Causes of Death and Pathologic Findings in 304 Cases of Bronchial Asthma*,**,†

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There is a widespread impression that bronchial asthma seldom causes death. This study shows clearly that the disease terminates fatally more often than is generally thought.

This paper summarizes the data obtained in a review of all cases in which the clinical diagnosis of bronchial asthma was made at the Mayo Clinic during the 40-year period 1916 through 1955 and in which necropsy was performed. The series totals 304 cases, and is the largest reported so far.

Incidence of Bronchial Asthma

Other than stating that the disease is frequent, the literature lacks information as to how common asthma is. The following data provide additional information as to the occurrence of the disease. During the year 1955, a diagnosis of bronchial asthma was made in 1667 of the

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119,000 patients who registered at the Mayo Clinic, giving an incidence of 1.4 per cent. The estimated incidence for 1954 was 1.3 per cent.

Of 743 known deaths occurring among all clinic patients seen during 1955, 25 (3.4 per cent) were among asthmatic patients. Four of the 25 patients died in status asthmaticus, two from complications of asthma (emphysema and cor pulmonale), and the remaining 19 from causes unrelated to asthma. Thus, 1.5 per cent of the 1667 asthmatic patients seen during 1955 died in that year.

**Duration of Bronchial Asthma**

The age at the time of death from status asthmaticus (group A) varied from 5 to 78 years (Fig. 1). Thirty-seven per cent of the patients in this group died before and 63 per cent during or after the age of 51 years. More than 50 per cent died in the age period 51 through 70 years.

The range in age at the time of death among patients dying from a complication of bronchial asthma other than status asthmaticus (group B) was very similar to the range for those with status asthmaticus.

Seventeen of the patients in group A were female and 18 were male. In group B, nine of the patients were female and 22 were male.

The duration of bronchial asthma in years before death varied from 1 to 66 years (Fig. 2). Of the patients dying of status asthmaticus, 20 per cent died within 5 years after the onset of asthmatic symptoms, 45.7 per cent within 10 years, 65.7 per cent within 20 years and 82.9 per cent within 30 years.

![Graph showing duration of bronchial asthma in years at death.](https://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21348/)
Of the deaths due to a complication of bronchial asthma other than status asthmaticus, 12.9 per cent occurred within 5 years after the onset of asthma, 32.2 per cent within 10 years, 51.6 per cent within 20 years and 67.7 per cent within 30 years.

**Causes of Death in 304 Asthmatic Patients**

During the 40-year period 1916 through 1955, there were 450 known deaths among clinic patients having had a diagnosis of "asthma" made sometime during their clinic visits. Seventy-seven of these cases were rejected from this study because necropsy had not been performed. An additional 69 cases were rejected because examination of the clinical records revealed a vague or equivocal history of bronchial asthma, or a diagnosis of "cardiac asthma."

The remaining 304 cases were divided into three groups, as shown in table 1. Four patients in group A and three in group B died soon after receiving 1/6 to 1/4 grain of morphine sulfate. Among the causes of death in group B were bronchiectasis, bronchopneumonia and emphy-
DEATH IN BRONCHIAL ASTHMA

TABLE 1—CAUSES OF DEATH (1916-1955) AMONG ASTHMATIC PATIENTS ON THE BASIS OF NECROPSY DATA

<table>
<thead>
<tr>
<th>Group</th>
<th>Patients</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Death during status asthmaticus</td>
<td>35</td>
<td>11.5</td>
</tr>
<tr>
<td>B. Death from complications of asthma</td>
<td>31</td>
<td>10.2</td>
</tr>
<tr>
<td>C. Death unrelated to bronchial asthma</td>
<td>238</td>
<td>78.3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>304</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>

Data on the causes of death in group C are given in Table 2. Cardiovascular and malignant disease accounted for approximately 60 per cent of the deaths in this group. Carcinoma of the lung was the most common malignant condition; it represented 34 per cent of the deaths from malignant disease in males. Cerebrovascular, renal and postoperative deaths were much less common. The incidence of suicide should be noted.

**Gross Findings in Groups A and B (Deaths From Status Asthmaticus or Complications Thereof)**

Gross emphysema (Fig. 3) was common in both groups. It was found in all but one (97.1 per cent) of the cases of status asthmaticus (group A), and in 52 per cent it was marked. It occurred in 81 per cent of the cases in which death resulted from some complication of bronchial asthma other than status asthmaticus (group B). The bronchial walls were thickened in 40 per cent of the cases in group A, and in 29 per cent of those in group B. Pulmonary edema was found in approximately one-fourth of the cases in each group.

Hydrothorax and pleural adhesions were each nearly twice as frequent in group A as in group B. Seventeen per cent of the patients in group A had these conditions.

Bronchopneumonia was found in nearly half of the patients in group B, in which it was more than five times as common as in group A. Atelectasis was uncommon in both groups; however, abnormal bronchial con-

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FIGURE 3: Gross emphysema.

