Inherited factors in diffuse bronchiectasis in the adult: a prospective study

F. Verra, E. Escudier, J. Bignon, M.C. Pinchon, M. Boucherat, J-F. Bernaudin, H. de Cremoux

ABSTRACT: To evaluate the prevalence of inherited respiratory ciliary structure and underlying mucus abnormalities in the diffuse bronchiectasis syndrome, we investigated 53 subjects comprising 38 patients with diffuse bronchiectasis confirmed by high-resolution thoracic computed tomography, ten with chronic bronchitis and no diffuse bronchiectasis and five healthy nonsmoking control subjects. The clinical history was determined by means of a standardized questionnaire. Axonemal abnormalities of respiratory cilia were evaluated on bronchial or nasal mucosa samples by transmission electron microscopy (structure) and stroboscopic observation (function). Cystic fibrosis (CF) and Young's syndrome were detected by means of the sweat test and semen analysis when male infertility was suspected.

Among the 38 patients with diffuse bronchiectasis, a primary ciliary dyskinesia (PCD) was detected in five (13%) with a high proportion (range: 55-100%) of cilia showing axonemal ultrastructural abnormalities always involving the dynein arms. The prevalence of this inherited condition was higher in North African (36%) than in European patients (4%) (p<0.01). After exclusion of the five patients with PCD, the patients with diffuse bronchiectasis showed axonemal ultrastructural abnormalities similar to those with chronic bronchitis.

The diagnosis of underlying mucus disorders was based on two types of criterion, i.e. for CF, sweat chloride levels >80 mmol·l⁻¹, or the combination of diagnostic criteria proposed by Stern et al. Respectively, five (three Young's syndrome and two CF) and seven (one Young's syndrome and six CF) cases of inherited mucus disorders were suspected.

Our results showed that PCD was highly prevalent among the adult North African patients with diffuse bronchiectasis but relatively rare in the Europeans.

Keywords: Adult cystic fibrosis; diffuse bronchiectasis; inherited disorder; primary ciliary dyskinesia; Young's syndrome.

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Bronchiectasis is defined on a pathological basis, as an abnormal, irreversible dilatation of the bronchial tree [1]. A large spectrum of etiological factors such as infectious insults during post-natal growth of the lung and genetic conditions are thought to induce the diffuse bronchiectasis syndrome.

Primary ciliary dyskinesias (PCD) form a group of genetic diseases characterized by ineffective ciliary beating [2-5]. In such disorders the absence of dynein arms is one of the main axonemal ultrastructural abnormalities (AUA). Kartagener's syndrome, associating situs inversus, diffuse bronchiectasis, pansinusitis and male infertility, is the classic clinical form of PCD and is observed in 1-4% of patients with diffuse bronchiectasis [6]. However, situs inversus is rare among Polynesian subjects [7] but common in Caucasian [3] patients with documented PCD, illustrating the heterogeneity of PCD and the difficulty of detecting such a syndrome on a clinical basis. Up to now, only one study has attempted to evaluate the prevalence of AUA in a series of consecutive patients with diffuse bronchiectasis. All were Polynesians and a lack of dynein arms was observed in every case; the authors concluded that such axonemal ultrastructural abnormalities were involved in the pathogenesis of diffuse bronchiectasis in this population [7].

Diffuse bronchiectasis has also been reported among adult males and females with an underlying mucus disorder. In males, obstructive azoospermia associated with diffuse bronchiectasis is suggestive of either Young's...
syndrome (normal sweat test) or an adult variant of cystic fibrosis (CF) (high sweat chloride levels) [8–13]. However, the differential criteria forwarded to distinguish between adult CF and Young's syndrome are debatable. In contrast to CF, a hereditary predisposition to Young's syndrome has not yet been demonstrated. There are several lines of evidence suggesting that the different CF subsets may result from several mutations [13–16]. In this regard, the recent discovery of a point deletion responsible for most classic forms of CF is of great importance [17–19]. However, in spite of recent advances in our knowledge of underlying disorders [2–5, 8–13] such as PCD, Young's syndrome, adult CF, alpha-antiprotease deficiency and hypogobulinaemia, the actual incidence of such aetiological factors has not yet been prospectively evaluated in adult patients with diffuse bronchiectasis. We thus investigated a series of patients with suspected diffuse bronchiectasis in order to evaluate the prevalence of underlying conditions and their role in the genesis of diffuse bronchiectasis.

