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AUTHORITY

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DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland
Bronchiectasis with situs viscerum inversus.

by M. Kartagener and K. Mully

From the Surgical Clinic of Zurich University. Schweizerische Zeitschrift für Tuberkulose, Vol. 13, No. 3 (1955) pp 166-191

The peculiar triade: Situs inversus, bronchiectasis and polyposis nasii or chronic sinusitis, to which one of us called attention in 1933, has been the subject of numerous publications during the past years. Previous literature has been summarized in 1935 by Kartagener, in 1939 by Hasler and in 1947 by Kartagener and Gruber. In the latter paper 88 cases were counted. Publications which have appeared since, and those overlooked previously, may be tabulated in chronological order as follows:

1937 Casaubon and Derqui (cited after Olsen)  evidently 1 case

1938 Cockayne  1 case (sister situs inversus without Eb)

Tempini  2 cases (one with simultaneous TB)

1939 Cole and Nalls  1 case

Natvig  2 cases (siblings)

1940 Dannenbaum (braunschweig)  1 case (personal report)

H.E. Keyer  1 case (isolated dextrocardia, mother Eb)

Perry and King  1 case (6 observations, of which 5 were already published 1937 by Adams, Churchill)

G.O. Wood and Blalock  1 case

W.B. Wood  1 case ("cystic disease" with dextrocardia, no further data)

1944 Richards  1 case

1946 Toscano  1 case (with congenital cardiopathy)

1947 Allende and Langer  2 cases
<table>
<thead>
<tr>
<th>Year</th>
<th>Authors/Details</th>
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<tbody>
<tr>
<td>1947</td>
<td>Lazeze and Buffard: 2 cases</td>
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<td>1948</td>
<td>Aimos: 2 cases</td>
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<tr>
<td></td>
<td>Benda and Huet: 1 case</td>
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<td></td>
<td>Hurter: 2 cases (third observation already published by Schaich in 1947)</td>
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<tr>
<td></td>
<td>Kluge: 1 case</td>
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<td></td>
<td>Shepard and Stewart: 2 cases (siblings, 1 other case questionable)</td>
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<tr>
<td></td>
<td>Tapie, Laporte, Pinel and Denard: 1 case (sister BE without inversion)</td>
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<td></td>
<td>Weill, Lallemand and Leveque: 1 case (brother: repeated bronchitis and agenesis of the frontal sinuses, one sister died of &quot;maladie bleue&quot;)</td>
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<tr>
<td>1949</td>
<td>Andrew: 1 case</td>
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<td></td>
<td>Assmann: 1 case (Fig. 270 in 6th ed. not identical with Fig. 216 in the 4th edition)</td>
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<tr>
<td></td>
<td>Eonhag: 2 cases (plus 1 case of TB with questionable BE)</td>
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<td></td>
<td>Churchill: 1 case</td>
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<tr>
<td></td>
<td>Fornara: 2 cases (3 observations, incl. Toscano’s case)</td>
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<tr>
<td></td>
<td>Langer: 1 case</td>
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<td></td>
<td>Mounier-Kuhn: 1 case (5th obs. in Soulas-Mounier-Kuhn)</td>
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<tr>
<td></td>
<td>Ochsner, De Bakey and De Camp: 3 cases</td>
</tr>
<tr>
<td></td>
<td>Santy, Berard and Galy: 1 case</td>
</tr>
<tr>
<td></td>
<td>Schettler and Klink: 1 case (with vascular deformity at fundus oculi)</td>
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<tr>
<td></td>
<td>Souders: 2 cases (may possibly include Adams and Ficarra’s case, 1947)</td>
</tr>
<tr>
<td>1950</td>
<td>Bergstrom, Cook, Scanell and Berenberg: 2 cases (siblings, 2 other siblings BE without inversion)</td>
</tr>
<tr>
<td></td>
<td>Blixenkrone-Moller: 1 case</td>
</tr>
<tr>
<td></td>
<td>Castanier, Vincent, Hadidi: 2 cases (brothers, simultaneously papillary edema of nervus opticus)</td>
</tr>
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<td>Rosass and Ripoll: 2 cases</td>
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</tbody>
</table>
1950 Cohen, Golstein and Hamill 1 case
Ferreira and Meira 1 case
Hogg 1 case
Jedlicka and Levinsky 11 cases (6 with complete triade, including two sisters, 3 with situs inversus and BE without sinusitis, 2 others by personal report)

1951 Chattas and Di Rienzo 2 cases
Conway 4 cases (1 case with polydactylyism both hands, cousin of one case also has situs inversus)
Fraga Filho, Nery and Maranhao 1 case
Kaye and Meyer 2 cases (siblings)
Murray 1 case
Sas (cited after Bolechowski and Jaroszewski) 1 case
Zuckermann and Wurtzebach 1 case (probably the oldest observed case, a 63 year old veteran of the First World War)

1952 Dassen and Gotlieb 1 case (second oldest case, 59 year old woman)
Ferrand, Sarrouy, Pierrou, Armand and Masson 3 cases (including 1 case without certain BE but with "deformations parietales des bronches de troisieme ordre" as "etat preliminaire a une dilatation bronchique vraie")
Hebel 2 cases (siblings, another sibling BE without inversion, another sibling asthmatic bronchitis. All four with simultaneous thorax deformities. Father: polyposis nasi)
Karani 2 cases (sisters. Father: chronic bronchitis. One brother with a "weak chest" —not examined—the heart was supposed to have been found "on the wrong side")
Pellnitz and Heyland 1 case (pyrgocephalus)
Pykoz (cited after Bolechowski & Jaroszewski) 1 case

