FETAL BRONCHIECTASIS *

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There are two types of congenital bronchiectasis: the atelectatic bronchiectasis first described by Heller and Francke, and the fetal bronchiectasis, the first detailed description of which was made by Meyer and Grawitz. The characteristic feature of the former is that, besides the development of an atelectatic condition in the affected part of the lung, there also occurs dilatation of the bronchi by a hypoplasia of the alveolar structure (Hondo). The dilatations are thus changed into various sized, multilocular cavities, with or without open connection with the larger bronchi; infiltration and pigmentation are then absent. On the other hand, there occurs an often marked growth in the cartilage of the bronchial walls. The mucosa is lined with stratified columnar epithelium, usually nonciliated. This type of bronchiectasis is said to appear in later adult life (over 45 years) and results in atrophy of the affected lung.

Fetal bronchiectasis is by far the more rare type. Since the first accurate work of Meyer and Kessler there have been a number of investigations of this interesting condition. Meyer cites Bartolinus, Fontanus, Fabricius, Ludovicus and Nonnus, who described cases which were apparently fetal bronchiectases. Humbert has gathered together several articles in his "*Malformation congenitales du poumon.*" These investigations are concerned, in the great majority of instances, with the possible etiologic factors leading to the production of the condition, and most of the reports of cases include detailed descriptions of the pathologic histology of the lung. However, little or no attention has been given by these observers to discussion of the symptomatology or of the causes of certain concurrent pathologic findings. Furthermore, the opinions as to the etiology of fetal bronchiectasis and its pathologic changes by no means agree.

It is my purpose here to review the literature on this subject, to present a case of this interesting lung abnormality, and to discuss briefly some of the points suggested by this case.

The lung changes occurring in fetal bronchiectasis may cause intra-uterine death, developmental malformations in the otherwise normal lung parts or thoracic contents, death at birth, or in infancy or early

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childhood, where the condition manifests itself after a shorter or longer period of latency. Moreover, there are certain cases which undoubtedly belong to this group, in which puberty or adult life has been reached, which have been described as adult forms of bronchiectasis, but which are probably of fetal origin (Schwalbe).

The condition is one in which there develops in the lung smaller or larger cavities, sometimes involving only part of a lobe, again the whole lobe, occasionally more than one lobe on one or both sides, and which, as Grawitz first ascertained, are of bronchiectatic nature. The affected portions are occasionally only slightly enlarged, but usually show great enlargement, sometimes causing considerable displacement of the heart and other thoracic contents, and at times, as in my case, consuming almost all of the space available in the thorax. Grawitz divided fetal bronchiectases into two types—"die telangiectatische angeborene und die universelle angeborene Bronchiectasien." The first type produces a cystic degeneration of a whole bronchus with all its branches and simulates an ovarian cystoma, while in the second type one finds small cystic ectasies which impress one as dilated lymph channels and are even more similar to a ranula pancreatica (Hondo). Kaufmann differentiates two types which are apparently but different grades of the same process, and which are seldom seen in the same case. In the one type, the affected portion is more or less completely composed of small cavities, those situated subpleurally and meeting with less resistance, becoming the largest, often attaining the size of a pea. The lung presents a spongy, emphysematous appearance, and the cavities, which, separated from each other by thin falciform septa, appear to lie in rows, may be connected with the larger bronchi or completely shut off from them (*Wabenlunge*). In the other and much more rare type, the entire lung segment is changed into a large cyst, on the inner wall of which numerous falciform septa form small pocket-like spaces or are completely flattened out (*Sacklunge*). There may be no connection whatever with the bronchi or there may be several small connections, which would indicate a single cyst resulting from the confluence of many smaller cysts. Whichever may be the case, the cyst is filled with a watery fluid, sometimes slimy, with air, or, as in my case, with both. This classification, although not exactly the same, seems to coincide with that of Grawitz.

