Electrocardiographic Changes in Induced Bronchial Asthma

Terumasa MIYAMOTO, M. D.*, Julian BASTAROLI, M. D.,** and Murray S. HOFFMAN, M. D.***

Asthmatic attacks were induced in 11 patients by the inhalation of the antigenic extracts. The electrocardiograms were recorded before, during and after the attacks for comparison. The significant changes during the asthmatic attack were as follows: (1) taller and more peaked P-waves in leads II, III and aVF, and the shifting of the mean vector of P-waves on the frontal plane towards the right; (2) generalized low amplitude of QRS-complexes, especially marked in left precordial leads and shifting of the mean vector of QRS-complexes on the frontal plane towards the right; (3) respiratory changes of QRS-complex which showed lower during the inspiratory phase and taller amplitude during the expiratory phase; (4) clockwise rotation of the heart along the longitudinal axis. Above findings were found in all cases and could be explained by the hyperinflation of the lung and strain of the right side of the heart by an increased pulmonary artery pressure, which were observed during cardiac catheterization.

A NAPHYLACTIC shock in the rabbit1) and the dog due to antigen-antibody reaction2) have produced definite cardiac disturbances as revealed by the electrocardiogram. These cardiac changes have been shown to consist of conduction disturbances and arrhythmias. Since the introduction of a provocative test for asthma consisting of the inhalation of specific antigenic extracts, the study of cardiovascular changes following such induced asthma as allergic reaction would appear to be a natural corollary. A study of the current literature, however, has failed to reveal any other electrocardiographic studies in this particular condition. This paper deals with the electrocardiographic changes following induced asthmatic attacks.

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MATERIAL

Three female and 8 male patients with a long standing history of bronchial asthma were the subjects in this study. They were all inpatients at the National Jewish Hospital, Denver, Colorado. Their ages ranged from 15 to 38, with a mean of 24. The duration of their asthma varied between 7 and 30 years with a mean of 18 (Table I). They were known to be sensitive to one of the inhalants (grasses, ragweeds, molds, etc.). Previous provocative tests with the inhalation of certain antigenic extracts produced asthmatic attacks. The patients studied were relatively free from asthma before the induction of an acute asthmatic attack.

METHOD

Standard complete electrocardiograms (6 standard and 7 precordial leads) were taken before the inhalation of antigenic extract. A control vital capacity (VC) and one second forced expiratory volume (FEV₁) were measured by the Stead-Wells respirometer with a kymographic speed of 1820 mm. per minute. The patients were then instructed to inhale antigenic extracts consisting of 10,000 protein nitrogen units per ml. Such inhalations were accomplished with the use of a nebulizer. The flow was adjusted to 5 to 6 L. per minute. The patients were instructed to hold their breath at the end of inspiration for a few seconds after each inhalation of the antigenic extracts to allow the mist to be more effective. Sufficient number of inhalations of the antigenic extracts were given to each patient to produce a “severe” asthmatic attack. The maximum air way obstruction was obtained between 12 and 18 minutes after the inhalation of the antigenic extract. Complete electrocardiograms and pulmonary function studies together with a constant recording of lead II were made during this latter period. Asthmatic attacks were relieved by the inhalation of isuprel 1:100. The complete electrocardiograms and pulmonary function studies were repeated 10 to 20 minutes after the attack was relieved by isuprel, thus minimizing the cardiac effects of isuprel. The pulmonary function studies were performed in a sitting position. The electrocardiograms were taken in a supine position. The skin markes were made on the chest in each individual in order to place the electrode exactly on the same spots during this study. The durations of P-waves, QRS-complexes, ST-segment changes, P/PR-segment ratio and the mean vector of P-wave and QRS-complex were measured. The widest P-wave and QRS-complex were chosen for the measurement of the duration. The mean vectors of P-wave and QRS-complex were determined in the frontal plane using lead I, II and III, with combination of 2 leads using the graph made by Carter and his co-workers. The mean value of these was considered to be the actual mean vector. If there were obvious respiratory changes of electrocardiographic complexes, the average of the figures were used for the measurement.
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**Mean Value**

<table>
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<tr>
<th>Age</th>
<th>Duration of Bronchial Asthma and Pulmonary Function, Before, During and After Induced Bronchial Asthma</th>
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**Note:** VC: vital capacity, FEV₁: one second forced expiratory volume.

* Number in ( ) expresses the actual value as percentage of normal predicted value.

** These patients had cardiac catheterization.
**RESULTS**

**P-wave:**

P-wave became significantly taller and more peaked in leads II, III and aVF during the induced asthmatic attack in all cases. This finding was not apparent in other leads (Fig. 1 and 2). The duration of P-wave and P/PR-segment ratio did not reveal any significant changes. The mean vector of P-wave in the frontal plane shifted rightward in all cases (Fig. 3). The height and mean vector of P-waves, however, did not return to the original value in all cases after the isuprel inhalation even though pulmonary function did improve significantly (in some cases, even better than control) (Table I).

