Morphogenesis of Human Bronchial Diverticulum

A Scanning Electron Microscopic Study

N. S. Wang, M.D.,** and W. L. Yung, M.D.†

Diverticulosis of the bronchial wall was found in patients not only with, but also without, chronic obstructive lung disease; it appeared to start as submicroscopic depressions and dilatations of the ducts of the bronchial gland on the mucosal surface. Multiple depressions and dilatations fused to form a diverticulum which herniated between and through the smooth-muscle cellular bundles. Rupture of the latter resulted in large diverticula. Cough and a weakened bronchial wall, from whatever causes, likely lead to bronchial diverticulosis. Exaggerated but unequal formations of bronchial diverticula at the sites of dichotomy suggest either that the effect of cough could be different between segments or subsegments, or that there are local differences in connective-tissue atrophy, inflammation, and structural defects. Mucous plugs, macrophages, red blood cells, inhaled particles, and probably carcinogens are accumulated at the bronchial diverticula, which apparently interfere with airway cleansing and also cause continuous local irritation. The relationship between bronchial diverticulosis and small-airway disease or lung cancer needs further clarification.

The "cystic enlargement" or dilated opening of the bronchial duct draining the hypertrophied mucous gland, a bronchographic as well as bronchoscopic sign, has been generally accepted as one of the hallmarks of chronic bronchitis. This sign was established mainly from examining groups of patients with varied types of respiratory diseases, such as tuberculosis and lung cancer, as well as bronchiectasis, emphysema, asthma, and chronic bronchitis; it was found in about 30 percent of these patients with chronic cough as the most common symptom. A synonym of this change, bronchial diverticulosis, illustrates an alternative theory of pathogenesis, that is, prolapse of the bronchial mucosa through dehiscent muscular bundles in the bronchus, presumably from the transient but repeated increase in the intrabronchial pressure with coughing. Scanning electron and light microscopic examinations of these lesions in lungs obtained at routine autopsy and surgery revealed a varied degree of submicroscopic alterations which may represent the early stage of the morphogenesis of bronchial diverticulosis.

Materials and Methods

Major, segmental, and subsegmental bronchi showing moderate to severe surface alterations were collected consecutively at routine reviewing sessions from eight lungs at autopsy and six surgically removed lungs. The brief clinical data obtained are summarized in Table 1.

All specimens were fixed either with 3.5 percent glutaraldehyde in 0.05 percent barbital (Veronal) acetate-buffered solution (pH 7.4) or 4 percent formaldehyde in neutral phosphate-buffered solution (pH 7.4) or 4 percent formaldehyde in neutral phosphate-buffered solution and were processed routinely for scanning electron and light microscopic studies.

Results

Grossly, the mucosal surface of all opened bronchi showed round or oval openings and surface depressions, varying in extent and distribution. Frequently, one of the subsegmental bronchi at the site of dichotomy was affected more than the other. Areas just beyond branchings were more frequently and severely involved than areas between branchings.

At scanning electron microscopic examination, round openings of the bronchial glands ranged from several micra in diameter to those obviously seen at the gross level, and the smaller ones were less than 500m apart in some areas. Mucosal depressions were frequently around a widened round opening often bordered by transverse or longitudinal mucosal bulges and sometimes showed multilevel depressions. In the overtly depressed...
Table 1—Summary of Cases