1953 Brusa 1 case
Dickey 5 cases (incl. 2 siblings, 1 partial situs inversus)
1953 Katz, Benzier, Nangeroni and Sussman

Laas (Hamburg) 1 case (personal report)

Negri 1 case

Nogueira da Silva and Chiaverini (cited after Cossio and Saul) 1 case

Di Rienzo 1 case

Welento (cited after Bolechowski and Jaroszewski) 1 case

1954 Katz, Benzier and Nangeroni

3 cases (including two siblings)

1955 Bolechowski and Jaroszewski

5 cases (1 other questionable case)

Fried 11 cases (roentgenogram examinations, "partial and complete pictures of Kartagener's syndrome"

Lindskog and Hubbell 3 cases

Luna 1 case (mother and one brother also BE)

Stutz and Vieten 2 cases (3rd observation is identical with 1 case of Hurter, according to personal report)

Taiana, Villegas and Schiepatti 1 case

1956 Finkler 2 cases (another questionable case)

Schmuckler 1 case

All together there have been reports of at least 216 individual cases of bronchiectasis with situs inversus (including the case to be described herein), considering the probability of some cases again escaping our attention. In the majority of these cases an involvement of the accessory nasal cavities has been observed as a complement of the triade proper. It follows beyond a doubt that simultaneous occurrence of bronchiectasis and situs inversus (and possibly of sinusitis) is not based on coincidence. Especially striking is the fact that
this anomaly occurs relatively frequently in several members of the same family. Bronchiectasis or a tendency to chronic bronchitis or chronic sinusitis without inversion also has been observed repeatedly among relatives, as have been siblings or ascending relationships with inversion but without involvement of the respiratory organs. The fact that a number of authors were able to report on several pertinent observations as soon as their attention was directed to this "lucus naturae," is worthy of special consideration. These authors have at times correlated the frequency of this combination to the total number of situs inversus cases seen by them, and have reached a remarkable agreement (with the exception of Finkler)(cf. Table 1).

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Frequency of situs inv.</th>
<th>Bronchiectasis with situs inversus absolute</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benda</td>
<td>1905</td>
<td>autops.2:10,000-0.02%</td>
<td>-</td>
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<tr>
<td>Sherk</td>
<td>1922</td>
<td>10:34,700-0.003%</td>
<td>-</td>
</tr>
<tr>
<td>Guenther &amp; Kegel</td>
<td>1923-1925</td>
<td>clinical 0.007%</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>autops. 0.013%</td>
<td>-</td>
</tr>
<tr>
<td>Lewald</td>
<td>1925</td>
<td>clinical (recruits)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1:35,000-0.003%</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>autops. 0.02%, roentg. 0.07%</td>
<td>-</td>
</tr>
<tr>
<td>Mandelstamm and Reinerberg</td>
<td>1928</td>
<td>roentg. 0.06%</td>
<td>-</td>
</tr>
<tr>
<td>Kartagener &amp; Hohlacher</td>
<td>1935</td>
<td>-</td>
<td>7:30</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>23.3</td>
</tr>
<tr>
<td>Adams and Churchill</td>
<td>1937</td>
<td>clin. 23:232,112-0.01%</td>
<td>5:23</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>21.7</td>
</tr>
<tr>
<td>Olsen</td>
<td>1943</td>
<td>-</td>
<td>14:85</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>16.5</td>
</tr>
<tr>
<td>Wegelin</td>
<td>1945</td>
<td>autops. 0.022%</td>
<td>2:10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>partial situs inv. 0.035%</td>
<td>20.0</td>
</tr>
<tr>
<td>Wayburn</td>
<td>1946</td>
<td>roentg. (flying personnel)</td>
<td>9:77,016-0.012%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>20.0</td>
</tr>
<tr>
<td>Taussig</td>
<td>1947</td>
<td>clin. 4:120,000-0.003%</td>
<td>-</td>
</tr>
</tbody>
</table>

5
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Frequency of situs inv.</th>
<th>Bronchiectasis with situs inversus absolute %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shepard and Stewart</td>
<td>1948</td>
<td>clin., partly roentg. 13:460,000-0.003%</td>
<td>2:13 15.3</td>
</tr>
<tr>
<td>Blegen (perspective)</td>
<td>1949</td>
<td>roentg. 0.015% autops. 0.016%</td>
<td>-</td>
</tr>
<tr>
<td>Jedlicka and Levinsky</td>
<td>1950</td>
<td></td>
<td>9:46 19.5</td>
</tr>
<tr>
<td>Tandos</td>
<td>1950</td>
<td>roentg. (soldiers) in Vietnam 0.03% in North Africa 0.02% in Europe 0.008%</td>
<td></td>
</tr>
<tr>
<td>Nogueira and Chiaverini</td>
<td>1952</td>
<td></td>
<td>2:10 20.0</td>
</tr>
<tr>
<td>Torgersen</td>
<td>1952</td>
<td>roentg. about 0.01%</td>
<td>about 25.0</td>
</tr>
<tr>
<td>Bolehowski and Jaroszewski</td>
<td>1955</td>
<td>EKG 7:66,000-0.012%</td>
<td></td>
</tr>
<tr>
<td>Fried</td>
<td>1955</td>
<td>roentg. about 1:16,000-0.06%</td>
<td>11:20# over 50%</td>
</tr>
<tr>
<td>Finkler</td>
<td>1956</td>
<td>roentgenograms about 50:250,000-0.02%</td>
<td>2:50 4.0</td>
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</tbody>
</table>

