

CILIARY STRUCTURE, ULTRASTRUCTURE & FUNCTION

1: Ups J Med Sci. 2006;111(1):155-68.

Transmission electron microscopy in the diagnosis of primary ciliary dyskinesia.

Roomans GM, Ivanovs A, Shebani EB, Johannesson M.

Primary ciliary dyskinesia (PCD) is an autosomal recessive disease with extensive genetic heterogeneity. Dyskinetic or completely absent motility of cilia predisposes to recurrent pulmonary and upper respiratory tract infections resulting in bronchiectasis. Also infections of the middle ear are common due to lack of ciliary movement in the Eustachian tube. Men have reduced fertility due to spermatozoa with absent motility or abnormalities in the ductuli efferentes. Female subfertility and tendency to ectopic pregnancy has also been suggested. Headache, a common complaint in PCD patients, has been associated with absence of cilia in the brain ventricles, leading to decreased circulation of the cerebrospinal fluid. Finally, half of the patients with PCD has situs inversus, probably due to the absence of ciliary motility in Hensen's node in the embryo, which is responsible for the unidirectional flow of fluid on the back of the embryo, which determines sidedness. PCD, which is an inborn disease, should be distinguished from secondary ciliary dyskinesia (SCD) which is an acquired disease. Transmission electron microscopy is the most commonly used method for diagnosis of PCD, even though alternative methods, such as determination of ciliary motility and measurement of exhaled nitric oxide (NO) may be considered. The best method to distinguish PCD from SCD is the determination of the number of inner and outer dynein arms, which can be carried out reliably on a limited number of ciliary cross-sections. There is also a significant difference in the ciliary orientation (determined by the direction of a line drawn through the central microtubule pair) between PCD and SCD, but there is some overlap in the values, making this parameter less suitable to distinguish PCD from SCD.

2: Am J Respir Crit Care Med. 2004 Feb 15;169(4):459-67. Epub 2003 Dec 4.

Primary ciliary dyskinesia: diagnostic and phenotypic features.

Noone PG, Leigh MW, Sannuti A, Minnix SL, Carson JL, Hazucha M, Zariwala MA, Knowles MR.

Primary ciliary dyskinesia (PCD) is a genetic disease characterized by abnormalities in ciliary structure/function. We hypothesized that the major clinical and biologic phenotypic markers of the disease could be evaluated by studying a cohort of subjects suspected of having PCD. Of 110 subjects evaluated, PCD was diagnosed in 78 subjects using a combination of compatible clinical features coupled with tests of ciliary ultrastructure and function. Chronic rhinitis/sinusitis (n = 78; 100%), recurrent otitis media (n = 74; 95%), neonatal respiratory symptoms (n = 57; 73%), and situs inversus (n = 43; 55%)

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are strong phenotypic markers of the disease. Mucoid *Pseudomonas aeruginosa* (n =12; 15%) and nontuberculous mycobacteria (n = 8; 10%) were present in older (>30 years) patients with PCD. All subjects had defects in ciliary structure, 66% in the outer dynein arm. Nasal nitric oxide production was very low in PCD (nl/minute; 19 +/- 17 vs. 376 +/- 124 in normal control subjects). Rigorous clinical and ciliary phenotyping and measures of nasal nitric oxide are useful for the diagnosis of PCD. An increased awareness of the clinical presentation and diagnostic criteria for PCD will help lead to better diagnosis and care for this orphan disease.

3: *Pediatr Res.* 2006 Mar;59(3):418-22.

Axonemal localization of the dynein component DNAH5 is not altered in secondary ciliary dyskinesia.

Olbrich H, Horvath J, Fekete A, Loges NT, van's Gravesande KS, Blum A, Hormann K, Omran H.

Primary ciliary dyskinesia (PCD) is a heterogeneous genetic disorder characterized by recurrent airway infections and situs inversus in half of affected individuals. Diagnosis currently relies on demonstration of abnormal ciliary ultrastructure or altered ciliary beat. Alterations encountered in secondary ciliary dyskinesia (SCD) caused by inflammation often complicate the diagnostic workup. We have recently shown that in respiratory epithelial cells from PCD patients with outer dynein arm defects the dynein protein DNAH5 is mislocalized and either completely or partially absent from the ciliary axoneme. In this study, we addressed the question whether SCD might affect axonemal DNAH5 localization in respiratory cells. To induce SCD *in vitro*, we treated primary human respiratory epithelial cell cultures with interleukin-13 (IL-13). Ciliary function and ultrastructure were assessed by high-speed videomicroscopy and transmission electron microscopy, respectively. For *in vivo* localization of DNAH5, we performed nasal brushing biopsies in patients with evidence of SCD. Expression of DNAH5 was analyzed by immunofluorescence microscopy. IL-13-treated cells showed evidence of SCD. Ciliary beat frequency was significantly reduced and ultrastructural analyses showed axonemal disorganization compared with control cells. High-resolution immunofluorescence studies of respiratory epithelial cells with SCD identified *in vitro* and *in vivo* normal axonemal DNAH5 localization. DNAH5 localization is not altered by SCD, indicating a high potential for immunofluorescence analysis as a novel diagnostic tool in PCD.