<table>
<thead>
<tr>
<th>Case</th>
<th>Surgical</th>
<th>Sex/Age</th>
<th>Clinical and Tissue Diagnosis</th>
<th>Smoking History*</th>
<th>Pulmonary Function Test</th>
<th>Clinical Respiratory Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 S</td>
<td>M/64</td>
<td>Epidermoid carcinoma of lung</td>
<td>Heavy smoker</td>
<td>Abnormal</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2 S</td>
<td>M/66</td>
<td>Epidermoid carcinoma of lung</td>
<td>40/day × 50 yr</td>
<td>Abnormal</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>3 S</td>
<td>M/69</td>
<td>Epidermoid carcinoma of lung</td>
<td>20/day × 55 yr</td>
<td>Normal</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>4 S</td>
<td>M/52</td>
<td>Old organized pulmonary infarct</td>
<td>Heavy smoker</td>
<td>Normal (probably)</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>5 S</td>
<td>M/70</td>
<td>Epidermoid carcinoma of lung</td>
<td>20/day × 7 yr</td>
<td>. . .</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>6 S</td>
<td>F/70</td>
<td>Undifferentiated large cell carcinoma of lung</td>
<td>15/day × 15 yr</td>
<td>. . .</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>7 A</td>
<td>M/57</td>
<td>Renal cell carcinoma with differentiated pulmonary metastases</td>
<td>20/day × 40 yr</td>
<td>Abnormal</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>8 A</td>
<td>M/56</td>
<td>Cirrhosis of liver; subdural hematoma</td>
<td>. . .</td>
<td>. . .</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>9 A</td>
<td>F/68</td>
<td>Chronic obstructive lung disease</td>
<td>Heavy smoker</td>
<td>Abnormal</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>10 A</td>
<td>M/80</td>
<td>Chronic bronchitis</td>
<td>Cigar smoker</td>
<td>. . .</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>11 A</td>
<td>F/72</td>
<td>Carcinoma of cervix with pulmonary embolism</td>
<td>. . .</td>
<td>. . .</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>12 A</td>
<td>M/71</td>
<td>Multiple myeloma</td>
<td>Nonsmoker</td>
<td>. . .</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>13 A</td>
<td>F/91</td>
<td>Congestive heart failure; pulmonary emphysema</td>
<td>. . .</td>
<td>. . .</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>14 A</td>
<td>M/80</td>
<td>Intracerebral hemorrhage</td>
<td>. . .</td>
<td>. . .</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

*Numbers in column are numbers of cigarettes.

mucosa, normal-sized openings of the bronchial duct were found at the lateral wall or at the bottom of the depression. Adjacent mucosal depressions apparently fused with each other beneath the bulges at some early stage so that the bulges hung over the depressed mucosa like a bridge over a valley (Fig 2).

The epithelial lining cells were demuded in many places, especially in the lungs obtained at autopsy, and were mostly ciliated in the relatively well-preserved areas. Goblet and squamous cellular metaplasia and dysplasia were usually found overlying the bulges (Fig 3), while ciliated cells with protruding goblet cells were common in the slope of the depressed area. Macrophages, red blood cells, bacteria, and foreign particles of unknown nature were frequently accumulated at the edge of the mucosal depression (Fig 4).

Histologic sections confirmed the epithelial denudation and goblet and squamous cellular metaplasia observed with the scanning electron microscope. The basal lamina was usually intact but thickened. The mucosal bulges observed at scanning electron microscopic examination were mostly submucosal aggregated bundles of smooth-muscle cells (Fig 5) and occasionally cartilage. The lamina propria was frequently thin due to decreased cellular and ground-substance components. A few mucous-plugged excretory ducts appeared to have ruptured into the interstitial space with an acute inflammatory reaction. More frequently, scattered chronic inflammatory infiltrates consisting mainly of lymphocytes, plasma cells, a few mast cells, and other cells.

![Figure 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/20976/ on 04/28/2017)

**Figure 1.** Segmental and subsegmental bronchi showing uneven distribution of mucosal lesions at site of dichotomy. Small openings of bronchial gland (*thin arrows at right*) are found on relatively normal mucosa. Mucosal depressions are mostly circular (transverse); they are usually short but probably fuse to form larger ones (*thin arrows at left*). Deep depressions are usually found immediately distal to site of bifurcation (*thick arrows*) (case 7) (× 4).

![Figure 2](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/20976/ on 04/28/2017)

**Figure 2.** Moderately advanced area. Mucosal depressions are evident between band-like bulges on bronchial mucosa. Depressions are multilevel, and some are located with openings of bronchial glands (O). One at center is plugged with mucus. Depressions may fuse beneath bulges (*arrows*) (case 8) (scanning electron microscopy, × 40).
cells, and eosinophils were seen. Not all depressions, especially the larger ones, were related to the ducts of the bronchial gland. The bronchial glandular mass was generally decreased, rather than increased, near these depressed areas and was formed predominantly by mucous-secreting cells. Fibrosis was prominent at the thinned and stretched portion of the depression. Ganglions, nerve fibers, and bronchial arteries were frequent and obvious, probably due to atrophy of the bronchial wall.

**DISCUSSION**

Our gross and scanning electron microscopic findings indicated that two different processes were present on the bronchial mucosa and that both dilatation of the openings of the bronchial glands and focal depression of the bronchial mucosa started at the submicroscopic level. In his book, von Hayek\(^7\) has estimated that openings of the bronchial glands in major human bronchi average one opening per square millimeter. The sizes of the openings were mostly under 20\(\mu\) in inner diameter but also varied, presumably reflecting the acinar mass that they drained. Nevertheless, it is probably appropriate to consider openings of 50\(\mu\) or more in inner diameter as dilated.