Grawitz considered his first four cases (two of these were in collaboration with Meyer) as similar cases of "hydropische Ansammlung bedingte Bronchiektasie," a 5 months fetus, a year old female infant, a new-born child, and a 25 year old male, since in each of these there were similar bronchial dilatations, a single main cyst into which all the side cysts opened. In each case the malformation was localized in a

single lobe which was markedly enlarged. The diagnosis of bronchiectasis was made by the presence of ciliated epithelium and communications with a bronchus. The fifth case of Grawitz, a 4½ months female

Fig. 1.—Gross photograph of thoracic and abdominal viscera, showing large size of lung cyst.

infant, is quite similar to those of Sandoz. Microscopically, the cysts were lined with ciliated epithelium and did not communicate with open

bronchi; the bronchial origin was further indicated by the presence of islands of cartilage.

Grawitz says, "These pictures differ from preparations of the higher grade emphysematous changes found in older people only in the absence of lung pigment." No mention was made of muscle and elastic fiber changes. Sandoz does not consider it improbable that this emphysema was the same as that which appeared in the same parts of his cases where the septa showed bundles of smooth muscle fibers. His cases, which he describes in great detail, were fetal bronchiectases occurring in twin sisters, 18 years of age, and were in many respects similar to those of Meyer and Grawitz.

The cavities are usually lined with ciliated columnar epithelium first described by Grawitz, in some cases flattened out to an endothelial-like thinness; however, they are not, as originally Virchow, and later Klebs, thought, lymphangiectases, since the structure of the walls clearly indicates their bronchiolar origin. The case of Virchow, which he calls a lymphangiectasis, is similar in many respects to Grawitz' last case. The airless lungs of a 9 months cretin had an almost emphysematous appearance, the outer as well as the inner surface showing "protruding cyst-like cavities, singly or in groups, which, when cut open, exhibited smooth-walled, empty cavities." No connection with air cells or bronchi was found, and no microscopic examination was made.

The presence of gland-like canals, supplied with smooth muscle, which have been described by some writers, could not be verified by many others. Sandoz describes narrow, branching, gland-like canals running in all directions, which opened either into the smaller bronchi or into the cyst cavities. The epithelium, where still present, was of the stratified columnar type, ciliated in many places, which, with the concentrically arranged smooth muscle fibers, indicated their bronchiolar origin. The mouths of these tubes frequently showed funnel-shaped widenings and occasionally gave the impression that they had been drawn into the cavities. No alveoli were present in their vicinity. Stoerk refers to them as proof of what he regarded as a tumor-like proliferation, while others describe them as undeveloped bronchi. Stoerk regarded his case as a cystic fetal broncho-adenoma. The right middle lobe of a new-born child contained a tumor the size of a hen's egg, made up of varying sized alveolar-like spaces which reminded him of emphysematous lungs. The cavities into which opened gland-like structures, were lined with simple columnar epithelium and showed muscle fibers in their walls. The connective tissue resembled the embryonic type. The bronchus to this lobe was not found. He described a second case, of the Vienna collection, similar to the first. These, like that of Frühwald, in contrast to Sandoz' cases, are localized

malformations of a part of a lung and not a diffuse disease of the whole organ.

The alveoli belonging to the dilated bronchi were often overlooked or not seen, even by careful examinations regarding the elastic structures, although references to well developed alveoli in connection with rudimentary bronchi are not infrequent. In some cases, only the finer, noncartilaginous bronchioles are considered; in others, only those supplied with cartilage are described (Arnheim). Functionally, a communication with a large bronchus is of considerable importance. In many of the cases, complete obliteration was found, the atretic bronchi being indicated only by scattered spots of cartilage. Schwalbe finds in this a great similarity to congenital atresia of the bile passages,

Fig. 2.—Photomicrograph, 4 mm. obj., showing ciliated columnar epithelium of cyst lining.

where, in spite of the closure, dilatation and other defects of the ducts, the remaining part of the gland and bile passages may be well developed, while in some of the cases glandular bronchial growths and bronchial dilatation are the prominent features; in others there appears to be a proliferation of the bronchial intermediates with a tendency toward obliteration.

Almost all of the investigators mention the marked decrease or even complete absence of pigment in the affected parts in contrast to the normal parts of lungs which had functioned for some time.