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4: Am J Physiol Renal Physiol. 2005 Dec;289(6):F1159-69.

An incredible decade for the primary cilium: a look at a once-forgotten organelle.

Davenport JR, Yoder BK.

Since the discovery that numerous proteins involved in mammalian disease localize to the basal bodies and cilia, these organelles have emerged from relative obscurity to the center of intense research efforts in an expanding number of disease- and developmental-related fields. Our understanding of the association between cilia and human disease has benefited substantially from the use of lower organisms such as *Chlamydomonas* and *Caenorhabditis elegans* and the availability of murine models and cell culture. These research endeavors led to the discovery that loss of normal ciliary function in mammals is responsible for cystic and noncystic pathology in the kidney, liver, brain, and pancreas, as well as severe developmental patterning abnormalities. In addition, the localization of proteins involved in rare human disorders such as Bardet-Biedl syndrome has suggested that cilia-related dysfunction may play a role in modern human epidemics such as hypertension, obesity, and diabetes. Although we have made great advances in demonstrating the importance of cilia over the past decade, the physiological role that this organelle plays in most tissues remains elusive. Research focused on addressing this issue will be of critical importance for a further understanding of how ciliary dysfunction can lead to such severe disease and developmental pathologies.

5: Acta Otolaryngol. 2005 May;125(5):571-6.

Comparison of ciliary wave disorders measured by image analysis and electron microscopy.

Lee CH, Lee SS, Mo JH, Kim IS, Quan SH, Wang SY, Yi WJ, Rhee CS, Min YG.

CONCLUSION: We have developed a simple, reliable method for the simultaneous determination of the ciliary wave disorder (CWD) and ciliary beat frequency (CBF) of actively beating cilia. **OBJECTIVE:** The CBF and the directions of beating cilia are two important components of mucociliary transport. Although lots of studies have been performed on the measurement of the CBF, there have been few studies on the direction of cilia, with the exception of those using electron microscopy (EM). EM takes too long to determine the directions of cilia, and it cannot determine the direction of actively beating cilia. The aim of this study was to develop an image analysis (IA) system to conveniently determine the wave directions of multiple actively beating cilia as well as the CBF. **MATERIAL AND METHODS:** Sphenoid sinus mucosae obtained from 10 patients undergoing pituitary tumor removal via a trans-septal trans-sphenoidal

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approach were divided into two 4 x 4 mm²-sized pieces. One piece was studied using IA, the other with EM. Using IA, ciliary wave directions were determined from 5 20 x 20 microm² regions of interest and the mean of 5 consecutive values was regarded as the CWD of each sample. The CBF was also measured. CWD was also measured using EM. RESULTS: The average number of cilia analyzed by EM was 102.50 (range 48-136). The mean CWDs determined using IA and EM were 28.25 \pm 4.84 degrees and 23.59 \pm 8.16 degrees, respectively. There was a significant correlation between the CWDs determined using these two methods (Spearman's correlation coefficient $t=0.648$; $p=0.043$). The mean CBF of sphenoid mucosa was 10.50 \pm 2.20 Hz.

6: Theriogenology. 2005 Aug;64(3):457-68.

Genetic sperm defects.

Chenoweth PJ.

Genetic sperm defects are specific sperm defects, which have been shown to have a genetic mode of transmission. Such genetic linkage, either direct or indirect, has been associated with a number of sperm defects in different species, with this number increasing with improved diagnostic capabilities. A number of sperm defects, which have proven or suspected genetic modes of transmission are discussed herein, with particular emphasis on cattle. These include: 1. Acrosome defects (knobbed, ruffled and incomplete); 2. Head defects (abnormal condensation, decapitated, round head, rolled head, nuclear crest); 3. Midpiece abnormalities ("Dag" defect, "corkscrew" defect, "pseudo-droplet" defect); 4. Tail defects ("tail stump" defect, primary ciliary dyskinesia).