* not for evaluation, selected material
** Adams and Churchill's data: 0.002%, should be a misprint

A really imposing confirmation of all these observations, which in the final analysis are still quite isolated, is represented by the systematic examination of Norway's extensive X-ray material by Torgersen. Among approximately 2 million roentgenograms, corresponding to about 2/3 of Norway's population, Torgersen found cases of situs inversus with a frequency of approximately 1:10,000, and among these about 25% with bronchiectasis or the complete triad. Exact, absolute figures are not available from Torgersen's paper. It is assumed to deal with about 200 cases of situs inversus and about 50 cases of situs inversus with bronchiectasis, partly with simultaneous sinusitis.
Similar, but less systematic examinations were conducted by Fried in Berlin and Finkler in Israel. Their results are shown in the table.

The following are considered questionable, more or less probable cases, listed in chronological order:

1884 Wehn
- clinical: left bronchiectatic cavity, autopsy points to more probable TB (no histologic examination, no bacteriologic evaluation)

1897 Vehseymeyer
- first roentgenogram of a case of congenital dextro-...x upon exposure lasting 13 minutes! (no inversion of abdominal organs, but the right diaphragm is lower; simultaneous chronic pneumonia of the left lung, chronic bronchitis)

1907 Aufdernau
- case 2, total situs inversus, "annoying and long-lasting pulmonary catarrh"

1907 Kehr, Liebold, and Neuling
- case 194, 55 year old man, bronchitis since childhood, copious sputum in the morning

1932 Cordier and Anstett
- emphysema with bronchial onsets

1934 Ellman
- complete situs inversus, large circular shadow upper left (cyst? cavity: no further data)

1941 Cohen-Tanugi
- among 4 cases of situs inversus one case with cough for years, one case with a chronically bronchitic mother.

1948 Shepard and Stewart
- case 12 (chronic sinusitis, productive cough, increased pulmonary markings, "suggestive of early bronchiectasis")

1949 Sonhag
- 1 case with TB and questionable bronchiectasis
- probably identical with the case published in 1948 by Welli, Lallemant and Leveque

1950 Jedlicka and Levinsky
- 6 cases of situs inversus with relapsing, chronic bronchitis (observations 5,7,25,32,35,42)

1951 Schier and Boucher
- simultaneous generalized Besnier-Boeck-Schaumann with cystic bronchiectasis in the anterior segment of the left superior lobe, diagnosed as postprimary bronchiectasis (calcified glands in the left hilus, sinusitis)

1952 Karani
- see above

1955 Boleschowski and Jaroszewski case 6

1956 Finkler
- case 3
With the exception of the cases of Kartagener and Horlacher (a) (case 1), Kartagener and Gruber, H.E. Meyer, H.B. Wood?, Dickey (case 2) and the questionable case of Vehsemayor, a total inversion of chest and abdominal viscera has always been involved.

Kartagener (a) points to the fact that a left-sided tracheal bronchus, which according to Bigler was observed only twice before 1924 with situs solitus, was described by Leboucq as early as 1881 in connection with situs inversus. The tracheal bronchus, according to Herxheimer and Gold, is important in genesis of accessory lungs or bronchial cysts, consequently also important for formation of bronchiectasis. In this connection the observation of Holinger, Johnston, Parchet and Zimmermann may be reported: Bilateral tracheal bronchi, which supply both superior lobes, in a 7 month old girl with dextrocardia and several other simultaneous anomalies.

With reference to pathogenesis, the majority of authors agree on the important role of a congenital factor in the appearance of this syndrome. The fact that generally anomalies are quite frequent in connection with situs inversus, that especially in cases of situs inversus with bronchiectasis anomalies are seen also in other organic systems, and particularly the familial occurrence of the triade speaks strongly for the significance of a congenital, possibly a hereditary factor.

Familial occurrence of the triade has been seen 33 times in 15 observations, and this by the following authors: Guenther, Graham, Nativig, Lopez-Areal (4 siblings), Torgersen (2 families with 2 and 3 siblings, respectively), Shepard and Stewart, Bergstrom et al (2 siblings and 2 other siblings with BE without inversion), Castanier et al, Jedlicka and Levinsky, Kaye and Kayer, Hebel (2 siblings and 2 siblings with suspected BE without inversion), Karani (2, perhaps 3 siblings), Dickey, as well as Katz, Benzler and Nangeroni.
Simultaneous other anomalies are quite frequently noted in the skeletal system: thorax deformities several times, polydactylist, pygoccephalus (Pellnitz and Heyland), further, atrophy of the right side of the body (Aimes), Fallot's tetrad (Toscano and Fornara), open septum ventriculorum and transposito vasorum (Dickey), abnormal origin of the left arteria subclavia (Haye and Neyer), vascular deformity at the fundus oculi (Schettler and Klink), papillary edema (Castanier et al), deafnessism (Kartagener(a), hypoplasia of the genitals and mental underdevelopment (several times).