Couvelaire describes at length the case of a new-born whose right middle lobe was markedly hypertrophic. Distributed irregularly throughout the entire parenchyma were small, air-containing cavities

not more than 1 cm. in diameter, lined with simple cuboidal epithelium. The connective tissue of the septa was of embryonal type. He also found small islands formed by canals lined by high columnar epithelium, which opened into the cyst spaces. None of the medium sized bronchi had the normal appearance. Although these cavities were extremely numerous, they did not prevent easy differentiation of the individual lobes. The alveoli in some places appeared quite normal. Couvelaire says in conclusion, "Il s'agit d'une malformation congénitale bronchopulmonaire aboutissant à des formations kystadénomateuses développées suivant le plan architectural ordinaire du poumon foetal."

Kaufmann mentions two cases and Peiser, one case of fully developed bronchiectases in fetuses. In one of Kaufmann's cases (Case 10) the left lung of a 42 cm. fetus presented the spongy appearance of the honeycombed lung (also described by Box); in the other case (Case 12), the left lung of a 35 cm. fetus was markedly enlarged, 5.5 by 2.5 cm., a typical *Sacklung*. On section, it had a reticulated appearance, large, branching, smooth-walled cavities occupying the place of the entire parenchyma. Here an open connection with the main bronchus was found.

Hondo's case was that of an infant which was born asphyxiated and died almost immediately. His description is much the same as the others of fetal bronchiectasis. Orth mentions a case of congenital emphysema in a 4 year old child, which he believed to be much like Kleb's case. Löhlein speaks of a cystic papillary lung tumor as the result of a fetal bronchiectasis. Dionisi studied two cases which he considered to be anatomically similar to congenital cystic kidneys, and which he described as congenital polycystic lung degenerations.

As I have mentioned, the opinions as to the cause or causes of the changes occurring in fetal bronchiectasis are widely divergent. The assumption of a merely passive dilatation after a primary bronchial closure is not sufficient explanation on account of the marked enlargement found in many cases, the glandular bronchial proliferation, and further, because in a number of cases there was no bronchial stenosis, Sandoz considers the cavities to be merely the dilated endings of the bronchi. Kaufmann wrote, "To understand this peculiar change one must think of an hypoplasia which permits of the greater development of the larger bronchial branches, but not of the alveoli." "In certain cases," he adds, "the bronchial dilatation occurs through the retention of secretion behind a bronchial stenosis." In this connection, Virchow and Klebs thought of lymphangiectasis.

Stoerk, observing a case of excessive epithelial proliferation, considered it a fetal broncho-adenoma, which Hondo agrees must be

thought of. However, even if it must be admitted that these changed lung parts may furnish the basis for lung tumors, it seems that an explanation of the development of fetal bronchiectasis by the presence of epithelial proliferation alone is not sufficient; the mesenchym and bronchial dilatation must also be considered. The opinions of Kimla and Couvelaire, that the condition results from a disproportion in the mesenchymal and endodermal anlage of the lung, seem very plausible.

Several writers assume, from the histologic pictures of their cases, that the condition is due to an inflammatory process. Hondo believes it to be due, not to a disturbance of secretion, but to an inflammatory

Fig. 3.—Photomicrograph, 32 mm. obj., showing character of cyst wall. Note cartilage and blood vessels.

process of early embryonic life. Sandoz described marked leukocytic and lymphocytic infiltration, cellular proliferation and degeneration, and concludes, "We have two processes here—the malformation of the bronchi and the inflammatory process." He adds that the air pressure of postfetal life must be considered a factor in the production of the bronchial dilatation in the malformed parts. He does not believe it possible for the retention of secretion to cause a bronchiectasis, and, in his cases, found open communications with larger bronchi. He says further, "The inflammatory process present in the malformed parts affects the bronchi and peribronchial connective tissue, and the lung parenchyma equally, and must be considered as well as the process of malformation."

