

CYSTIC ENLARGEMENT OF THE MUCOUS GLANDS OF THE BRONCHUS ASSOCIATED WITH CHRONIC BRONCHITIS

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The behaviour of mucous glands situated in the bronchial walls and found in cases of chronic bronchitis or bronchial inflammation associated with bronchiectasis has been the basis of research in which the six separate methods of investigation have been used simultaneously, namely bronchoscopy, bronchography, the examination of fresh post-mortem lungs, the examination of dried specimens prepared after the technique of Fischer (1933), the preparation of bronchial casts with acrylic resins (Duprez, 1951a), and serial sections.

BRONCHOGRAPHY

The information obtained by bronchography is mainly morphological and not always constant owing to physical variations in the bronchial tree and in the contrast filling media. A bronchogram shows dilatation, stenosis, or obstruction of bronchi. It does not show the nature of the anatomical substratum.

Many bronchograms performed for various reasons were carefully reviewed to try to discover any previously undetected abnormalities, and in a few cases minute patches of lipiodol outside the bronchi, some of them looking like isolated droplets of oil, others like small crypts or diverticula (Fig. 1), were identified. When there was only a thin layer of oil along the walls of the tracheo-bronchial tree, these abnormalities first appeared like a rain of dark droplets disposed transversely along the trachea and main bronchi (Fig. 2).

In other cases, under the carina or under any of the bifurcations in the larger (lobar or first segmental) bronchi, there were small diverticula, generally connected to the wall by a narrow pedicle (Fig. 3).

A few radiographs showed a completely serrated bronchial wall, some of the crypts even dividing into two branches: such was the bronchogram in one of our series (Fig. 2a and 2b). The patient in this case suffered from severe bilateral bronchiectasis with the dilatation extending to the lower part of the trachea. He sometimes coughed up a pint of

fetid, mucopurulent sputum. The walls of the trachea and main bronchi showed the most extensive picture of what could be referred to as a diverticulosis of the bronchial wall. Huizinga and Smelt (1949) recently produced a very similar picture.

However, with the bronchogram alone it is impossible to tell whether these cyst-like structures are folds of the mucous membrane or true cysts. We were of the opinion that they represented dilated mucous gland ducts, and proceeded to investigate this point by other techniques.

The bronchographic pictures were always associated with chronic bronchitis or bronchiectasis, and on some of the bronchograms it was possible to observe long black lines running all along the trachea and main bronchi (Fig. 4) corresponding to the ridges observed on bronchoscopy and in the dried specimens.

BRONCHOSCOPY

A certain number of patients who had long-standing fibrous tuberculosis or chronic bronchitis showed a bronchial mucosa which appeared nacreous and atrophic. Long parallel ridges ran from the larynx into the lobar bronchi.

The larger bronchi in these patients were carefully studied at bronchoscopy using a telescope, and a few small round apertures leading to narrow ducts in the bronchial wall were observed. Usually these ducts opened into the bottom of a large anfractuosity, and sometimes a bifurcation could be observed through the aperture. They were mostly located in the neighbourhood of the bronchial bifurcations. These openings could only represent mucous gland ducts. With an oedematous or even normal mucous membrane, these ducts are hidden by the turgescence of the cells and by the protective mucous layer which covers them.

EXAMINATION OF POST-MORTEM LUNGS

A number of lungs derived from necropsy were carefully dissected and the tracheo-bronchial tree