7: Ultrastruct Pathol. 2005 Jan-Feb;29(1):3-8.

Ultrastructural patterns of primary ciliar dyskinesia syndrome.

Carda C, Armengot M, Escribano A, Peydro A.

Clinical presentation, ciliary ultrastructure, and nasal mucociliary transport by a radioisotopic technique were analyzed in 14 Kartagener syndrome patients. In this study the most common pattern was the absence of outer and inner dynein arms in 57% of cases. Also reported are 14% patients with short inner dynein arms. A total of 29% of the patients showed normal dynein arms. Mucociliary stasis was observed in 13 cases. Primary ciliary dyskinesia syndrome and Kartagener syndrome are clinically homogeneous and morphologically heterogeneous. The authors conclude that a typical clinical presentation with an altered mucociliary transport obtained by radioisotopic technique is diagnostic although ciliary ultrastructure is normal.

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8: Acta Otolaryngol. 2004 May;124(4):527-31.

The secondary nature of ciliary (dis)orientation in secondary and primary ciliary dyskinesia.

Jorissen M, Willems T.

OBJECTIVE: Ciliary orientation (COR) is an important parameter of mucociliary clearance and ciliary disorientation has been reported in cases of acquired abnormalities [secondary ciliary dyskinesia (SCD)] and in a very few cases as the single abnormality in primary ciliary dyskinesia (PCD). The etiology, pathogenesis, consequences and relevance of ciliary (dis)orientation are still unclear. **MATERIAL AND METHODS:** To elucidate the primary or secondary nature of ciliary (dis)orientation, COR was measured in 179 non-PCD and 59 PCD patients. COR was measured in biopsies and after ciliogenesis in culture and was correlated with a number of functional and ultrastructural parameters. COR was defined as the SD of the angles of lines through the central pair of microtubules using transmission electron microscopy. Internationally accepted normal values for COR are $< \text{ or } = 20$ degrees; COR values of 20-35 degrees indicate increased disorientation; and COR values > 35 degrees represent a random orientation. **RESULTS:** For non-PCD biopsies, COR increased with increasing SCD, from 15 ± 7 degrees ($n = 54$) for normal ($< 5\%$) SCD to 28 ± 8 degrees ($n = 16$) for severe ($> 25\%$) SCD. No correlation was found between COR and ciliary beat frequency. However, increased COR values (28 ± 8 degrees) were found for immotility ($n = 8$), compared to (coordinated) ciliary activity (19 ± 9 degrees) ($n = 121$). After ciliogenesis no ultrastructural abnormalities were found and COR was normal (13 ± 5 degrees; $n = 308$). COR can therefore be considered to be secondary in non-PCD and correlates with SCD percentage and ciliary motility. In biopsies from PCD patients with dynein deficiency and with normal ultrastructure, COR was increased, to 28 ± 11 degrees ($n = 32$) and 21 ± 7 degrees ($n = 15$), respectively, and in cases with central pair abnormalities COR was random (38 ± 11 degrees; $n = 12$). After ciliogenesis COR remained random in the PCD group with central pair abnormalities (38 ± 9 degrees; $n = 15$), and was increased in the PCD groups with dynein deficiency (24 ± 10 degrees; $n = 35$) and normal ultrastructure (25 ± 8 degrees; $n = 17$). Ciliary disorientation was never found as the single abnormality. **CONCLUSION:** COR can be considered to be secondary in PCD. Both ciliary (im)motility and SCD percentage contribute to COR.

9: Paediatr Respir Rev. 2004 Mar;5(1):69-76.

Cilia, primary ciliary dyskinesia and molecular genetics.

Chodhari R, Mitchison HM, Meeks M.

Primary ciliary dyskinesia (PCD) is a phenotypically and genetically heterogeneous condition in which three genetic mutations have already been identified. The primary defect is in the ultrastructure or function of cilia,

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highly complex organelles that are structurally related to the flagella of sperm and protozoa. The clinical features of PCD include recurrent sinopulmonary infections, subfertility and laterality defects; the latter due to ciliary dysfunction at the embryological node. Completion of the human genome sequence has accelerated the identification and characterisation of disease genes, and the current molecular strategy in PCD includes candidate gene analysis, positional cloning, model organism analysis and proteomic analysis. The identification of these genes will provide new insights into the molecular mechanisms involved in the assembly and function of cilia and the pathway that determines left-right axis in man. This may also allow the development of new methods for diagnosis, prevention and treatment of PCD.