**Methods**

**Study population**

**Patients.** From January 1987 to December 1988, 48 consecutive adult out-patients were included in the study. All were referred by their general practitioners to our chest department for the investigation of chronic sputum production. After chest X-rays and clinical examination, patients were included if diffuse bronchiectasis was suspected. Apart from two patients with situs inversus and two others with previously documented male infertility, none of the patients had a clinical or family history suggestive of an inherited disorder. Thirty five patients from Europe and 13 from North Africa were studied.

**Controls.** Five healthy nonsmoking European adult volunteers (age: 28±5 yrs) with no history of chronic or current sputum production were included as controls.

**Clinical investigations**

Clinical histories, i.e. acute respiratory tract infections in early childhood, age at onset of chronic bronchial symptoms, daily amount of sputum production, past and present smoking habits, suspicion of male infertility (absence of conception after at least 2 yrs of unprotected sexual intercourse), were taken using a standardized questionnaire.

**Radiology.** High-resolution thoracic computed tomography (1.5 mm thick sections and 10 mm intervals) was used to detect bronchiectasis [20]. The findings were interpreted independently by two researchers and the diagnosis was established according to the criteria described by NAIDICH et al. [21]. Two criteria were required to classify the bronchiectasis as diffuse: 1) bilateral process; 2) 4 of 6 distinct lung areas involved (the three lobes of the right lung, the left lower lobe, the lingula and the culmen). No clinical history or chest X-ray findings suggestive of past tuberculosis or bronchial obstruction were observed in this series of patients. Radiographs of the paranasal sinuses were obtained in every case.

**Pulmonary function tests (PFT).** The vital capacity and forced expiratory volume in one second were measured by means of spirometry (PK Morgan spirograph) and total lung capacity by helium dilution. Results were expressed as a percentage of the predicted values [22].

**Ultrastructural and functional studies of respiratory cilia**

Bronchial mucosa samples were obtained by brushing or biopsy during routine fibroscopic examination performed under local 2% lidocaine hydrochloride anaesthesia (Xylocaine, Roger Bellon). When this procedure was not indicated or when bronchial samples were not adequate, specimens from the inferior nasal turbinate were obtained under local 5% lidocaine with naphthazoline anaesthesia (Xilocaine with naphthazoline, Roger Bellon) as described previously [23, 24].

**Ultrastructural analysis**

Samples for transmission electron microscopy were fixed in 2.5% glutaraldehyde 0.045 M cacodylate buffer, pH 7.4, for 2 h at 4°C. They were then post-fixed in OsO₄ and processed routinely. Ultra-thin sections were studied with a final magnification of 60,000. At least 30 transverse sections through the body of ciliary shafts of different cells were examined in each specimen. Internal axonemal structure was studied using a quantitative method [24, 25]. Briefly, dynein arms, radial spokes and nexin links were considered to be absent from sections if the structure was missing from at least 6 of the 9 peripheral doublets. In order to facilitate the definition of axonemal abnormalities, the radial spokes and nexin links were combined under the term "peripheral junctions". The central structures (central microtubules and central sheath) were termed the "central complex". The numbers of cilia with abnormal axonemal ultrastructure were expressed as a percentage of the number of cilia examined.

**Ciliary beat frequency.** The ciliary beat frequency was measured by means of stroboscopic illumination of ciliated epithelial cells maintained in tissue culture medium (IP 199, Eurobio France) at 37°C for 1–5 h [26]. After estimating the proportion of motile cilia in each sample, measurements were made at room temperature on at least three different areas of bronchial or nasal samples. Beat frequency was expressed in hertz (Hz) as the mean of the measurements. The presence of ciliated cells was confirmed by centrifuging the cell suspensions at 500 rpm for 10 min, then staining with
May-Grünwald-Giemsa and Wright’s method and examining them under a light microscope.

Evaluation of other underlying factors

Serum alpha-1-protease inhibitor (concentration and isoelectric focusing phenotype), and immunoglobulin concentrations were assessed in every case. The sweat test of Gibson and Cooke [27] was also performed systematically: chloride levels >80 mmol·l⁻¹ in duplicate tests were considered diagnostic for CF. Semen analysis was only proposed in cases of clinically suspected male infertility. Criteria defining Young’s syndrome were: 1) azoospermia; 2) absence of significant AUA; and 3) sweat chloride level <80 mmol·l⁻¹ [8, 9]. As differential criteria between CF and Young’s syndrome are debatable, CF was also diagnosed on the basis of a previously proposed combination of diagnostic criteria [28].