![Image of electrocardiogram](image_url)
Fig. 2. P-wave changes in 2 cases, J. D. (right) and R. R. (left). The taller P-waves during the attack should be noted.

Fig. 3. The mean vectors of P-waves before, during and after the induced bronchial asthma. The mean vectors of P-waves shifted rightwards during the asthmatic attack.
QRS-complex:
Low amplitude of QRS-complexes were quite evident in lead I and left precordial leads (V₃, V₄, V₅ and V₆) during the induced asthmatic attack (Fig. 2, 4 and 5). There were neither significant changes of Q-
wave nor change in the duration of QRS-complex. S-waves became deeper in the left precordial leads ($V_4$, $V_5$ and $V_6$) and R-waves became of lower voltage in lead I and in the left precordial leads ($V_3$, $V_4$, $V_5$ and $V_6$) in all cases during the attack suggesting the clockwise rotation of the heart along its longitudinal axis (Fig. 5). In addition, induced attacks produced significant changes in the amplitude of QRS-complexes during respiration that was not evident in the controls. This finding was more obvious in the precordial leads, particularly $V_{3R}$, $V_1$ and $V_2$ (Fig. 6 and 7). Lower amplitude of QRS-complexes was observed during the

![Fig. 6](image)

Fig. 6. Respiratory variation of QRS-complexes in lead $V_1$ before, during and after the induced bronchial asthma in case A.P.

![Fig. 7](image)

Fig. 7. Respiratory variation of QRS-complexes in the right precordial leads during the induced asthmatic attack in case C.G. Lower amplitude of QRS-complexes was observed during the inspiratory phase and higher amplitude during the expiratory phase.
inspiratory phase and higher amplitude during the expiratory phase. Most of the above findings during the attack resumed the original values after the administration of isuprel except for the mean vector of the QRS-complexes in the frontal plane, which did not return to the baseline but, in some cases, shifted further rightward (Fig. 8).

ST-segment:
Though there was very slight ST segment depression in II, III, and aVF in some cases, no significant ST-segment deviation was noted (Fig. 1).

Rhythm:
In 2 cases out of 11, frequent ventricular extrasystoles and atrial premature beats were observed for 5 to 10 minutes after the inhalation of the antigenic extract, while the airway obstruction was becoming more severe, but once airway obstruction presumably reached its maximum, these ectopic beats disappeared (Fig. 9 and 10).
Fig. 9. Ectopic beats during the induced bronchial asthma. Frequent occurrences of ventricular extrasystoles should be noted. "During 1" was taken 7 minutes after inhalation of antigenic extract and "During 2" 15 minutes.

Fig. 10. Ectopic beats during the induced bronchial asthma. Frequent atrial premature beats should be noted. "During 1" was taken 7 minutes after inhalation of antigenic extract and "During 2" 15 minutes.

**Discussion**

**P-waves:**

There are 3 factors, which are said to produce changes in the height of P-waves and shift in the P-vector secondary to the diseases of the lungs: (1) By changes of the anatomical position of the heart in the thorax;
(2) Hypoxia; (3) Right atrial overloading. In the P-wave changes during the asthmatic attack, all of 3 factors may play a role: During the asthmatic attack, because of air trapping and overinflation of the lung, the diaphragm has a tendency to be displaced downward, causing changes in anatomical position of the heart. Since the outstanding changes in the electrocardiogram due to the upright position of the heart are an increase in the amplitude of the P-waves in leads II and III, and since the prominent P-waves in leads II, III and aVF in pulmonary emphysema have been thought to result from the extreme vertical position of the heart, it is quite conceivable that the exaggerated P-waves during induced bronchial asthma were partly due to the vertical displacement of the heart caused by downward displacement of the diaphragm.

Arterial desaturation has been commonly observed in spontaneous and provoked bronchial asthma. The mechanism of the tall and peaked P-waves that have been observed in arterial desaturation is not well understood at the present time.

The pulmonary artery pressure as well as the effective pulmonary artery pressure (difference between the actual pulmonary artery pressure and the corresponding esophageal pressure) increased significantly in all cases during the induced asthmatic attack. Although the atrial pressures were not measured, it is quite conceivable that functional tricuspid insufficiency might have occurred, because of the increased pulmonary artery pressure, producing an increased atrial pressure. Since the atrium is a thin-walled chamber, an acute distention of the atrium may appear before any dilatation of the right ventricle. In some cases, the changes in the height of P-waves during an attack were not evident, although peaked P-waves were observed invariably. From this observation, it might be considered that peaked P-waves may be the good index of right atrial "strain" since the height of P-waves can be damped by the hyper-inflation of the lungs.