The earlier investigators, among whom existed the tendency to attribute the condition to intra-uterine inflammatory processes, soon brought forward the explanation of congenital syphilis as the causative factor. Sandoz emphasizes the point that his cases were twin sisters, and that the cause of the bronchiectasis occurring in both cases must have been some influence either transmitted to the ovum or forced on the embryos during pregnancy. Although he had no proof for an assumption of syphilis, either from the histories of the cases or from the examination of the other organs, he suggests syphilis as a probable explanation, and finds a similarity in his cases to the lung findings in congenital syphilis.

Stroebe and Spanudis mention the interesting point that syphilitic lungs now and again do not attain alveolar development. Arrest in development certainly occurs in the lungs, as in the kidneys, etc., but what happens later is not known. Bronchiectasis has, however, been described by the French writers in connection with hereditary syphilis. Aufrecht also described a marked dilatation of the smaller bronchi in congenital syphilis. Balzer and Grandhomme described a case of a luetic child, which died soon after birth, and whose upper left lobe had the appearance of a greatly enlarged cystic kidney. The hazelnut sized cysts contained a cloudy liquid, and microscopically appeared to be of bronchial origin. They suggest the similarity of this case with the first case of Grawitz, who, however, made no mention of syphilis. They describe ampulla-like dilatations of the smaller bronchi in the normal lobes, and found, also, a chronic bronchopneumonia with prominent foci in the peribronchial and perivascular connective tissue, and less marked foci in the alveolar septa. They considered that in their case syphilis was merely a coincidence.

Spanudis lays stress on the fact that in luetic lung processes, the proliferation and desquamation of the epithelium go hand in hand with the interstitial process. Birch and Hirschfeld emphasize the peribronchial and perivascular localization of syphilitic interstitial pneumonia.

There are very few descriptions of the lung findings in late hereditary syphilis, and these are quite brief. Fournier found in 212 such cases that the lungs were involved in only five cases. Gummas occurred in four cases; in a fifth case (Lancereaux), in a 41 year old woman, the right lung was partly involved by bronchiectatic cavities the size of a pigeon's egg or smaller, lying in indurated tissue. Unfortunately, no microscopic description was given by Lancereaux. Virchow described an alveolar catarrh in connection with white hepatization.

Aufrecht, referring to other observations (Rollet, Schnitzler, Hiller, Pavlinoff), says that syphilis may be looked on as the basis of all

diffuse pneumonic diseases. Stoerk describes processes quite like peribronchitis and periphlebitis. Flockemann concludes, however, that the indurative fibrous process does not simulate syphilis, and that the changes described by investigators of bronchiectasis may well be affected by other disease causes, but he does not suggest specifically what causes.

Pepere and Dionisi are of the opinion that this condition is due to congenital disease. Pepere also suggests that many cases appear to be the result of a congenital lack of resistance of the whole lung tissue, particularly the stroma.

Regarding the effect on the normal lung parts, it is quite possible that the rapid and increasing enlargement of the bronchiectatic lung part may have an injurious effect on the normal parts, and, as in the case of such spreading processes, produce a circulatory disturbance. Frühwald speaks of a case of intercostal lung hernia due to fetal bronchiectasis.

The tendency of most of the modern writers is to assume that the change is the result of a developmental derangement through which the different parts of the bronchial tree reach an incomplete and disproportionate development, in which the formation of alveoli is absent. The different appearances in the various cases may, according to Schwalbe, be explained by the site and degree of the dilatation. The microscopic proof of nondevelopment or maldevelopment and the simultaneous occurrence of other abnormalities favor this theory of a primary maldevelopment.

A congenital basis for some cases of bronchiectasis is accepted, partly occasioned by the reference to an instance of heredity (Neisser and others). The French writers in particular assume a congenital "debilitas pulmonalis," "maladie kystique" (Peiser, Humbert), a congenital lack of resistance which, on account of the normal requirements of the lungs, points the way to the development of a bronchiectasis, and Humbert suggests an inhibition of the postembryonal growth of the bronchial wall.

My case is that of a new-born child and is in many respects similar to the other cases of fetal bronchiectasis of the *Sacklung* type. Nowhere, however, have I found an analysis of the cyst fluid such as I have made.

REPORT OF CASE

History.—A new-born child (W.) whose family history was negative for syphilis, malignancy, tuberculosis, etc.