Data analysis

Data are expressed as mean±SEM. Comparisons between patient groups were made using the Mann-Whitney test, Chi² test and analysis of variance (ANOVA). The Spearman rank correlation was used to assess inter-observer variations in evaluating the number of involved lung segments.

Results

Demographic and clinical data (table 1)

Patients were separated in two groups according to computed tomography findings (fig. 1), as follows: diffuse bronchiectasis group (n=38 patients; 27 Europeans; 11 North Africans) and bronchitis group (n=10 patients with no computed tomography evidence of diffuse bronchiectasis, 8 Europeans; 2 North Africans). No significant difference was observed between the two observers with respect to the type and presence or absence of bronchiectasis. Moreover, the assessment of the number of involved lung segments by the two observers was well correlated (r=0.83; p<0.01). Infertility was suspected in 10 of the 21 evaluable male patients with diffuse bronchiectasis and was more frequent in the North Africans (6 out of 7) than in the Europeans (4 out of 14) (p<0.02).

Table 1. - Demographic, functional and clinical data

<table>
<thead>
<tr>
<th></th>
<th>DBS group n=38</th>
<th>Chronic bronchitis</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Cryptogenic n=28</td>
<td>PCD n=5</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male patients n</td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td>Age yrs</td>
<td>47±3</td>
<td>46±4</td>
</tr>
<tr>
<td>Age at onset of chronic symptoms yrs</td>
<td>21±3</td>
<td>17±5</td>
</tr>
<tr>
<td>Past smoking habits pack-years</td>
<td>7±3</td>
<td>31±10</td>
</tr>
<tr>
<td>Early respiratory infection n</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Daily sputum production ml</td>
<td>25±3</td>
<td>50±6</td>
</tr>
<tr>
<td>AUA mean %</td>
<td>10±1</td>
<td>80±7†</td>
</tr>
<tr>
<td>Male infertility n</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Sinus X-ray changes n</td>
<td>16</td>
<td>5</td>
</tr>
<tr>
<td>Number of involved segments</td>
<td>13±1</td>
<td>17±0.9†</td>
</tr>
<tr>
<td>Cylindrical + varicose / cystic bronchiectasis</td>
<td>15/13</td>
<td>2/3</td>
</tr>
<tr>
<td><strong>PFT data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TLC %</td>
<td>80±4</td>
<td>85±7</td>
</tr>
<tr>
<td>FVC %</td>
<td>73±5</td>
<td>64±11</td>
</tr>
<tr>
<td>FEV₁ %</td>
<td>57±6</td>
<td>35±11</td>
</tr>
<tr>
<td>Pao₂ mmHg</td>
<td>77±3</td>
<td>60±3*</td>
</tr>
</tbody>
</table>

DBS: diffuse bronchiectasis syndrome; Cryptogenic: DBS without demonstrable inherited origin; PCD: pulmonary ciliary dyskinesia; IMD: inherited mucus disorders; AUA: axonemal ultrastructural abnormalities; PFT: pulmonary function test; TLC: total lung capacity; FVC: forced vital capacity; FEV₁: forced expiratory volume in one second; Pao₂: arterial oxygen tension. Significance versus cryptogenic DBS: †: p<0.05; ††: p<0.005 (Mann-Whitney test).
Ciliary disorders

Axonemal study. The ciliary ultrastructure and beat frequency studies were done on bronchial samples from 34 bronchiectasis patients and on nasal samples from the remaining four and on bronchial samples from 8 chronic bronchitis patients and on nasal samples from the remaining two. Bronchial samples from all of the healthy volunteers were studied.