After an asthmatic attack was relieved by the inhalation of isuprel, the mean vector of the P-wave in the frontal plane and the amplitude of P-waves in leads II, III and aVF did not return to their original values in all cases. Moreover, in some cases P-waves became taller than that of during the attack. In order to clarify this finding, isuprel was given to normal subjects in exactly the same way, and the electrocardiograms were taken 10 to 15 minutes afterwards. The P-waves in leads II, III and aVF became taller and the mean vector in the frontal plane shifted towards the right (Fig. 11). Since isuprel accelerates the heart beat and increases stroke volume, the above findings may well have been due to right atrial "strain" associated with isuprel administration.

There were no significant changes of P/PR-segment ratio before, during
and after the induced bronchial asthma. In spite of the increased pulmonary artery pressure and the great possibility of right atrial strain during the asthmatic attack, atrial enlargement could not be detected by P/PR-segment ratio, a previous standard electrocardiographic criterion for the recognition of atrial enlargement.15)

Fig. 11. Electrocardiogram before and after inhalation of isuprel in normal subject. The taller P-waves in leads II, III and aVF, and the rightwards shift of the mean vector of P-wave should be noted.

QRS-complex:

The generalized low amplitude of QRS-complexes in left precordial leads and the trend of lower amplitude in other leads were probably due to positional changes of the heart and the hyperinflation of the lungs.16)

The mean QRS vector on the frontal plane had a tendency to move towards the right during the asthmatic attack, but did not return to their original value after the attack was relieved by isuprel inhalation. This could be explained by the same explanation used previously in P-waves,
Respiratory changes in QRS-amplitude:

The lung is considerably overdistended in the inspiratory phase of the asthmatic attack and the heart is displaced vertically and posteriorly. Considering the electrical conductivity of the hyperinflated lung, it seemed to be thus quite evident why QRS-amplitudes became smaller during the inspiratory phase, particularly in the right precordial leads. This finding seemed to be more apparent when the induced asthmatic attack was more severe.

ST-segment:

There seemed to be a trend of ST-segment depression in leads II, III and aVF during the asthmatic attack although the findings were not always present. ST-segment depressions might have been due to the low oxygen tension in the arterial blood, which was a common finding during the attack.9),10),17)

Rotation of heart:

Clockwise rotation of the heart was observed in all cases during the asthmatic attack. If the lung is over distended and the diaphragms are displaced downwards, clockwise rotation of the heart along the longitudinal axis is commonly found as seen in cor pulmonale or emphysema.8),9) Clockwise rotation of the heart during the asthmatic attack was, therefore, believed to be produced by overdistention of the lung and the lowering of the diaphragms. This is believed to be the reason why the heart resumed the previous position after the attack was relieved by the inhalation of isuprel.

Acute right ventricular enlargement might be another possibility for the clockwise rotation of the heart, yet this is believed to be unlikely, as other electrocardiographic changes which might indicate right ventricular enlargement or dilation could not be detected.

Ectopic beats:

While the airway obstruction was becoming increasingly severe, there should be significant changes in cardiopulmonary hemodynamics. During a Valsalva maneuver, similar electrocardiographic changes have been observed, including extrasystoles and partial heart block.16),17) Since the forced breathing during the asthmatic attack simulates a Valsalva maneuver, it was quite conceivable that the ectopic beats observed in this study were due to the acute changes in cardiopulmonary hemodynamics. When the airway obstruction stabilized and the body seemingly adjusted to a new condition, the ectopic beats all disappeared.
SUMMARY

Asthmatic attacks were induced in 11 asthmatics by the inhalation of the antigenic extracts. The electrocardiograms were obtained before, during and after the attacks for comparison. The significant changes during the asthmatic attack were as follows: (1) taller and more peaked P-waves in leads II, III and aVF, and the shifting of the mean vector of P-waves on the frontal plane towards the right; (2) generalized low amplitude of QRS-complexes, especially marked in left precordial leads and shifting of the mean vector of QRS-complexes on the frontal plane towards the right; (3) respiratory changes in QRS-amplitude which was lower during the inspiratory phase and taller during the expiratory phase; (4) clockwise rotation of the heart along the longitudinal axis. The above findings were observed in all cases and could be explained by the hyperinflation of the lung and “strain” of the right side of the heart by the increased pulmonary artery pressure, which was observed during cardiac catheterization.

Ectopic beats were observed in 2 cases among 11, while the airway obstruction was becoming progressively severe, but disappeared after the airway obstruction reached a maximum. From the present study, it was also believed that there seemed to be no direct cardiac danger of the provocative study by the inhalation of the antigenic extracts.

REFERENCES

11. Under progress at National Jewish Hospital.