It is difficult to decide just how this congenital (possibly hereditary) factor influences the genesis of bronchiectasis. In regard to the bronchiectasis one of the following may be involved: a true deformity (congenital bronchiectasis in a narrower sense) or inadequate arrangement (defaut original of Bards) of the supporting apparatus of the bronchial wall (musculature, elastic fibres, cartilage) or a distinct "secretory hyperactivity of the bronchial mucous membrane" (Churchill). The latter possibility is supported by very frequent (but not obligate) involvement of the mucous membrane of the upper air passages noted in early reports of bronchiectasis with situs inversus (Siewert 1904). Rounier Kuhn (cf. also Gregoire) also supposes a "niopragia" of the bronchial and nasal mucous membranes which is congenitally caused, possibly on the basis of hereditary syphilis. Benda and Huet's and Ferrand's et al "predispotion tissulaire" must be interpreted in the same sense. Similar meaning must be ascribed to the questionable or "early" bronchiectasis in the aforementioned cases of Shepard and Stewart, Bolesowski and Jaroszewski, Finkler.

The majority of authors assume — at least in the cases with situs inversus—that the alterations in the nasal cavities are coordinated with bronchiectasis (cf. Kartagener and Ulrich). According to Ferrand et al the manifestations in the upper air passages are more intense and precede bronchiectasis considerably.
In their case sinusitis maxillaris and agenesis of sinus frontalis were present, while the bronchi only showed a "deformation parietale" as a forerunner of true bronchiectasis. Similar interpretations were made by Benda and Huet, who in their case found sinusitis maxillaris, nasal polyps and absence of frontal sinuses, but only slight bronchiectasis. Considering the age of the patient (7 years), they believe this to be a "borderline case," meaning probably that bronchiectasis has not yet fully developed.

Sohier and Boucher even rejected the congenital nature of bronchiectasis due to absence of sinusitis!

Conversely, sinusitis is caused by bronchiectasis according to Dickey and Hogg. Sinusitis is said to grow out of coughing up of infectious bronchiectatic pus. Hogg was able to prove by X-ray the presence of lipiodol in the sinus maxillaris following bronchography (cf. also Brock).

Direct anatomical proofs of the congenital nature of bronchiectasis are hard to find. So far no related observations of fetuses and newborn are known, which would prove the congenital nature of bronchiectasis by means of its congenitateness. Still, cases of pulmonary cysts or honeycomb-lung in which the congenital moment is probable from the start should be noted here in particular. First the autopsy and biopsy cases: In Wehn's case tubercular cavities seem more likely. Geri, whose observations were later identified as bronchiectasis by Kartagener, describes "a large cavity" in the left superior lobe. Kartagener's (a) case 4 (autopsy Prof. Uehlinger) showed generalized bronchiectasis of all pulmonary lobes and honeycomb-lung in the left middle lobe; however, the diagnosis is not quite unequivocal due to secondary tuberculization. According to Inghram (cited in Zuckerman and Wurtzbach, the original unfortunately was not available to us) the whole picture gave the impression of a "congenital deformity with persistence of peribronchial connective tissue and underdevelop-
ment of the alveolar structure." The remaining anatomical examiners (cf. especially Oettli and Wegelin) cannot find signs of disturbed development. Findings by Sauerbruch and Lotzing, such as: no important inflammation, complete confusion of elements used in the buildup of bronchial walls, drastically called "pale-pale" by Renault, have not been noted. Dickey's findings will be discussed later.

Clinically, i.e. roentgenologically, pulmonary cysts and honeycomb-lung were noted by:

Perrault ("cystes pulmonaires congenitaux"), Lageze and Duffard (case 2 "voluminous cystic bronchiectasis" lower left), Weill, Lallemant and Leveque ("enorme poche iuxtacardiaque"), Kluge (walnut-sized circular shadow" upper left), Jedlicka and Levinsky ("cystosis pulmonum" in two sisters), Hagen (honeycombs upper left). Even the uncertain cases of Elman, Sonier and Boucher (cf. table) may be mentioned here.

The remaining pathologic-anatomical findings do not deviate from those which are usually found with "commonly acquired" bronchiectasias. The same applies to the clinical picture. Anamnestically the leading symptoms, cough and sputum, can be followed into earliest childhood. Characteristically the histories of these cases often show phrases such as: Cough "immediately after birth" (Siewert), the illness is said to have commenced "on the day of birth" (Kartagener (a), or bronchitis "all his life" (Conway), "cough since birth" (Dickey), or "a toujours toussé" (Jeill et al). But such information is not less rare in other cases of bronchiectasis, even without inversion. The remaining symptomatology: Copious sputum, mouthfuls of expectorations, possibly hemoptysis and relapsing onsets of fever, is completely identical with that of other bronchiectasias.
Even roentgenologically and bronchographically speaking, cases of honeycomb-lung and pulmonary cysts (cf. above) showing the character of congenitalness from the start are quite rare. Frequently — in our case — triangular shadows in the paramediastinal area are reported or depicted as an expression of atelectasis (cf. Kartagener and Horlacher (b). Various authors have tried therefore to interpret bronchiectasis, even in cases with situs inversus, as being the secondary effect of atelectasis, without, however, being able to explain the marked increase in these atelectases, especially in those cases where a factor of predisposition cannot be denied. Elsewhere one of us (Kartagener (c) has exhaustively treated the importance of atelectasis in the genesis of bronchiectasis, considered significant and even dominating by other authors, especially anglo-saxons (e.g. Lander and Davidson, Ogilvie, Andrus, Mullory, Perry and King), and has arrived at the following conclusion: Causally, atelectasis as such is not set above bronchiectasis.