FIGURE 4: Heart showing grade 3 right ventricular hypertrophy with grade 2 dilatation.
TABLE 2—CAUSES OF DEATH UNRELATED TO ASTHMA AMONG 238 ASTHMATIC PATIENTS (GROUP C)

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease</td>
<td>64</td>
<td>18</td>
<td>82</td>
<td>34.4</td>
</tr>
<tr>
<td>Malignant disease</td>
<td>47</td>
<td>11</td>
<td>58</td>
<td>24.3</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>10</td>
<td>8</td>
<td>18</td>
<td>7.6</td>
</tr>
<tr>
<td>Renal disease</td>
<td>9</td>
<td>6</td>
<td>15</td>
<td>6.3</td>
</tr>
<tr>
<td>Postoperative condition</td>
<td>11</td>
<td>4</td>
<td>15</td>
<td>6.3</td>
</tr>
<tr>
<td>Periarteritis nodosa</td>
<td>5</td>
<td>4</td>
<td>9</td>
<td>3.8</td>
</tr>
<tr>
<td>Trauma</td>
<td>5</td>
<td>0</td>
<td>5</td>
<td>2.1</td>
</tr>
<tr>
<td>Suicide</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>2.1</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>1.3</td>
</tr>
<tr>
<td>Other causes</td>
<td>17</td>
<td>11</td>
<td>28</td>
<td>11.8</td>
</tr>
<tr>
<td>Total</td>
<td>173</td>
<td>65</td>
<td>238</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Tents (mucus, purulent exudate, or both) were found in 97.2 per cent and 71.0 per cent of the cases in groups A and B respectively.

Bronchiectasis occurred in nearly one half of the cases in group B, but in less than 15 per cent of those in group A. Healed tuberculosis was evident in 26 per cent and 39 per cent, respectively, of the cases in groups A and B. These figures do not begin to approach those found by Terplan as representing the incidence of tuberculosis in consecutive necropsy material studied by him during the decade 1930 to 1940. For adult patients, his incidence of positive results was 71 per cent in the age group 18 to 30 years and 90 per cent in the age group 40 to 50.

The incidence of abnormally heavy hearts was 58 per cent and 75 per cent respectively in groups A and B.

Right ventricular hypertrophy (Fig. 4) occurred in 90 per cent of the cases in group B and in nearly 70 per cent of those in group A.

Laryngeal edema and obstruction were noted in three cases of group A (Fig. 5).

**Microscopic Findings**

Complete obstruction of bronchial lumina by mucous plugs was the most common microscopic lesion in group A, being present in all cases (Fig. 6). It was a less common finding in group B. Extensive numbers

*FIGURE 5: Edema of larynx viewed from below. Patient died suddenly during a paroxysm of asthma.*
of goblet cells in the bronchial epithelium were also less commonly found in group B than in group A. This finding was usually associated with hyperplasia of bronchial mucous glands.

Hyperplasia of bronchial epithelium was evident in approximately a third of the cases in each group, and frank metaplasia (squamatization) of bronchial epithelium was evident in nearly three fourths of the cases in each group. Figure 7 shows an abrupt change from normal bronchial to metaplastic epithelium, and marked thickening of the basement membrane of the bronchial epithelium. There was a definite relation between the presence of bronchiectasis and the occurrence of metaplasia of the bronchial epithelium, for it was rare to find metaplasia in any case in

![Figure 6A](image_url)

**FIGURE 6A**: Bronchus showing complete obstruction by a mucous plug, excessive mucus in the bronchial epithelium, and grade 3 hypertrophy of the bronchial smooth muscle (mucin stain; ×30).

![Figure 6B](image_url)

**FIGURE 6B**: Smaller bronchus showing complete obstruction by a mucous plug that contains many leukocytes. Also shown are a thick-walled pulmonary capillary, grade 2 hypertrophy of bronchial smooth muscle, and grade 3 thickening of the basement membrane (hematoxylin and eosin; ×50).
which there was not also microscopic evidence of severe or moderately severe bronchiectasis.

Hypertrophy of bronchial smooth muscle was common in both groups, although severe hypertrophy was about twice as common in group A (34 per cent) as in group B (16 per cent).

The severity of bronchial smooth-muscle hypertrophy could not be correlated with duration of asthmatic symptoms; however, those pa-

![FIGURE 7: Metaplasia (squamatization) of bronchial epithelium with grade 3 thickening of basement membrane (hematoxylin and eosin; x90).](image)

![FIGURE 8: Eosinophilic infiltration beneath basement membrane of bronchial epithelium (Dominici stain; x350).](image)
tients with the severest hypertrophy usually also had rather severe thickening of the epithelial basement membrane.

Severe bronchial eosinophilic infiltration (Fig. 8) was much more common in group A than in group B (in 60 and 16 per cent of the cases respectively). No correlation between the severity of bronchial eosinophilic infiltration and duration of asthma was evident.

Bronchial fibrosis was observed in more than 80 per cent of the cases in both groups. Bronchiectasis (Fig. 9) was less common in group A than in group B; in group A more than a third of the patients had no evidence of bronchiectasis, and a little more than half had only minimal bronchiectasis.