Past History of Mother.—Para I, 26 years of age; had the usual diseases of childhood, but no serious illnesses. Her first labor terminated thirty months previously by a difficult midforceps delivery; she had a nonfebrile puerperium and nursed her child for eight months; the child is in excellent condition at present.

Present History.—Multigravida. Last period occurred Sept. 29, 1917; she felt life eighteen weeks later. Pregnancy was normal throughout, with no vomiting; urine was normal on weekly examination; blood pressure, systolic, ranged from 115 to 120. Since the baby was estimated to be considerably larger than the first child, which weighed 3,210 gm., and the labor which was due July 15 had not started, the patient was given 10 grains of quinin sulphate and 2 ounces of castor oil at 9 a. m. July 16, and the quinin repeated in one hour. Labor started at 10 a. m.

The baby, a female, weighed 3,438 gm., and was 52 cm. in length. It was noticed that the child exhibited a very slight bluish tinge; however, it cried quite normally. No abnormality was detected by casual examination. The child was apparently well formed and well developed. No special examination of heart or lungs was made.

One hour after delivery it was noticed that the child was dyspneic and markedly cyanotic. All efforts to overcome the apparent asphyxia were unsuccessful and included artificial respiration, hot tubbing, oxygen, and intramuscular administration of camphor oil. The respiratory efforts came at increasing intervals and the child died one hour and thirty minutes after birth.

Necropsy.—The body is that of a female, newly-born infant, 52 cm. in length, apparently well developed and well nourished. The skin is elastic and everywhere markedly cyanotic. No edema, eruptions, abrasions, hemorrhages, desiccation, or other abnormal discoloration.

The head is well formed, of normal size and shape, and covered with a moderate amount of brown hair. The sutures and fontanels are of normal size. The pupils are equal and normal in size and shape. The sclerae are of normal appearance. The neck, thorax, abdomen, genitals and extremities present no abnormalities or malformations.

The pericardium presents the normal size, appearance and relations, and contains the normal amount of fluid.

Lungs: No pleural adhesions or fluid. The right lung presents a normal appearance and weighs 7 gm. On section, a small amount of whitish, foamy material can be expressed from the bronchioles. The lower left lobe presents an atelectatic appearance. The upper left lobe presents a large air- and fluid-containing cyst with the unexpanded lung tissue spread out over its surface. The cyst contains 75 c.c. of fluid (described later) and a lesser quantity of air. No connection between the cyst and a bronchus can be determined. The wall of the cyst is covered irregularly, but completely, with strands of white, fibrous tissue of varying thickness and irregularly distributed, incomplete, falciform septa, partially walling off varying sized pockets from the main cavity. No secondary cysts are to be seen. Sections of lung tissue from this lobe sink in water, whereas other sections float.

Heart: The heart, in situ, lies with its base in the right anterior axillary line and its apex in the midsternal line; no pericardial fluid, adhesions, or thickening. The size, color, shape, and consistency are normal and it weighs 13 gm. The ductus arteriosus and foramen ovale are patent and normal.

Measurements:	Mm.
Thickness of wall of left ventricle.....	2.5
Thickness of wall of right ventricle.....	3
Circumference of mitral orifice.....	32
Circumference of tricuspid orifice.....	38
Circumference of aortic orifice.....	20
Circumference of pulmonary orifice.....	21

The peritoneal cavity is free from adhesions, exudation, etc. No distention, contraction, or abnormal development of the intestines is present. The lymph nodes are of normal size and color. The intestines are 4.45 meters long. Mucous membranes present a normal appearance throughout.

The spleen lies in its normal position and presents no abnormalities in color, etc. The capsule is normal; the trabeculae, lymph nodules, pulp and blood vessels are normal. The spleen weighs 10 gm. and measures 5 by 3 by 1.7 cm.

The liver shows no enlargement or other abnormal appearance and cuts with normal resistance. It weighs 100 gm. and gives the following measurements:

	Cm.
Length, right to left.....	9
Vertical diameter of right lobe... ..	6
Vertical diameter of left lobe.....	4.7
Average thickness.....	3.5

The adrenals present no abnormalities and together weigh 4 gm.