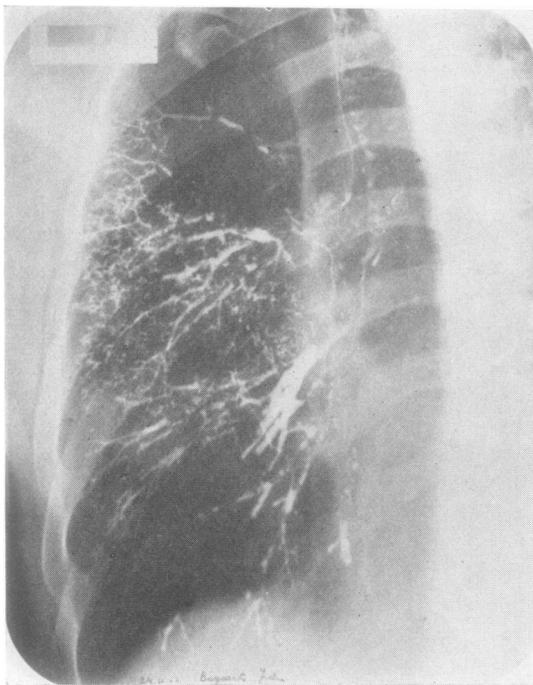


FIG. 1

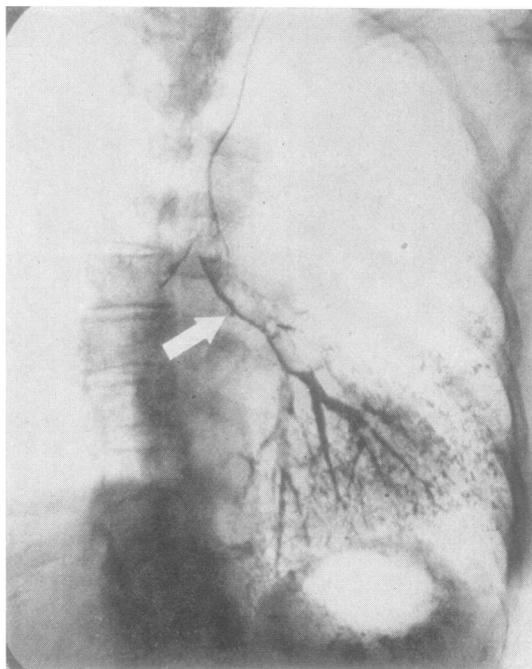


FIG. 3



FIG. 2a



FIG. 2b

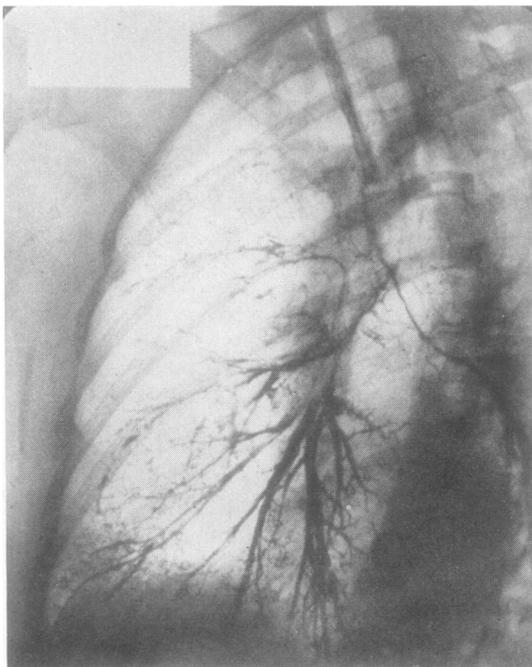


FIG. 4

FIG. 1.—Glandular cyst in the wall of the right main bronchus opposite the upper lobar bronchus immediately under the carina.
 FIG. 2a.—A completely serrated bronchial wall (diverticulosis of the bronchial wall) in a case of severe bilateral bronchiectasis.
 FIG. 2b.—Diagram of Fig. 2a.
 FIG. 3.—Two glandular cysts in the wall of the left main bronchus.
 FIG. 4.—Longitudinal ridges, which represent fasciculi of elastic fibrils, visualized by bronchography.

isolated from its parenchyma as far as the end of the subsegmental divisions. The specimens were further treated by the method of Fischer (1933) as described by Baud (1945), consisting in a progressive dehydration by alcohol solutions of increasing concentrations. The bronchial trees were then immersed for 24 to 48 hours, according to their size, in three solutions of alcohol (30, 70, and 96°), plunged for 24 to 48 hours in turpentine in order to prevent excessive hardening, and, finally, dried in the open air for 48 to 72 hours. Such preparations can be preserved indefinitely.

The internal surface of the bronchi prepared in this way appears perfectly white and smooth. The walls are stiff, but the mucosa keeps a certain degree of suppleness and it is possible to take out large pieces with forceps.

The specimens were split into two equal parts in a sagittal plane. The anterior half carries with it the larger part of the cartilaginous rings, whereas the posterior one includes the membranous part and the groove which lies between the latter and the cartilaginous one.

These preparations, including bronchial trees from adults and from newborn babies who died of extra-pulmonary diseases, were studied through a dissecting microscope with lateral illumination. The mucous membrane showed a definite structural pattern which could be divided into longitudinal ridges, transverse ridges, and round apertures.

LONGITUDINAL RIDGES.—On the internal surface of the membranous portion of the trachea and of the large bronchi there are longitudinal and parallel ridges running from the larynx into the segmental bronchi. When these near the carina or the lobar bifurcations they divide into two equal bundles and pass on down the branches. In the bronchi of the newborn this is even more striking. The same patterns were observed by bronchoscopy and were sometimes visible on bronchograms in the form of black lines, as already mentioned. They represent the well-known fasciculi or elastic fibrils in the submucosa (Bariety, Paillas, and Levy, 1951; Miller, 1947).