When both changes frequently occur at the same time, they are often coordinated effects of the common cause: Bronchiostenosis. However, there is a reciprocal relationship between bronchiostenosis and bronchiectasis, regardless whether the latter is positioned distally, as is usually the case, or proximally to the bronchiostenosis, i.e. bronchiostenosis may be the cause as well as the result of bronchiectasis. A bronchial wall weakened endogenically or exogenically in its apparatus may lead through collapse of the bronchial wall to collapse of pulmonary parenchyma (atelectasis, cf. bronchial tuberculosis), similarly an infected or toxically damaged bronchial mucous membrane may by increased production and retention of secretion obturate the bronchial lumen and thereby cause atelectasis (cf. postoperative atelectasis). Both conditions: The weakening of the bronchial wall and retention of secretion in the bronchial lumen are met in every bronchiectasis, regardless of genesis. As it is custo-
mary since Legendre and Baily (1844) to consider early childhood bronchiectasis with its accumulation of secretion (due to inadequate respiratory movements or insufficiently vigorous coughing) a frequent cause of atelectases, the more the possibility of secondary genesis of atelectases should be evaluated in already established bronchiectasis.

Aside from other arguments dealt with elsewhere, the frequent findings of atelectasis in the presently discussed case of bronchiectasis with situs inversus as well as in familial bronchiectasias (a report on which is forthcoming in this journal), i.e. in bronchiectasias which were generated on the basis of an idiotypically caused anomaly, is an especially important support of the assumption of secondary atelectasis founded on already existing bronchiectasis.

The findings of Dickey are particularly illuminating in this connection:

During the autopsy of a 14 months old child (case 1) with the complete triad we found a defect of the ventricular septum and transposition of the large vessels with a dilated heart. Right lung collapsed, right principal bronchus collapsed, without cartilage in the posterior wall.

Fig. 1 a. Sch. . . ., 21 year old girl, roentgenogram on 13 Nov 1949. Situs inversus, atelectasis (triangular shadow) lower left. — Fig. 1 b. Same case. Exposure on 21 Dec 1954: Status after resection of the left middle and inferior lobes as well as the right lingula. — Fig. 2. Same case. Bronchogram of the right lung on 20 Feb 1950. — Fig. 3. Same case. Bronchogram of the left lung on 27 Feb 1950.

In case 2 (with atelectasis of the left middle lobe) the histologic examination of the dissected left middle lobe and the inferior segments of the left superior lobe revealed the "absence of muscular and cartilaginous tissue in the majority of the peribronchial regions."
In case 3 (atelectasis of the left middle lobe, lobectomy): "Distinct reduction and destruction of the elastic tissue and smooth musculature in the bronchial wall. Several bronchial cartilages were partially destroyed. The brother of this case (case 4) also was subjected to lobectomy of the atelectatic left middle lobe. Histologic: "Extensive alteration of the pulmonary architecture."

In spite of these marked changes in the bronchial wall, corresponding with Engel's "broncho-malacia" (cf. also Pohl's "tracheo-bronchopathia malacica"), and although within the discussed syndrome "heredity is usually the primary factor or at least the predisposing cause and although it is possible that early development of bronchiectasias is influenced by a developmental shortcoming of the bronchi themselves," Dickey believes that atelectasis precedes bronchiectasis or that bronchiectasis is the result of atelectasis!

A similar role is ascribed to atelectasis by Conway (4 of his own cases, partly with other deformities!), although "a congenital factor may be of importance." On the other hand, Richards rejects the causal importance of roentgenologically proved collapse to the origin of bronchiectasias precisely because of the absence of the other two components of the triade, although in his case the possibility of a postprimary collapse is evident (cf. also Lageze and Buffard).

Blixenkrone-Moller, too, unequivocally favors the secondary nature of atelectasis. In his case the X-ray revealed a basal triangular shadow on the right, representing atelectasis of the right inferior lobe. Bronchoscopic: Mucus in the right bronchus, no compression, no obturation. Lobectomy: No interthoracic adhesions, no middle lobe, no glands, bronchi not compressed, right inferior lobe airless, cylindric dilatation of all bronchi. Histology: Dilatation, especially of the respiratory bronchioles, leukocytes and eosino-
phils in the lumen. Epithelium highly cylindrical, cilia preserved in places, copious lymph follicles in the bronchial wall, resembling an appendix. Alveoli atelectatic, or filled with serum and erythrocytes, no pneumonia, no old blood pigment. The findings are interpreted by Stixenkrone-Moller as congenital, the pulmonary collapse as secondary.

Fig. 4. Same case: Picture of the accessory nasal cavities on 11 Feb 1950: Antro of Hughmore are light, frontal sinuses large. — Fig. 5. Same case. Solid epithelial cords surrounding bronchiectases (280 X).