10: Cell. 2004 Jun 11;117(6):693-7.

Cilia and flagella revealed: from flagellar assembly in *Chlamydomonas* to human obesity disorders.

Snell WJ, Pan J, Wang Q.

The recent identification in *Chlamydomonas* of the intraflagellar transport machinery that assembles cilia and flagella has triggered a renaissance of interest in these organelles that transcends studies on their well-characterized ability to move. New studies on several fronts have revealed that the machinery for flagellar assembly/disassembly is regulated by homologs of mitotic proteins, that cilia play essential roles in sensory transduction, and that mutations in cilia/basal body proteins are responsible for cilia-related human disorders from polycystic kidney disease to a syndrome associated with obesity, hypertension, and diabetes.

11: Am J Respir Crit Care Med. 2004 Mar 1;169(5):634-7.

Central microtubular agenesis causing primary ciliary dyskinesia.

Stannard W, Rutman A, Wallis C, O'Callaghan C.

Primary ciliary dyskinesia is an autosomal recessive disorder characterized by chronic upper and lower respiratory tract symptoms. We report the diagnosis of primary ciliary dyskinesia associated with a circular ciliary beat pattern in three siblings. This beat pattern is consistent with a ciliary transposition defect, where a peripheral microtubule doublet is transposed to the center of the ciliary axoneme to replace the absent central microtubule pair. However, in these siblings, ultrastructural analysis of the cilia revealed an absence of the central microtubule pair only. This variant of transposition with a circular ciliary beat pattern has not been described previously. In addition, this defect, together with the transposition defect, may help explain the mechanism of the circular beat pattern and also the absence of situs inversus in these patients.

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12: J Allergy Clin Immunol. 2003 Sep;112(3):518-24.

Ciliary beat pattern is associated with specific ultrastructural defects in primary ciliary dyskinesia.

Chilvers MA, Rutman A, O'Callaghan C.

BACKGROUND: The main symptoms of primary ciliary dyskinesia (PCD) are nasal rhinorrhea or blockage and moist-sounding cough. Diagnosis can be difficult and is based on an abnormal ciliary beat frequency, accompanied by specific abnormalities of the ciliary axoneme. It is unknown whether determining ciliary beat pattern related to specific ultrastructural ciliary defects might help in the diagnosis of PCD. **OBJECTIVE:** We sought to determine ciliary beat pattern and beat frequency (CBF) associated with the 5 common ultrastructural defects responsible for PCD. **METHODS:** Nasal brushings were performed on 56 children with PCD. Ciliary movement was recorded using digital high-speed video imaging to assess beat frequency and pattern. Electron microscopy was performed. **RESULTS:** In patients with an isolated outer dynein arm or with an outer and inner dynein arm defect, 55% and 80% of cilia were immotile, respectively. Cilia that moved were only flickering. Mean CBF (\pm 95% CI) was 2.3 Hz (\pm 1.2) and 0.8 Hz (\pm 0.8), respectively. Cilia with an isolated inner dynein arm or a radial spoke defect had similar beat patterns. Cilia appeared stiff, had a reduced amplitude, and failed to bend along their length. Immotile cilia were present in 10% of cilia with an inner dynein arm defect and in 30% of radial spoke defects. Mean CBF was 9.3 Hz (\pm 2.6) and 6.0 Hz (\pm 3.1), respectively. The ciliary transposition defect produced a large circular beat pattern (mean CBF, 10.7 Hz [\pm 1.1]). No cilia were immotile. **CONCLUSIONS:** Different ultrastructural defects responsible for PCD result in predictable beat patterns. Recognition of these might help in the diagnostic evaluation of patients suspected of having PCD.

13: Ultrastruct Pathol. 2003 Jul-Aug;27(4):243-52.

Clinico-pathological evaluation of ciliary dyskinesia: diagnostic role of electron microscopy.

Pizzi S, Cazzato S, Bernardi F, Mantovani W, Cenacchi G.

From November 1995 to May 2002, the authors studied 59 children with suspected primary ciliary dyskinesia (PCD). Samples of ciliated respiratory epithelium were obtained by nasal brushing from 44 patients and by biopsy of bronchial mucosa from 15 patients. Thirty-four/Fifty-nine samples were suitable to obtain a qualitative-quantitative evaluation of ultrastructural ciliary abnormalities. Many ciliary and axoneme alterations were described. This study revealed that

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quantitative and qualitative ultrastructural assessment of respiratory epithelial cilia plays an important role in the differentiation between primary, secondary, and borderline ciliary abnormalities. Early diagnosis of PCD with appropriate clinical follow-up and treatment is important to prevent irreversible lung tissue damage, namely bronchiectasis.