Quantitative ultrastructural changes (fig. 2 and table 1). The mean number of transverse ciliary sections studied in the healthy control group was 227±56 (range: 65–376). The mean number of AUA in this group was 0.7±0.2% (range: 0–1%). Among the 38 patients with diffuse bronchiectasis, the mean number of sections studied was 123±11 (range: 15–331); a mean of 18.9±4.2% (range: 1.7–100%) ciliary abnormalities was found. The distribution of AUA is shown in figure 2: five patients had a high percentage of AUA in bronchial samples (range: 55–100%). The remaining 33 had a percentage of abnormalities (9.2±1.2%; range: 1.7–24%) similar to that in the bronchitis group (10.7±3.6%; range: 0–33%). These percentages were significantly higher than in the controls (p<0.005 and p<0.025, respectively). When the percentage of AUA in bronchial samples was compared in terms of smoking habits, after exclusion of the five patients with a high percentage of abnormalities, nonsmokers with diffuse bronchiectasis had a smaller proportion of abnormalities (5.23±1.5%) than smokers with either diffuse bronchiectasis (14.4±2.1%; p<0.005) or chronic bronchitis (16±3.8%; p<0.025).

Qualitative ultrastructural changes (table 2). Defects in the dynein arms (always involving the outer arms) were the predominant changes in patients with high percentages of AUA. Patients with low percentages of AUA showed heteromorphic defects. It is noteworthy that, after exclusion of the dynein arm defects, quantitative and qualitative changes were similar between the patient groups.

Table 2. Mean percentage of cilia with qualitative axonemal ultrastructural abnormalities

<table>
<thead>
<tr>
<th></th>
<th>Central complex</th>
<th>Peripheral junction</th>
<th>Peripheral microtubules</th>
<th>Dynein arms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Central microtubules</td>
<td>Central sheath</td>
<td>Radial spokes</td>
<td>Nexin links</td>
</tr>
<tr>
<td>Cryptogenic</td>
<td>2.65</td>
<td>2.79</td>
<td>0.39</td>
<td>0.98</td>
</tr>
<tr>
<td>PCD</td>
<td>4.7</td>
<td>1.3</td>
<td>0</td>
<td>12.3</td>
</tr>
<tr>
<td>IMD</td>
<td>2.6</td>
<td>2</td>
<td>0.66</td>
<td>0.88</td>
</tr>
<tr>
<td>CB</td>
<td>5.06</td>
<td>1.22</td>
<td>0</td>
<td>2.62</td>
</tr>
<tr>
<td>p</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

n: total number of ciliary transverse sections examined in each patient group; Cryptogenic: diffuse bronchiectasis syndrome without demonstrable inherited origin; PCD: primary ciliary dyskinesia; IMD: inherited mucus disorders; CB: chronic bronchitis; ns: nonsignificant.
Ciliary beat frequency. The ciliary beat frequency in the controls and the patients with bronchiectasis were similar, ranging between 8.7-13 and 8-9.8 Hz, respectively. The mean ciliary beat frequency in PCD patients was low (5.1±2.4 Hz) with wide inter-individual variations. No ciliary beat was detected in the two patients (one with Kartagener's syndrome) with 100% of AUA; three patients (one with Kartagener's syndrome) had a beat frequency within the normal range (9.1-11.1 Hz), despite high levels of AUA (range: 55-77%). All four male patients with PCD-associated disorders had clinically suspected infertility, documented by immotile spermatozoa in two cases.

Primary ciliary dyskinesia syndrome and geographic origin. It is noteworthy that PCD-associated disorders were more frequent in the North African (4 out of 11) than in the European patients (1 out of 27, p<0.01).

Mucus disorders

According to the above criteria, in the bronchiectasis group there were three male patients with Young's syndrome (32, 49 and 59 yrs old, all with a characteristic clinical scrotal examination) and two patients with CF (a 45 yr old male patient with a normal scrotal examination including a palpable vas deferens, and a 46 yr old female patient). In two other patients (75 and 59 yrs old) with sweat chloride levels <80 mmol/l and a history consistent with infertility, no definitive diagnosis could be made because they refused semen analysis. Using other criteria [28], CF was diagnosed in four additional cases, corresponding to two patients in the "Young's syndrome" group (both had chronic Pseudomonas aeruginosa bronchial infections and one had 70 mmol/l sweat chloride) and two in the "unexplained diffuse bronchiectasis" group (both had chronic Pseudomonas aeruginosa infection and borderline sweat chloride levels of 70 and 68 mmol/l).

Mucus disorders and geographic origin. Whatever the criteria used, the North Africans (1 out of 11 or 2 out of 11) and Europeans (4 out of 27 or 5 out of 27) were affected at similar rates by these inherited mucus disorders.