We may be permitted to point out the similarity to the findings of Whitwell in connection with what he calls follicular bronchiectasis, in which obstruction of the bronchi is found distal to bronchiectasis, however.

Compared to the relatively large amount of material dealing with clinical observations, as listed in the table, the autopsic and especially the biopsic material is quite scanty. Since biopsic findings are superior to autopsic ones in pathogenic clarification of bronchiectasias, we believe to be justified in reporting the following case, which was approached 3 times operatively and which offers other interesting pathogenetic aspects.

Own observation (cited by A. Brunner and Wegmann. The second case of bronchiectasis with situs inversus reported by these authors is identical with the case published by Wernli-Haessig, 1937):

Sch. A., girl, born 1928: First admission to the surgical clinic on 7 Feb 1950. Anamnesis: Parents (not related by blood) and 2 brothers healthy, no pulmonary diseases in the family. As a child had measles, mumps, whooping cough, pneumonia twice. In 1942 angina followed by nephritis. In 1948 appendectomy.

Since childhood persistent cough and copious sputum, evening temperatures, fatigue, no hemoptysis, never TB bacilli. In 1949 the Thurgau-Schaffhaus Sara-
torium at Davos diagnosed bilateral bronchiectasis. The patient is referred for lobectomy.

Findings: Good nutritional condition, paleness, no clubbed fingers. Clinically and roentgenologically situs viscerum inversus totalis. Typical EKG. Plentiful rales over both lungs. Sputum 40-60 cm$^3$ daily, purulent, at times fetid, without tubercle bacilli, without elastic fibers.

Thorax X-ray (Fig. 1): Hilir markings not increased, distinct paracardiac triangular shadow lower left (corresponding to atelectasis of the left inferior lobe or a segment of the inferior lobe.) Coronary waist filled on the right, possibly as a result of lingular atelectasis.

Bronchography (Fig. 2 and 3, oblique exposures) reveals marked bronchiectasis in both lingular segments on the right. Left lung (Fig 3) bronchiectasis in the region of the inferior and middle lobes.

The rhinologic examination at the Otolaryngologic Polyclinic (Prof. Ruedli) gave no evidence of sinusitis, no polyposis nasi. On the X-ray film (Fig. 4) the accessory nasal cavities are light, the frontal sinuses large.

On 8 Mar 1950 lobectomy of the left middle lobe and resection of the lower segments of the right inferior lobe were accomplished (Prof. A. Brunner). No significant malformations in the pleura. Basal segments of the left inferior lobe as well as the middle lobe are quite extensively atelectasic. Resection of the basal segment of the inferior lobe, closure of the bronchial stump. Extirpation of the left middle lobe. Coverage of bronchial stumps with a pedunculated flap of the pleura parietalis.

The apical segment of the left inferior lobe is twice the size of a fist and almost completely fills the cavity in the inferior lobar area. Rubber tube to the pleural cavity, instillation of penicillin, stratified closure of the wound. In the dorsal position Monaldi’s catheter in the first IAR in front.
Postoperative progress without complications (penicillin aerosol).

The histologic examination of the resectional preparation resulted in the following findings: Fairly well developed pulmonary tissue with numerous cylindrical, sacular and fossulate bronchi. The bronchiectasis in the majority is without cartilages. The bronchial walls are strongly reinforced and the mucous membrane considerably folded. The epithelial lining consists primarily of single or multiple layers of ciliated epithelium, partly of multiple layers of pavement epithelium. The tunica propria is strongly thickened, vascularized almost angiomatously, and showing dense lymphoplasmacellulare infiltration, partly with follicular accumulation. The tunica propria is outwardly connected to the muscular layer, which is settled by radial vascular loops. The muscular layer, without sharp demarcation, leads into a covering layer with collapsed alveoli. These are lined largely with a single layer of pavement epithelium. Sporadically, larger solid epithelial buds are found, surrounded by connective tissue with lymphoplasmacellular infiltration (Fig. 5). The interlobular septa show a slightly edematous loosening. The vessels do not show marked intimal thickening.

On 24 Nov 1950 a right lingulectomy was effected (Prof. Brunner). The pleura was free. Lingula slightly larger than a thumb, brown-red (Fig. 6). Remaining lung a pale pink, inflates very nicely. Ligature of arteriae and venae, clamping and severance of the bronchus. Provision of the slightly over 1 c long bronchial stump. Coverage with a freely transplanted pleural flap, stratified closure of the wound.

Fig. 6. Same case. Dissected lingula. — Fig. 7. Same case. Cut through the lingula: Numerous irregularly formed tongues of cartilage, plentiful mucous glands. Mucous membrane thickened, folded.
The histologic examination of the dissected lingula (Fig. 7) reveals numerous bronchiectases in immediate proximity. The tongues of cartilage are irregularly formed, partly at angles to each other, slightly bent, unequally thick. The mucous membrane is thickened and folded everywhere. For the most part it carries a multi-row, single layer ciliated epithelium, seldom multi-layer, single row. No pavement epithelium can be found. Between epithelium and tongues of cartilage and between the individual tongues there are massive deposits of mucous glands.

Postoperative progress was satisfactory in the sense that a distinct decrease in the amount of sputum occurred. Coughing persisted, however, as did the secretion of yellowish-green, rather foamy sputum.