TRANSVERSE RIDGES.—Transverse ridges are also present in the bronchi. More numerous in the smaller bronchi, and thinner than the longitudinal ridges, they intersect with the latter to form a typical chequer pattern. They represent the circular muscle fasciculi which were described by Reissesen in 1822.

ROUND APERTURES.—Besides these ridges there were many round apertures, large and small, which could be separated into two categories according

to their diameter (Fig. 5). The small openings are about 0.2 mm. wide and are the more numerous. They are set regularly in transverse lines on the two slopes of the cartilaginous rings of the trachea and of the larger bronchi (Fig. 5). They are often found and are the most clearly marked in the groove which lies between the membranous and the cartilaginous portions of the walls.

The larger group of openings has a diameter between 0.7 mm. and 1.2 mm. (Fig. 5), and there did not seem to be any systematic topography in any one of the specimens observed, nor was the same pattern found in any two specimens.

The round apertures are more frequently observed in the larger bronchi than in the trachea, and are more numerous in the neighbourhood of the bronchial bifurcations (Fig. 6). Sometimes two or three of them are found together in the bottom of a deep crevice, lying between two transverse ridges (Fig. 7). If a transverse section of the bronchial wall is made along the main axis of one of these crevices, it is possible to see that the round apertures are the openings of long ducts which branch off in the depth of the bronchial wall, often beyond the level of the cartilaginous rings.

These specimens constitute, so far as we know, the first anatomical demonstration of the topography of the mucous gland ducts.

The findings are consistent with the observations which one of us has previously reported on bronchial casts (Duprez, 1951a). When studying the anatomy of bronchiectasis by means of specially prepared bronchial casts in resected lobes, minute prickles were noticed on some of the bronchi which were interpreted as enlarged gland ducts (Fig. 8). Their location and structure are the same as has now been observed in the dry specimens.

HISTOLOGY OF THE BRONCHIAL GLANDS

The mucous glands of the bronchi are composed of mucous, serous, and mixed acini. They lie in the depth of the submucosa, in the fibrocartilaginous layer, and even extend to the peribronchial fat. They are mostly located between the cartilaginous rings and around the bronchial bifurcations. They are more numerous in the larger bronchi. They disappear in the bronchioles at the same level as the cartilaginous rings, that is to say, in the 1 mm. diameter bronchi (Möllendorff, 1936). The ducts of these glands run through the muscular layer, and then turn sideways under the mucous membrane (almost parallel to it) before opening in a hollow which is covered with ciliated columnar cells (Policard and Galy, 1945). The portion of the duct which is near the bronchial lumen is also



FIG. 5.—Apertures of enlarged glandular ducts as observed in the dry specimens, $\times 4$.



FIG. 7.—Glandular duct opening in the bottom of a crevice (dry specimen), $\times 10$.



FIG. 6.—Normal and enlarged glandular ducts in the neighbourhood of a bifurcation (dry specimen), $\times 4$.

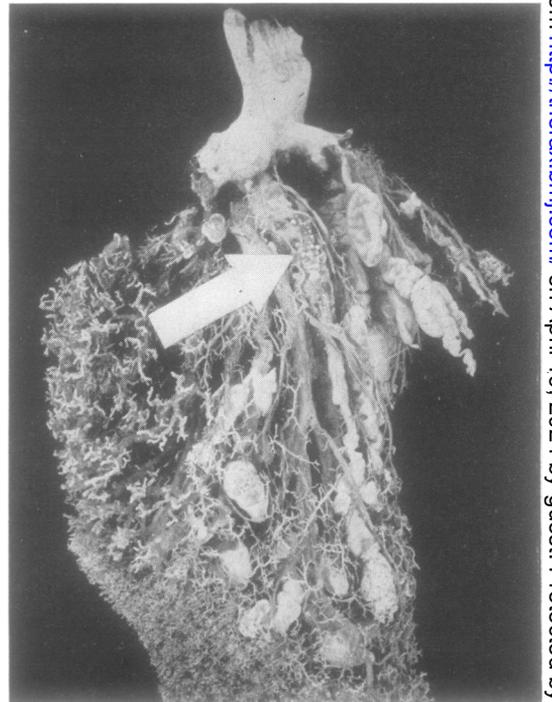


FIG. 8.—A bronchial cast of bronchiectasis with evidence of cystic enlargement of the glands.

covered by a layer of ciliated columnar cells, extending as far as the neck, a narrow passage bordered with prismatic cells, whose outer end shows a thickened cuticular border, but no cilia. These cells of the neck have been described by Bonne (1901). They may be responsible for the development of the so-called "bronchial adenoma" (Policard and Galy, 1945). Beyond the neck, the main duct spreads out into many smaller branches ending in the acini.