Hypogammaglobulinaemia and low alpha-1-antiprotease levels

No patient with bronchiectasis in this series had hypogammaglobulinaemia and no major quantitative alpha-1-antiprotease defect was observed (2.18±0.1 g/l; range: 1.13-3.91 g/l; normal range for M-phenotype subjects: 1.9-3.5 g/l). The phenotypes were mostly M, with six exceptions (MS: five cases; ML: one case).

Clinical implications of underlying factors

With the exception of male infertility and situs inversus, no difference was observed between the patients with demonstrable inherited disorders with regard to the rate of early acute respiratory tract infections, age at onset and sinus abnormalities in patients with bronchiectasis (table 1). There was a trend toward poorer PFT results in patients with PCD relative to those with unexplained diffuse bronchiectasis (only significant for arterial oxygen tension (Pao2); a history of heavy smoking was observed in patients with PCD (table 1).

Moreover, the number of involved lung segments was higher in patients with PCD (n=17±0.9) and in those with underlying mucus disorders (n=18.2±0.7) than in patients with unexplained diffuse bronchiectasis (n=13.1±0.7; p<0.01 for both comparisons).

Discussion

Although rare in Western countries, bronchiectasis is a common disabling disease in other populations. In this study we attempted to assess the prevalence of underlying conditions (PCD, CF, Young's syndrome, hypogammaglobulinaemia and major quantitative alpha-1-antiprotease defect) responsible for this so-called "orphan disease" [6]. Ultrastructural studies of cilia and semen analysis are mandatory to assess the prevalence of such conditions. The sophisticated and time-consuming nature of techniques such as electron microscopy, and the fact that semen analysis is often declined by this typically middle-aged population may explain why so few studies of the frequency of such aetiological factors have been performed. In the present work 48 patients with chronic sputum production and suspected of having diffuse bronchiectasis were investigated by means of thin-section computed tomography. Using this sensitive and accurate method [20], 38 patients were found to have diffuse bronchiectasis, and a congenital ciliary or mucus defect was detected in ten of these (26%), comprising five patients with PCD (most prevalent among North African subjects) and five with an inherited mucus disorder (no ethnic difference). It is interesting to note that, despite a careful study based on available criteria, the majority of the cases of bronchiectasis (28 out of 38) remained cryptogenic. Unrecognized underlying conditions affecting the entire respiratory mucosa may be present in these patients.

Clinical implications of inherited disorders

There was a trend toward poorer PFT results and a more extensive process in patients with PCD or mucus disorders compared to subjects with unexplained diffuse bronchiectasis. This feature in PCD patients contrasts with previous observations of mild and stable disease in similar cases [3, 29]. However, in this series the relationship between poor respiratory status and PCD is unclear, since the two groups of patients were also different in respect of smoking history, socioeconomic status and geographic origin.
Ciliary abnormalities

We found five patients (two with Kartagener's syndrome) with more than 50% of abnormal cilia, associated with a lack of outer dynein arms in every case. Previous studies have suggested a genetic basis for such AUA, identical to those found in other species [30,31]. Moreover, similar changes in axonemal ultrastructure have been observed in Kartagener's syndrome and familial PCD-associated disorders. A lack of dynein arms is the most common defect associated with PCD [2-4, 24, 25, 32-37]. The other AUA observed in this series was mild and diverse, suggesting an acquired nature [37]. Our data suggest that tobacco plays a role in the genesis of acquired AUA, since smokers without PCD had a higher rate of such abnormalities than corresponding nonsmokers. The ciliary beat frequencies (measured at room temperature) were somewhat lower in our study than in others [3,4,23,37,38]; local anaesthesia [39] and in particular ciliary beat frequency temperature-dependence may account for this.

Indeed, the frequencies that we observed are similar to those generally obtained at room temperature [40-42]. Moreover, our inclusion of control subjects permitted accurate inter-group comparisons. The stroboscopic method is, in our experience, somewhat disappointing: the observed beat frequency was normal in three patients despite high degrees of AUA. However, in Kartagener's syndrome, there is a wide intra-individual and inter-individual range of beat frequency [3,4,26,32-37]. Other approaches such as the microphoto-oscillographic technique [35], video motion analysers [36] and laser light-scattering spectroscopy [38] might be helpful for detecting more subtle qualitative changes in ciliary motion such as asynchrony and abnormal wave shapes.