The kidneys exhibit the surface markings of the fetal lobulations, but no pathologic appearance as to size, shape, color, or consistency. The capsule strips easily. The cut surface presents a normal appearance; the cortex measures 2 mm. and the entire kidney substance, 12 mm. The kidneys measure 4.3 by 2.7 by 1.9 cm. and weigh 10 gm. each.

The thymus presents no abnormality and weighs 5 gm.

Anatomic Diagnosis.—1. Cyanosis of the skin. 2. Cyst and atelectasis of the upper lobe of the left lung. 3. Incomplete expansion of the lower left lobe. 4. Hypertrophy of the right ventricle.

The sections cut for microscopic examination were fixed in formaldehyd solution, imbedded in paraffin and stained by the usual hematoxylin-eosin technic.

Microscopic Examination.—The sections of kidney, spleen, liver, pancreas, intestine, thymus, and suprarenal exhibit no pathologic appearances other than the usual post mortem changes. Sections of lung and liver, stained according to the method of Levaditi, exhibited no treponemata. In the sections of suprarenal body may be seen a rather distinct zona glomerulosa, said not to appear until the second or third year.

Heart: Sections of the right ventricular wall show an increase in the transverse diameter of the muscle fibers and well stained, square-end nuclei. Otherwise these and other sections are quite normal.

In order to avoid repetition I will describe the microscopic appearance of the various cyst wall sections as a composite picture. In some places the flattened pleural epithelial cells and the underlying thin layer of connective tissue have a normal appearance, in others they are absent, while frequently the pleura may be seen to be somewhat thickened. Beneath the pleura lie various sized areas of unexpanded lung tissue, some very large areas showing no alveoli whatever, or only indications of them. They appear to be areas of undeveloped lung in which there remains considerable mesoblastic tissue, a rudimentary type of connective tissue, considerable lymphocytic infiltration, especially about the blood vessels, a few leukocytes, and occasional plasma cells. The nuclei of the stromal cells are large, round and well stained. The round or spindle shaped cell bodies stain rather poorly. The stroma is relatively rich in blood vessels, mainly small arterioles and capillaries. Most of the alveoli which are present are unexpanded; the epithelium, which has largely desquamated, appears irregularly cuboidal in places, and the nuclei occasionally seem to bulge into the lumina. Here and there throughout the stroma are small plaques of irregularly arranged smooth muscle fibers. Blood pigments may be seen in some places; anthracotic pigment is, of course, absent. The bronchi show dilatation and, in some places, epithelial proliferation, and the normal bronchial glands are frequently to be seen. The cyst wall is made up of fibrous tissue in which occur smaller or larger pieces of hyaline cartilage, the connective tissue between them being extensively infiltrated with lympho-

cytes and a few leukocytes. Here, also, varying sized plaques of smooth muscle fibers are frequently seen, in some places lying between the cartilage and the epithelium. No secondary cysts were seen.

The epithelium, largely desquamated, is of the ciliated columnar type, sometimes appearing as a single layer and sometimes stratified, where the underlying cells assume a cuboidal or round shape. In a few places the epithelium appears to lie on a well developed basal membrane. Beneath lies a thick layer of connective tissue quite infiltrated with lymphocytes and a few leukocytes.

Lying among the islands of cartilage, are rows of cells with heavily staining nuclei, which seem to be of bronchiolar epithelial origin. Here, also, are various sized areas of glandlike tissue.

Sections from the right lung show slightly dilated alveoli, the inter-alveolar connective tissue with the contained blood vessels being somewhat thinned, indicating a moderate grade of emphysema.

Sections from the lower left lobe show large areas of unexpanded lung tissue similar to those mentioned before in the upper lobe.

Microscopic Diagnosis.—1. Fetal bronchiectasis, forming a cyst of the upper lobe of the left lung. 2. Atelectasis of both left lobes. 3. Alveolar dilatation of the right lung, slight. 4. Slight myocardial hypertrophy of the right ventricle.