14: Ultrastruct Pathol. 2003 Mar-Apr;27(2):123-6.

Absence of nexin links as a possible cause of primary ciliary dyskinesia.

Carlen B, Lindberg S, Stenram U.

Transmission electron microscopy of nasal cilia was performed in three patients, two of them siblings, with repeated respiratory infections. Number of microtubuli and dynein arms were within normal limits and they had an ordered arrangement except for a disarray of the microtubuli in some areas of the biopsies from two of the patients. In the normal areas radial spokes and sheaths were easily found but nexin links could not be discerned in any of the patients. The orientation of the cilia was partly random. As all patients repeatedly and constantly had very low nasal NO (range 9-15 ppb; normal findings for persons <10 years old are > 50 ppb), the diagnoses were very likely primary ciliary dyskinesia (PCD). Absence of nexin links may be an ultrastructural variant of PCD. Deficiency of these structures might be the cause of the microtubular disarray observed in some areas of the biopsies.

15: Trends Genet. 2003 Mar;19(3):162-7.

Lateralization defects and ciliary dyskinesia: lessons from algae.

El Zein L, Omran H, Bouvagnet P.

Flagella and cilia are two very similar organelles that "beat" to move cells and to propel fluid over tissues. They are highly conserved, being found in organisms ranging from prokaryotes to plant and animal eukaryotes. In humans, cilia are present in almost every organ, and several human conditions involve dysfunctional cilia; for example, lateralization defects, where the positions of organs are reversed, and primary ciliary dyskinesia, a rare condition where patients suffer from recurrent respiratory infections. In this article, we will discuss how information gained from studies on algae has aided research into these human diseases. These studies found a variety of functions that was previously unsuspected, renewing interest in cilia.

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16: Am J Respir Crit Care Med. 2002 Nov 1;166(9):1257-62.

Computer-assisted analysis helps detect inner dynein arm abnormalities.

Escudier E, Couprie M, Duriez B, Roudot-Thoraval F, Millepied MC, Pruliere-Escabasse V, Labatte L, Coste A.

The diagnosis of primary ciliary dyskinesia is based on demonstration of ciliary defects, mainly concerning dynein arms. Whereas the absence of outer dynein arms can be easily distinguished, the absence of inner dynein arms is difficult to confirm because of their low contrast on electron microscopy. Ciliary ultrastructure was studied in 40 patients suffering from respiratory tract infections. Conventional transmission electron microscopy showed normal cilia in 6 patients, confirmed a diagnosis of primary ciliary dyskinesia in 26 patients, and was inconclusive in 8 patients. All doubtful cases were related to inner dynein arm determination. Conventional electron microscopic analysis was able to define the ultrastructural phenotype of inner dynein arms in 40.5% of cases (6 presence of inner dynein arms, 13 absence of inner dynein arms). We developed computer-assisted analysis of electron microscopic micrographs to improve inner dynein arm visualization. Computer-assisted analysis consisted of image transformations designed to enhance the signal/noise ratio, based on the symmetry of ciliary axonemes. The sensitivity and specificity of computer-assisted analysis were 100 and 98%, respectively. The efficiency of computer-assisted analysis to visualize inner dynein arms, evaluated in the patients with undetermined phenotype after electron microscopy, was 86% (three normal cilia, seven primary ciliary dyskinesia with absence of outer dynein arms, three primary ciliary dyskinesia with absence of inner dynein arms, five partial absence of inner dynein arms). Computer-assisted analysis of ciliary micrographs improves the characterization of inherited axonemal defects.

17: Pediatrics. 2001 Nov;108(5):E86.

Abnormal central complex is a marker of severity in the presence of partial ciliary defect.

Tamalet A, Clement A, Roudot-Thoraval F, Desmarquest P, Roger G, Boule M, Millepied MC, Baculard TA, Escudier E.