PCD was unusual in the European subgroup (3.7%) but common in the patients from North Africa (36.4%). This higher prevalence of PCD, although not previously reported, may reflect the well-known high degree of consanguinity in part of the Moslem Magreb population which would tend to exacerbate the expression of what is probably an autosomal recessive disorder [3]. However, differences in the prevalence of one or several abnormal genes can not be excluded. This finding, like the observation by Warne et al. [7] concerning New Zealand Polynesians, highlights the need to focus on ethnic factors in such studies.

Mucus disorders

In this series, using two different sets of criteria for the diagnosis of inherited mucus disorders, we observed particularly wide discrepancies in the recognition of adult CF. Our data confirm that, in populations of adult patients with diffuse bronchiectasis, Stern's criteria are more effective in identifying CF patients than is the standard sweat test. However, the accuracy of this combination of criteria is open to criticism and requires confirmation by comparison with an unambiguous diagnostic test. Unfortunately, other procedures which assess chloride channel function, e.g. bioelectric potential difference measurement, have not been extensively used or validated in such borderline adult syndromes [40]. Our results, thus, emphasize the lack of well-defined limits between Young's syndrome, adult CF and some types of so-called unexplained diffuse bronchiectasis. The hypothesis that a subset of CF may correspond to Young's syndrome is also supported by a recent report of relatively low sweat chloride levels, late onset, and mild respiratory impairment among CF patients characterized by normal pancreatic function and lacking the common mutation (A F508) [43]. Taken together, these findings suggest that, in the absence of differential criteria, adult CF and Young's syndrome should be combined within an "adult mucus disorder syndrome". Better understanding of the mechanism(s) underlying bronchial and seminal mucus abnormalities in adult patients with CF and Young's syndrome and/or the identification and analysis of the gene(s) involved will permit the separation or unification of CF and Young's syndrome and help to identify "Young's syndrome" in female patients with diffuse bronchiectasis.

References


Facteurs héréditaires dans les bronchiectasies diffuses de l'adulte: une étude prospective. F. Verra, E. Escudier, J. Bignon, M.C. Pinchon, M. Boucherat, J.F. Bernaudin, H. de Cremoux. RÉSUMÉ: Afin d'apprécier la prévalence des anomalies sous jacentes responsables du syndrome de dilatation diffuse des bronches (DDB), nous avons étudié 38 patients atteints de DDB authentifiées par tomodensitométrie en haute résolution, 10 patients atteints de bronchite chronique obstructive sans DDB et 5 sujets sains non fumeurs. Les données cliniques ont été recueillies par un questionnaire standardisé. Les anomalies ultrastructurales des cils ont été appréciées par microscopie électronique et leur fonction par un système stroboscopique. Les maladies génétiques du mucus (mucoviscosidose et syndrome de Young) ont été recherchées par un test à la sueur et un spermogramme était recommandé en cas de suspicion clinique de stérilité masculine.

Parmi les 38 patients avec DDB, 5 (13%) étaient atteints d'un syndrome de dyskinésie ciliaire (avec dans tous les cas un haut pourcentage (55–100%) de cils atteints d'anomalies ultrastructurales indépendant dans tous les cas les bras de dynastine. Cette affection était plus fréquente parmi les sujets nord-africains.
(36%) que chez les européens (4%) (p<0.01). Après exclusion de ces 5 syndromes de dyskinésie ciliaire, on a observé que les anomalies ultrastructurales étaient identique en cas de DDB et de bronchite chronique.

Concernant la diagnostic des maladies sourcées du mucus, deux types de critères ont été appliqués (soit une concentration en chlore supérieure à 80 mmol·L⁻¹ de sueur soit un faisceau d'arguments proposé par Stern). Ainsi respectivement 5 (3 Young et 2 mucoviscidoses) ou 7 (1 Young et 6 mucoviscidoses) cas de maladie congénitale du mucus ont pu être suspectés.

Ainsi cette recherche systématique des facteurs génétiques responsables de DDB souligne l'importance de la dyskinésie ciliaire parmi la population maghrébine et sa rareté chez les européens. Nous soulignons aussi l'absence de critère diagnostique pour apprécier la fréquence relative de la mucoviscidose et du syndrome de Young.