A control bronchography on 8 Nov 1954 (Fig. 8 and 9) revealed unmistakable bronchiectases in the apical segment of the left inferior lobe.

On 2 Dec 1954 segmental resection of the remaining apical segment of the left inferior lobe was accomplished (Mully). The lung was completely fused with the parietal pleura, the apical segment of the inferior lobe was not atelectatic, saccular bronchiectases were well palpable. The segment was severed. The vessels were found in the interlobar fissure, they were callously fused with lymphatic glands. The bronchi were severed peripherically and the segment removed, the the apical segmental bronchus leading to the trunk was found, isolated, severed and closed after Klinkenbergh. Coverage with mediastinal pleura and lymphatic glands. Superior lobe emphysematous, fills the entire pleura. Vena azygos is situated on the left, no anomalies of the heart and the pericardium. Bronchial arteries enlarged but not pathologically changed.

The dissected, fixed resectional preparation can be seen in Fig. 10. Above all it shows 3 strongly distended bronchi with greyish-white surrounding mantles of tissue, in places up to 1-2 mm thick.
Histologically speaking, the distention in the peripheric bronchial sections also amounts to many times that of the norm. Thus the corresponding pulmonary arteries are about 1/20 narrower than the bronchi. The epithelium generally consists of a multi-row ciliated epithelium. The cilia can still be recognized. The epithelium, however, is rather strongly permeated by lymphocytes and plasma cells, in part also by polymuclear leukocytes with short gaps in the epithelial cover.

In close proximity there are broad mantles of tissue, which are densely infiltrated by lymphocytes. Centers of reaction are distinctly recognizable (cf. Fig. 11). But here, too, infiltrations by polymuclear lymphocytes are seen in places. Finally there follow cuffs of connective tissue, radiating like fingers into the bordering pulmonary tissue. The latter has alternatively wide alveoli, septa usually narrow. But here, too, small star-shaped scars appear.

Fig. 8. Same case. Bronchogram of the apical segment of the left inferior lobe on 8 Nov 1954. — Fig. 9. The same, oblique exposure. — Fig. 10. Same case. Apical segment of the left inferior lobe, fixed and dissected.

Mantles of connective tissue are especially distinct in the medium-sized bronchi. On the other hand, infiltrations of lymphocytes decrease. Here the epithelium shows distinct metaplasia of pavement cells (cf. Fig. 12). Cartilages are rare, muscle fibers also are quite scanty. The elastic fibers are severely splintered and preserved only in small bunches or in the form of islands (cf. Fig. 13). The larger bronchi still show a distinct ciliated epithelium. Cartilages are well recognizable here, but slightly separated. Bundles of muscle fibers are also distinct. The elastic fiber system is rather meagre (cf. Fig. 13).
Further postoperative progress was satisfactory in every way. The thorax X-ray film on 21 Dec 1954 (Fig. 1 b) still shows a small residual effusion in the left sinus. The left superior lobe is well inflated and fills the entire pleural cavity.

In short summary, the medical history of our patient, 22 years old at the time of first admission, reveals the classic symptomatology of bronchiectasis: Cough and sputum since childhood, subfebrile temperatures of long duration, two pneumonic attacks as well as "traditional pneumopathies" (Marquezy and Renaut) in the anamnesis. Frank broncho-blennorrhea. Acoustics: Expansive bilateral bronchitic syndrome. Bronchography revealed bronchiectases (Fig. 2 and 3); on the right side a diffuse distension of the superior and inferior lingular segment, no certain bronchiectasis in the inferior lobe, on the left side diffuse, cylindrical bronchiectases in the left inferior and middle lobes with moderate shrinkage of the inferior and middle lobes. The superior lobar bronchi rather stretched out. In addition situs viscerum inversus totalis. However, the triad is incomplete due to the absence of involvement of the accessory nasal cavities. Frontal sinuses and processi mastoidei are well pneumatized. Further, on the negative side, the absence of clubbed fingers is remarkable.

Within 4½ years the patient is three times subjected to thoracotomy: In the first operation on 8 Mar 1950 the left middle lobe and the lower segment of the left inferior lobe are dissected, on 13 Nov 1950 right lingulectomy is effected, in the third operation on 2 Dec 1954, i.e. at age 26, resection of the left apical inferior lobar segment is accomplished.

Histologic examination of the extirpated lobes and segments revealed no direct evidence in favor of congenitalness, nor did it support the acquired nature of bronchiectasis; in particular, no intra, endo or exo-bronchial
causes of roentgenologically and biopsically diagnosed atelectasis could be determined. Only the increased and irregularly ordered cartilaginous plates, and possibly the uncommonly numerous mucus glands in Fig. 7 could be admitted to a certain degree as an expression of "dysembryoplasia." On the other hand, the proliferations of the epithelium (Fig. 5), which for Garnier is a sign of the congenital origin of bronchiectasis, should not be evaluated in this sense. They are of frequent occurrence in inflammatory changes of different genesis in various parenchymatous organs (cf. Oudendal, Pagel, Planchu, Policard and Galy), F. Muller has mentioned them in connection with bronchiectasis as early as 1907.

On the other hand, the severe inflammatory alterations connected with bronchiectasias should not be interpreted to mean that the inflammation is the cause and the dilatation its result. Even assuredly congenital, connatally occurring bronchiectasias will quite naturally be infected in the course of life or — as put by Debre and Gilbrin — will disinfect themselves with great difficulty and will reveal correspondingly severe inflammatory changes.