Analysis of the Cyst Fluid.—Amount, 75 c.c.; specific gravity, 1.009; reaction, slightly alkaline (litmus); appearance, slightly cloudy or opalescent fluid, of light-yellowish color, noncoagulated after standing at room temperature for five days.

Microscopic examination showed an occasional polymorphonuclear leukocyte, less than 3 per cubic millimeter, which may be due to error in collecting the fluid, and fat globules which stained well with Sudan III; no crystals were to be seen. Quantitative determinations of the cyst fluid constituents gave the following results calculated in parts per 1,000:

Water	987.77
Total solids.....	12.23
Fibrinogen ¹	trace
Albumin ²	2.38
Fats and lipoids ³	0.26
Water extractives.....	9.61
Ash from water extractives.....	8.85 }
Ash from water insoluble bodies.....	0.62 }
	9.47

The ash yielded 3.79 parts chlorin⁴ per 1,000 and qualitatively showed a small amount of sodium. Cholesterol, lecithin, uric acid and urea determinations were, unfortunately not made.

Most of the histologic features of this case are quite similar to those found by most of the observers; for example, the somewhat thickened pleura, the areas of unexpanded lung, the cellular infiltration, the irregularly distributed muscle fibers in the stroma, the dilatation of the smaller bronchi, the epithelial proliferation, the plaques of smooth muscle fibers lying between the epithelium and cartilage, the cartilage islands, the thick connective tissue layer below the epithelium, and the

1. Determined according to the method of Whipple.

2. Determined by Scherer's method (Webster).

3. Determined by Röse-Gottlieb method (Rupp-Müller).

4. Precipitated as silver chlorid (AgCl); calculated as chlorin.

ciliated columnar epithelium lining the cyst. Addison and How have described the cuboidal epithelium of fetal alveoli such as I have mentioned above. Concerning the bronchiolar epithelial cells, the islands of cartilage and the intermingled plaques of smooth muscle fibers, I have considered these in relation to the cyst wall, partly because of the comparatively large size of these areas, whereas one must also consider the possibility of their relation to imperfectly developed bronchioles in the cyst wall, perhaps interfered with in their development by the enlargement of the cyst. That the increasing enlargement of the cyst could produce a mechanical interference in the development of neighboring bronchi is readily conceivable, as I have indicated before. Furthermore, the increased resistance offered to the circulation by the development of the cyst, as is the case in almost every instance of a growing process occurring in the thorax, as well as by the atelectatic lung, may be quite sufficient to cause the myocardial hypertrophy apparent in the preparations of the right ventricle.

If it is proper to interpret the muscle and cartilage as belonging to the cyst, then there can be no doubt as to its bronchial origin. Proof of such origin, however, is certainly to be had in the ciliated columnar epithelium of the lung and in the thick layer of connective tissue beneath it. The fetal alveolar epithelium is not of the ciliated columnar type and it is difficult to conceive of a metaplasia into a more highly differentiated form. Hence, it is quite justifiable to assume that we are dealing in this case with a fetal bronchiectatic cyst. Furthermore, if it is true that the lungs may be said to have completed their development by the sixth week of intra-uterine life (Ballantyne), then the cause or causes of the condition must have been present in the ovum or forced on the embryo during the first six weeks.

As to the etiology of this condition nothing positive can be said. Syphilis, I think, can be eliminated; it is certainly not pneumonia gelatinosa specifica, there are no miliary syphilomas with signs of neighboring interstitial pneumonia, nor is there the connective tissue hyperplasia indicating a clearly marked interstitial fibroid pneumonia—pneumonia interstitialis fibrosa chronica congenita. The areas of undeveloped lung with remaining mesoblastic tissue, which I have mentioned before, may suggest pneumonia alba syphilitica, but the other features of the case, together with the absence of any positive evidence of syphilis in the family, and of treponemas in the liver and lung, clearly point against syphilis.

One feature of this case is of particular interest, namely, the composition of the cyst fluid, which so closely approximates that of amniotic fluid. Liquor amnii is described in various places as a

serous fluid of slightly alkaline reaction, and has a specific gravity varying from 1.006 to 1.013. Its composition at term has been determined as the following.