**FIGURE 9:** Moderately severe bronchiectasis with medial hypertrophy and intimal fibrosis of a pulmonary arteriole (Verhoeff's elastic tissue stain with van Gieson counterstain; x85).

**FIGURE 10:** Grade 3 emphysema. The clubbed ends on the broken septa represent attempts at healing, and show that the broken septa are not artifacts secondary to preparation of the slide (hematoxylin and eosin; x40).
Microscopic evidence of emphysema was present in essentially all cases (Fig. 10). No correlation between severity of emphysema and duration of asthma was apparent.

Focal atelectasis was common in both groups. Pulmonary arteriolar intimal proliferation was more common in group B, being present in nearly half the cases of that group. Medial hypertrophy was present in more than a third of the cases in both groups.

SUMMARY

One and one half per cent of all patients that come to the Mayo Clinic have bronchial asthma.

Bronchial asthma terminates fatally more often than is generally thought. In 304 necropsy cases, 17 per cent of the deaths related to asthma occurred within five years after the onset of asthma, and 35 per cent occurred before the age 51.

Of 304 asthmatic patients examined at necropsy, 11.3 per cent died of status astmaticus and 10.4 per cent died of some other asthmatic complication. The remaining 78.3 per cent died of causes unrelated to asthma.

Oclusion of bronchial lumina with thick, tenacious, mucin-staining material is responsible for death in status astmaticus.

The pathologic anatomy of bronchial asthma is that of emphysema, bronchial mucous plugs, bronchial fibrosis, thickening of bronchial base of membrane, and hypertrophy of bronchial smooth muscle.

ACKNOWLEDGEMENT: The authors wish to express their appreciation to Dr. Louis E. Prickman for the initiation of work leading to this report.

RESUMEN

Uno y medio por ciento de los enfermos que vienen a la Clínica Mayo, tienen asma bronquial.

El asma bronquial termina fatalmente más a menudo de lo que se piensa. En 304 necropsias, el 17 por ciento de las muertes relacionadas con el asma, ocurrieron cinco años después del principio del asma y 35 por ciento acontecieron antes de la edad de 51 años.

De 304 asmáticos examinados por autopsia, 11.3 por ciento murieron en status astmaticus y 10.4 por ciento murieron de otra complicación asmática.

Los restantes 78.3 por ciento murieron de causas sin relación con el asma.

Las obstrucción de la luz bronquial con material espeso, adherente, que se tife como mucina, es responsable de las muertes en status astmaticus.

La anatomía patológica del asma bronquial, es la del enfisema, tapones mucosos, fibrosis bronquial, espesamiento de la membrana basal bronquial y la hipertrofia de los músculos lisos bronquiales.

RESUMÉ

1.5% de la totalité des malades qui viennent à la Mayo Clinique sont atteints d'asthme bronchique.

L'asthme bronchique a une issue fatale plus fréquente qu'on ne le pense. Dans 304 cas ayant pu être autopsiés, 17% des décès rapportés à l'asthme survinrent moins de cinq ans après l'apparition de l'asthme et 35% avant l'âge de 51 ans.

Sur les asthmatiques examinés à l'autopsie, 11.3% moururent d'état de mal asthmatic et 10.4% moururent de quelque autre complication due à l'asthme. Les 78.3% restant moururent de causes sans rapport avec l'asthme.

L'obstruction de la lumière bronchique par une matière épaisse, adhérente, se colorant par la mucine, est responsable de la mort dans l'état de mal asthmatique.

L'anatomie pathologique de l'asthme bronchique est la même que celle de l'emphysème: remaniement de la muqueuse bronchique, fibrose bronchique, épaisseissement de la membrane basale bronchique et hypertrophie des muscles lisses bronchiques.

ZUSAMMENFASSUNG

1½% aller Patienten, die in die Mayo-Klinik eingewiesen wurden, leiden an Bronchialasthma.

Bronchialasthma endet häufiger tödlich als man allgemein annimmt, und von 304 Sektionen ereigneten sich 17% der durch Asthma bedingten Todesfälle innerhalb von 5 Jahren nach Beginn des Asthmas. 35% traten vor dem 51. Lebensjahr ein.

Von 304 asthmatischen Patienten, die autopsi sch untersucht worden waren, starben 11.3% im status asthmaticus; 10.4% starben infolge anderer Komplikationen des Asthmas. Die übrigen 78.3% starben aus Gründen, die mit dem Asthma nicht in Zusammenhang standen Verschluß, der Bronchiallumina mit dickem, scharf und sich wie Mucin getarbtes Material ist verantwortlich für den Tod im status asthmaticus.

Die pathologische Anatomie des Bronchialasthmns ist diejenige eines Emphysem, bronchialer Schleimfropfen, bronchialer Fibrose, Verdickung der Basalmembran der Bronchien und Hypertrophie der glatten Bronchialschleimhaut.

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