BACKGROUND: Ciliary ultrastructural defects with total lack of dynein arms (DA) cause abnormal mucociliary function leading to the chronic infections observed in primary ciliary dyskinesia. The role of partial ciliary ultrastructural defects, especially those involving the central complex, and their relationship with respiratory symptoms have been less thoroughly investigated. **OBJECTIVE:** In a pediatric population with partial ciliary defects, we determined the relationship(s) between ultrastructural findings, ciliary motility, and clinical and functional features, and evaluated the outcome of this population. **DESIGN:** We analyzed the clinical presentation and pulmonary function of 43 children with chronic bronchitis and partial ultrastructural defects (from 15% to 90%) of

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their respiratory cilia demonstrated on bronchial biopsies. The study population was divided into 3 groups according to ciliary ultrastructure: the main ultrastructural defect concerned the central complex in 23 patients (CC group), peripheral microtubules in 8 patients (PMT group), and DA in 12 patients (DA group). RESULTS: The percentage of ciliary defects was lower in the PMT group than in the CC and DA groups. Patients in the PMT group had less severe disease with frequent normal ciliary motility. Patients in the CC group had initially a higher incidence of respiratory tract infections, extensive bronchiectasis frequently requiring surgery, and arguments in favor of a congenital origin (high proportion of sibling form). Partial absence of DA, although of congenital origin, was associated with a good prognosis. In all groups, follow-up showed that the functional prognosis remained good with appropriate treatment. CONCLUSIONS: In children with chronic respiratory infections, presence of situs inversus, sibling form, obstructive pulmonary syndrome, or bronchiectasis required ultrastructural analysis, regardless of ciliary motility. Detection of CC abnormalities is a marker of severity and required intensive therapy and close follow-up.

18: Acta Otorhinolaryngol Belg. 2000;54(3):343-56.

Ultrastructural expression of primary ciliary dyskinesia after ciliogenesis in culture.

Jorissen M, Willems T, Van der Schueren B, Verbeken E, De Boeck K.

During the period 1990-1999 84 PCD patients were identified and characterized. The expression of inherited abnormalities in primary ciliary dyskinesia after ciliogenesis was investigated in 41 patients with dynein deficiency, 6 patients with absence of the central pair of microtubules and 24 PCD patients with normal ultrastructure. In patients with dynein deficiency, the outer dynein arms counts were 1.9 ± 1.0 in the biopsies and 1.6 ± 0.7 after ciliogenesis. Secondary abnormalities were found in $15.8 \pm 20.4\%$ of the transverse sections of cilia and only in $1.0 \pm 1.3\%$ after ciliogenesis. Ciliary orientation was 28 ± 11 degrees and 24 ± 10 degrees respectively in biopsies and cultures. In patients with absence of the central pair this was found in $15 \pm 16\%$ in biopsies and $21 \pm 19\%$ after ciliogenesis. The values for the outer dynein arm were 8.4 ± 0.3 and 8.7 ± 0.2 and for the secondary abnormalities were $11.7 \pm 7.3\%$ and $0.5 \pm 1.3\%$ in the biopsies, respectively after ciliogenesis. In patients with normal ultrastructure the scores for the dynein arms were similar. Secondary abnormalities were found in $12.2 \pm 11.7\%$ in the biopsies and $0.6 \pm 0.9\%$ after ciliogenesis while ciliary orientation was respectively 21 ± 7 degrees and 25 ± 8 degrees. In conclusion, inherited abnormalities in primary ciliary dyskinesia are expressed after ciliogenesis, while secondary abnormalities are virtually absent, thereby facilitating the ultrastructural diagnosis.

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19: Acta Otorhinolaryngol Belg. 2000;54(3):333-42.

Secondary ciliary dyskinesia is absent after ciliogenesis in culture.

Jorissen M, Willems T, Van der Schueren B, Verbeken E.

Ultrastructural secondary ciliary dyskinesia (SCD) was measured using transmission electron microscopy in 301 biopsies and 439 samples after ciliogenesis in the sequential monolayer-suspension culture. Biopsies were taken in the context of exclusion of primary ciliary dyskinesia. SCD was frequently found in the biopsies: only 30% of the samples were normal (SCD < 5%), the mean percentage of SCD abnormalities was 11.9 +/- 12.9%. In 1/8 of the samples severe SCD (> 25%) was present. The most frequently encountered SCD abnormality was the membrane bleb, followed by the various peripheral microtubular abnormalities. With increasing total SCD the absence of the central pair became more important. After ciliogenesis in culture SCD was virtually absent: 1.0 +/- 1.8% for all 439 samples, 96% of the samples were within limits of normality (SCD < 5%). Moderate (15-25%) and severe SCD (> 25%) were never found. In more than 50% of the samples not one abnormality was found. There was no relation between the SCD in the biopsy and that after ciliogenesis. The absence of SCD after ciliogenesis is a major advantage for the diagnosis of PCD, specifically in cases with central pair abnormalities, peripheral microtubular pair abnormalities and those without a primary ultrastructural abnormality.