FIG. 9.—Normal mucous gland and its duct.

The peculiar anatomical pattern of a long and narrow duct, running parallel to the mucosa before opening into the bronchial lumen by a neck, is not favourable to the outward passage of the mucous secretions. It is more liable to lead to obstruction of that duct (Fig. 9).

DISCUSSION

Some authors have already observed similar bronchographic pictures. Huizinga and Smelt (1949) regarded the abnormalities as herniae of the

mucous membrane between the cartilaginous rings, or more probably small retention cysts of the mucous glands which had broken through into the bronchial lumen. They generally noticed these pictures on patients who were suffering from chronic cough.

Stutz (1948) and Fischer (1950) also observed similar patterns associated with chronic bronchitis or bronchiectasis, and believed them to represent dilated gland ducts. The histology and topography of the mucous glands and their ducts in the bronchi are well established, but the changes after acute or long-standing bronchopulmonary diseases are less well known. In 1838 von Rokitsansky commented on hypertrophy of the mucous glands after chronic bronchitis. Gruber (1869) showed true glandular cysts on the posterior aspect of the trachea, one of them being as long as 1.1 cm. Later he described a retrotracheal cyst which was 2.4 cm. long (Gruber, 1875). Gruber regarded this cystic degeneration of the glands as being due to chronic bronchitis, which leads to the obstruction of the duct by mucous plugs and by oedema of the mucosa. Such glandular hypertrophies have also been found in patients who died from croup (Borel, 1918) or from acute necrotizing tracheo-bronchitis (Hart, 1915). The pictures observed in the dry preparations were probably produced by the same mechanism. The small aper-

tures which are regularly arranged on the two slopes of the cartilaginous rings correspond to the normal gland ducts. The larger ones, sometimes as wide as 1.2 mm. and scattered in the bronchial wall, represent dilated ducts from the glands. They are more numerous near the bifurcations, but are absent in the lungs of the newborn.

The process of cystic dilatation probably results from repeated attacks of bronchitis, which are accompanied by increased secretion of mucus. Sometimes if a mucous plug remains lodged in a

duct the mechanism alleged by Gruber (1869) would account for dilatation of the whole duct system behind the obstruction and for cystic degeneration of the gland. If, on the other hand, oedema and swelling are reduced the mucous plug is coughed out, but a small diverticulum similar to those described may persist.

It is possible to visualize these enlarged ducts by bronchoscopy, and we feel that this should be borne in mind when interpreting the bronchoscopic appearances thought to be due to a bronchial fistula produced by the rupture of a tuberculous lymph node, particularly as there are an increasing number of records of such ruptures in the literature of the past few years.

Enlargement of the tracheo-bronchial lymph nodes after a primary tuberculous infection is common, and when it is extensive it may produce a bronchial stenosis with the subsequent development of atelectasis or bronchiectasis. A breaking-down caseous lymph node, or even a calcified one, sometimes ulcerates through the adjacent bronchial wall and caseous material or broncholiths are coughed up. The condition is potentially dangerous, since the foreign matter and tubercle bacilli can be aspirated into different parts of the lung and produce a tuberculous spread. Though this condition is not uncommon we do not believe, as G6rgenyi-G6ttche and Kassay (1947) say, that "bronchial rupture belongs to the phenomena occurring every day." An estimate of the incidence is given by Jeune, Mounier-Kuhn, and Potton (1951), who recently found 13% of lymph node ruptures in children with a primary tuberculous infection, and think this figure to be below the true percentage. Lemoine and Fayance (1950) found ruptures in 21% of similar cases in children. Boucher (1951) inspected 100 young soldiers with a primary complex, and he claims to have found symptoms of fresh or old rupture in 30 of them. However, he reports positive bronchoscopic findings in one half of the cases only and admits that in the other half there was no anatomical evidence of a fistula.

The localization, the scarcity in the trachea, the frequency in the main bronchi and around the bronchial bifurcations which, according to the above-mentioned authors, are pathognomonic of bronchial fistulae, are strikingly similar to the localization and frequency of the small glandular cysts observed by us.