Close association of small depressions and dilated openings of the bronchial gland suggests that they fuse to form the classic diverticulum. Loss of noncellular ground substances in the “caved-in” area simulates subsidence of the earth following excessive extraction of underground water or oil.

Both smooth-muscle cells and cartilage appeared to be the remaining rigid skeleton in the bronchial wall. If intrabronchial pressure is raised only when the smooth-muscle cells are in the contracted state, smooth-muscle cells will hold out among the other tissues in the bronchial wall. The raised pressure may push the mucosa through the weakened gap between the smooth-muscle bundles. Cough with spasmodic contraction of smooth-muscle cells and intramural inflammatory or degenerative changes of the bronchial wall, therefore, are implicated in the genesis of bronchial diverticula.\(^1,5,8\) Rupture of smooth-muscle bundles resulted in an excessively large depression. Fragmented elastica, peripheral fibrosis, degeneration, and calcification of the cartilage most likely represent a secondary degenerative process.\(^9\)

Diverticulosis is usually rare in the trachea, mild in the lobar bronchi, but prevalent in segmental and subsegmental bronchi, probably reflecting the fact that different sites of the airway receive different expansile forces at coughing, or that there are focal differences in the severity of connective tissue atrophy, inflammation, or structural defect. Indeed, branching sites with prominent circular muscular

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**Acknowledgments**

The authors are grateful to Dr. Peter D. Dell, M.D., for many helpful discussions, to Dr. Lewis F. Miller, M.D., for his encouragement, and to Mrs. Janet M. S. Dell for her expert secretarial assistance. Photographs were taken by Dr. J. L. Curtiss and Dr. J. N. Frome, M.D. in the Department of Pathology.

**References**


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**Figure 3.** Lining cells at boundary of bulges and depressions are mostly nonciliated with irregular sizes, suggesting dysplasia. Two openings of bronchial glands are also seen, one with mucous plugging (case 5) (scanning electron microscopy, \(\times 1,120\)).

**Figure 4.** Macrophages, red blood cells, and other materials of unknown nature tend to accumulate at edge of depression (case 6) (scanning electron microscopy, \(\times 1,200\)).

**Figure 5.** Cross sections of mucosal bulges are formed by aggregated smooth-muscle bundles; some depressions are, and others are not, related to duct of bronchial gland (arrows) (case 11) (Hematoxylin and eosin, \(\times 32\)).
bulges usually had adjacent marked depressions, suggesting this is a site of excessive focal strain or weakness.

Despite the fact that most of our cases with diverticula were not bronchitic clinically and that not all bronchitic patients had bronchial diverticula, the deformities in the bronchi are the site for repeated and obstrinate infections and irritations, as attested by the local collections of inflammatory cells and epithelial metaplasia. The changes were most prominent in cases with cancer of the lung, suggesting the perpetuating and progressing nature of the lesion if untreated. Bronchial diverticulosis, therefore, should not be considered as the hallmark of an irreversible chronic obstructive lung disease; rather, in less symptomatic patients, it should be sought at bronchoscopic and bronchographic examinations as a serious warning sign and used in a constructive sense in the prevention of chronic obstructive lung disease and probably lung cancer.

ACKNOWLEDGMENT: We wish to thank Mr. Francis Wei and Miss Monique Charbonneau for their technical assistance.

REFERENCES

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Technology of Ancient China

In the field of mechanics, seventeenth-century China matched the main advances of seventeenth-century Europe. Modern historical research has demonstrated that the Chinese were responsible for developing a crucial element of the watch, namely the escapement, the part that prevents the spring from unwinding faster when it is tightly wound. Ironically, it was the Chinese who invented the gunpowder, which the Europeans used in their conquest of the Orient. Because of investments in government-controlled dams, canals, and irrigation systems, the Chinese excelled the Europeans in many types of water mills. Joseph Needham, the great historian of Chinese science and technology, regards the Chinese water-powered metallurgical blowing machine as the direct ancestor of the steam engine. Needham also credits the Chinese with the invention of the first computer, the canal lock gate, the iron chain suspension bridge, the first true mechanical crank, the stern-post rudder, and the man-lifting kite.

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