Fig. 11. Same case. Apical segment of the left inferior lobe, dense infiltration by lymphocytes with follicular accumulation and centers of reaction in the tunica propria. — Fig. 12. Same case. Metaplasia of pavement cells in bronchiectasis. — Fig. 13. Same case. Elastica stain.

Special attention is due in our case to the bronchiectases in the apical segment of the left inferior lobe, which made the third operation necessary. We believe ourselves justified in assuming, on the basis of the first broncho-ography and especially on the basis of the histologic changes in the preparation of the last (third) resection, that the bronchiectases were already present at the time of the first hospitalization of the patient. Nevertheless the question of postoperative development of bronchiectases in previously healthy bronchi must be aired. Unequivocal observations of this type have been made several
times (cf. among others Brunner, Nally, Crollin, Lehman, Katon and Curry).

Even in cases with situs inversus, postoperative bronchiectases in segments and lobes previously proved healthy by means of bronchography have been reported by Di Rienzo: The left middle lobe of a 15 year old girl with a complete triad was dissected because of bronchiectasis. The other bronchi, "very closely studied," were normal. A few months later "bronchiectases of the alveolo-agenetic type, which generally are considered congenital" were found in the right inferior lobe and the lingula. In the right inferior region a paracardial, triangular shadow had appeared. According to Di Rienzo these findings proved that the bronchiectases, "which accompany inversion of the thoracic viscera, can regenerate themselves within a short time during life, and that the genesis of bronchiectasias is associated with a bronchial functional syndrome. Stutz and Viiten interpret these findings of Di Rienzo as well as their own observations of minor bronchiectasis in the left inferior lobe, which "obviously had developed only in childhood," in a 14 year old boy with situs inversus and polyposis nasii, as idiopathic bronchiectasis in the sense of Bard. Without mentioning Bard, Segalin also believes in a "morphologically indeterminable disposition." In a quite general way postoperatively diagnosed bronchiectasias remind of Policard and Galy's "bronchiectasies en puissance." Recently Cooley, Ginsburg, Olsen, Kirklin and Clagett tried to explain the frequency of postoperative bronchiectasis in children (16.6%) by the fact that development of the lung and with it, of bronchiectasis, is not yet completed in childhood.

Since to our knowledge bronchiectasis has not been proved in newborn with situs inversus, and no anatomical findings (with the possible exception of the observations of Ingraham) on the roentgenologically diagnosed development of cysts and honeycombs in situs inversus intra vitam are available, the consequential result of the examinations, even the anatomical ones, is this:
It is impossible to differentiate bronchiectasis with situs inversus from "common" bronchiectasis found in the autopsic and biopsic material. Taiana, Villegas and Schiepatti also stress the curious fact that pathologic-anatomical findings of the resection specimen in their case could not be differentiated from those of "common bronchiectasis of the acquired type."

And yet one cannot doubt an endogenically or idiotypically caused predisposition to bronchiectasis on the basis of extra-pulmonary findings: Situs inversus, involvement of the accessory nasal cavities, frequent simultaneous deformities and conspicuous familial occurrence. From this factor of predisposition ("defaut original" or "malformation en puissance" of Bard) during the course of life, gradually but irresistibly, the disease of bronchiectasis itself may develop without intervention of an inflammatory or mechanical cause (idiopathic bronchiectasis Bard). In other cases (Churchill, Ferrand et al) the development of bronchiectasis must be ascribed to an inflammatory-infectious genesis, similar to the origin of inflammations of the accessory nasal cavities. However, a constitutional anomaly must be held responsible for the persistence and the progression of the inflammation. Olsen, too, presupposes a "deformity of the bronchial trunk as a prime factor" and a release by exogenous moments (obturation, atelectasis and bronchial infection), consequently "congenital and acquired components" of bronchiectasis in his 14 cases of bronchiectasis with situs inversus. Likewise Karani speaks of a congenital defect of the bronchial wall, "perhaps aided by chronic infection." This form of bronchiectasis Kartagener (c) calls "bronchiectasias of mixed etiology" or, paraphrasing an expression of Volharda, endogenically caused, exogenically effected bronchiectasias.

All three possibilities of not acquired bronchiectasis: Congenital bronchiectasis in the proper sense, idiopathic bronchiectasis (Lard) and bronchiectasis
of mixed etiology consequently are realized in bronchiectasias with situs inversus. No anatomical verification exists as yet for the first form. The two last mentioned forms (idiopathic and bronchiectasis of mixed etiology), while they cannot be differentiated from acquired bronchiectasias either clinically, roentgenologically, bronchographically or anatomically, must nevertheless be postulated, on the ground discussed above in detail. This point of view, which shifts its center of gravity to extrapulmonary and even extra-individual considerations, shows many cases of seemingly acquired bronchiectasis, even with situs solitus, in an entirely new light. The pathogenetic relativity of atelectasis, genuine bronchial stenosis, and bronchiectasis, as well as their possible reciprocity are especially illuminated thereby.

SUMMARY

Detailed description of a case of bronchiectasis and situs inversus with reference to the complete bibliography and discussion of the pathogeny of the triade of Kartagener.