The bronchoscopic findings are identical, and the interpretation of an aperture a few tenths of a millimetre wide observed at the end of a tube 40 cm. long is rather a matter of guesswork. Jeune,

Mounier-Kuhn, and Potton say there must be some caseous matter in the bronchi to confirm the diagnosis of a lymph node rupture. They were, however, only able to collect caseum in 24 of their 41 cases, with acid-fast bacilli present in only five. There is no dispute about the fact that a lymph gland can rupture into the bronchial tree, and there are numerous accurate observations of bronchial fistulae, both post-mortem and clinical. We personally encountered two such clear-cut cases.

Apart from the clinical cases in which caseous material containing acid-fast bacilli is recognized when a tuberculous lymph node breaks into the lumen of a bronchus, it is dangerous to make the bronchoscopic diagnosis of rupture based on the presence of a minute fistula or a scar. Similarly, the possibility of a mucous gland cyst must be borne in mind before diagnosing a true congenital diverticulum of the bronchus. Bremer (1932) was able to show accessory bronchial buds in human embryos. These buds eventually disappear during the growth of the embryo, but may, not infrequently, develop into diverticula, accessory bronchi, or cysts.

One of us (Duprez, 1951b) recently collected six cases of congenital bronchial anomalies. In one instance a man had been operated on for cancer of the lung, and inspection of the resected lung revealed a small accessory bronchus, 7 mm. wide and 3 mm. long, opening into the main bronchus not far from the carina and ending in a small cystic mass. The structure was lined by ciliated columnar epithelium, and could be described as a congenital accessory bronchus, because there were traces of cartilaginous rings, muscle, and elastic tissue. When these elements are missing, or if the investigations are incomplete, the differential diagnosis between a cystic gland and a congenital anomaly may be impossible.

Some of the histological evidence points to inflammatory changes persisting round these dilated ducts and glands, and it is possible that they may play a role in reinfection of the lung in cases of long-standing bronchitis, and indeed of maintaining an infection which otherwise would have subsided. Evidence for this hypothesis is being explored at the present time.

SUMMARY

The main topographical and histological characteristics of the mucous glands in the tracheo-bronchial tree have been summarized.

It has been shown that chronic bronchitis leads to cystic degeneration of some of the glands; the latter are then observed by bronchoscopy and bronchography.

Bronchial casts, and a technique for dehydration of the bronchi, which is described in the paper, are the best methods for investigating dilated glands.

Some of the aspects of these glandular cysts have been pointed out in relation to the differential diagnosis of lymph gland ruptures in the bronchi and true diverticula of the bronchi.

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REFERENCES

- Bariety, M., Paillas, J., and Levy, M. (1951). *La trachée et les bronches cartilagineuses*. Paris.
- Baud, C. A. (1945). *Recherches sur l'histomécanique des capsules d'organes*. Thesis. Lyon.
- Bonne, C. (1901). *Bibliogr. anat.*, **9**, 97.
- Borel, F. E. (1918). *Les glandes muqueuses des voies respiratoires dans la diphtérie*. Thesis. Geneva.
- Boucher, H. (1951). *Rev. Tuberc., Paris*, **15**, 712.
- Bremer, J. L. (1932). *Anat. Rec.*, **54**, 361.
- Duprez, A. (1951a). *J. franç. Méd. Chir. thorac.*, **5**, 442.
- (1951b). *Acta chir. belg.*, **50**, 65.
- Fischer, E. (1933). *Z. Anat. EntwGesch.*, **101**, 168.
- Fischer, F. K. (1950). *Fortschr. Röntgenstr.*, **72**, 653.
- Görgenyi-Göttche, and Kassay, D. (1947). *Amer. J. Dis. Child*, **74**, 166.
- Gruber, W. (1869). *Virchows Arch. path. Anat.*, **47**, 1.
- (1875). *Ibid.*, **65**, 227.
- Hart, C. (1915). *Berl. klin. Wschr.*, **52**, 402.
- Huizinga, E., and Smelt, G. J. (1949). *Bronchography*. Van Gorcum, Assen, Netherlands.
- Jeune, M., Mounier-Kuhn, P., and Potton, F. (1951). *Sem. Hôp. Paris*, **27**, 1428.
- Lemoine, J. M., and Fayance, R. (1950). *Rev Tuberc. Paris*, **14**, 117.
- Miller, W. S. (1947). *The Lung*. Charles C. Thomas 1948.
- Möllendorff, W. von (1936). *Handbuch der mikroskopischen Anatomie des Menschen*. Springer, Berlin.
- Policard, A., and Galy, P. (1945). *Les Bronches*. Paris.
- Reissesen, F. D. (1822). *Über den Bau der Lungen*. Rücker, Berlin.
- Rokitansky, C. von (1838). *Osterr. Jahrbücher*, **16**, 382.
- Stutz, E. (1948). *Röntgenpraxis*, **17**, 91.