Investigator	Water Per Cent.	Solids	Albumin	Water Ext.	Fats and Lipoids	Salts	Chlorids
Ballantyne.....	97 to 99	1 to 3	0.6 to 1	0.03 to 0.7		0.3 to 0.9	0.586 (NaCl)
Labruhe	99.15		0.082	0.06		0.706	
	98.793	1.207	0.2533	0.1689	0.0368	0.1464	0.5596
Winckel			0.24			(Sod. Phos.)	
			0.22				

The question arises as to the possibility of the cyst fluid being liquor amnii. Addison and How found that during prenatal life the future respiratory passages are filled with a liquid, which, with the first inspirations, is drawn into the lungs. Intra-uterine respiratory movements have been described by several clinical observers (Ferroni and others). Howell expresses the opinion that the mammalian fetus under normal conditions makes no respiratory movements while in utero. Ballantyne accepts the results of the clinicians, but says it is doubtful that they are strong enough to draw liquor amnii into the lungs. Addison and How add that if the movements are really similar to respiratory movements, "they are not to be compared in point of intensity with the postnatal efforts, and do not affect the structure of the lung to any extent." Leclard, on opening the trachea of a still living guinea-pig fetus, found a fluid analagous to amniotic fluid, and that when colored fluid was injected into the amniotic fluid, that in the bronchi was also colored. This was verified by Preyer and added to by Geyl.

The presence of fluid in the alveoli and bronchioles does not seem to me to be entirely dependent on respiratory efforts, in that the normal development of the growing air spaces could well explain it. The fluid must be either liquor amnii or that secreted by the bronchial glands; its composition in this case and the observations noted strongly suggest the former, but this cannot be definitely proved. However, its composition is quite unlike the secretions.

Lastly, I wish to suggest certain possible explanations for the child's air hunger and cyanosis. These can be explained, according to the recent work of R. G. Pearce, as due to increased carbon dioxide tension in the blood, and anoxemia, respectively. In this case the cyanosis appeared immediately after birth and increased in intensity until death. Three factors may contribute to the production of the cyanosis in this case: First, the atelectasis prevented the aeration of the blood passing through that part of the lung; second, the increased resistance to the circulation on the affected side may have been suffi-

cient to cause the flow of considerable unrespired blood through the patent ductus arteriosus into the systemic circulation. Both of these causes could have brought about the presence of unrespired blood in the general circulation, that is, blood with a low oxygen content. Added to these is the third factor, that the great size of the cyst was enough to prevent the advent of a sufficient quantity of air for the proper oxidation of the blood even if it could have been available to the blood, as in cases of congenitally large thymus, congenital stenosis of the upper respiratory passages, or any condition preventing the easy ingress of air. Also, it must be remembered that no open connection could be found between the cyst and the larger bronchi, so that complete bronchial stenosis other than that produced by pressure of the cyst must also be considered. It is, of course, impossible to say which of these factors was responsible for the cyanosis; all of them must be considered and probably each had a part.

It is quite probable that the slight alveolar dilatation observed in the right lung was due to forcible respiratory effort, and that the hypertrophy of the heart muscle was due to the increased resistance offered to the pulmonary circulation by the cyst, atelectasis and excess of mesoblastic tissue.

CONCLUSIONS

1. The cause of fetal bronchiectasis is unknown, although the opinion of a primary maldevelopment seems to be current among most modern investigators.

2. The bronchial origin can be said to be proved.

3. The composition of the cyst fluid found in this case strongly suggests the possibility of its being liquor amnii.

4. It appears that there occurred a slight alveolar dilatation of the right lung, probably due to increased respiratory effort, that the myocardial hypertrophy was due to increased resistance to the pulmonary circulation; that the dyspnea was due to increased carbon dioxid tension of the blood, and that the cyanosis can be explained by any or all of three factors—the prevention of oxidation of the blood by the atelectatic state of the lung, the circulation of unrespired blood due to increased resistance to the pulmonary circulation and the patent ductus arteriosus, and the obstruction to the ingress of air by the pressure of the cyst on the large bronchi or by the developmental bronchial stenosis.

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