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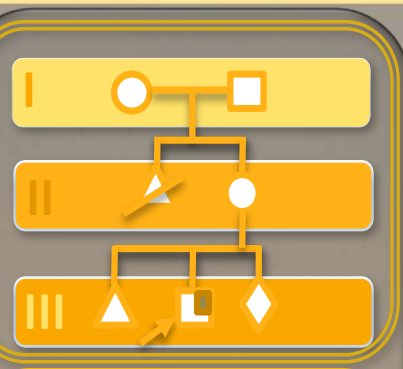

From the desk of Editor

The genetic division of the Pediatric Department publishes a monthly newsletter for all Medical Professionals. The newsletter is related to genealogical parlance and is a deliberate attempt to enhance awareness of genetic disorders with recent updates.

Author: Prashant Kumar Verma[1], Dr. Khushboo Kamal Taneja[2]
[1]Chairperson of Medical Genetic division,
[2]Senior resident in Pediatric Pulmonary Medicine
Department of Pediatrics, AIIMS Rishikesh, Uttarakhand, India

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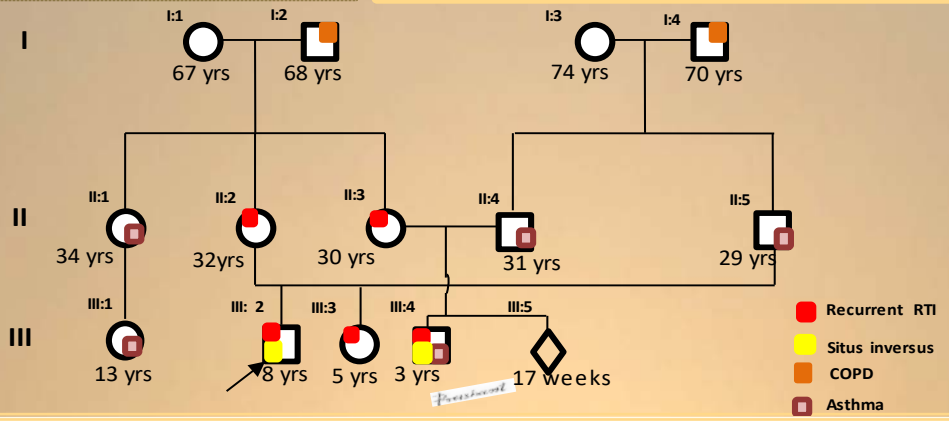
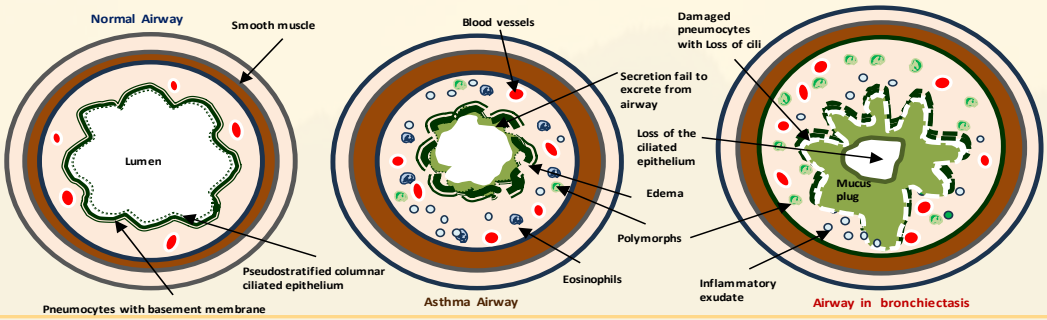
Reviewer: Dr. Raksha Ranjan,
[1]Department of Pediatrics, AIIMS Bathinda, Punjab, India

Pulmogenetics-VIII / Hereditary Ciliopathies & Bronchiectasis / Primary CILiary Dyskinesia (PCD or CILD) /DNAI1 & OTHERS



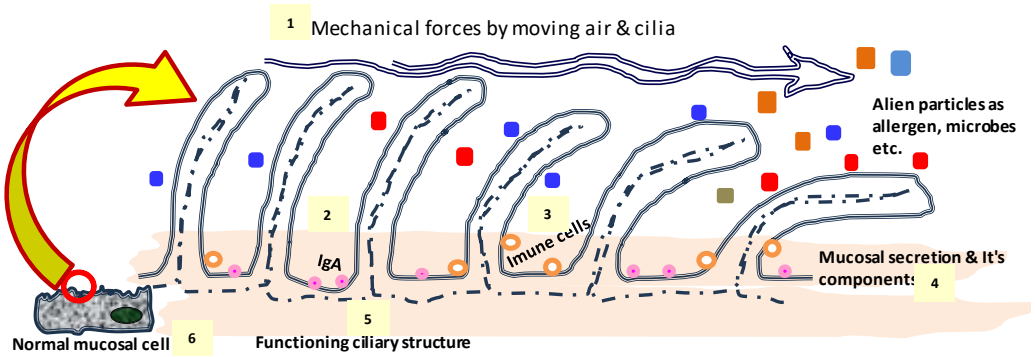
Impact on airways due to dysfunction of Cilia & its pathways related to airway changes



Insight:

1. How does ciliary dyskinesia affect innate immune mechanism?
2. When would you suspect a case of Primary CILiary Dyskinesia (PCD or CILD)?
3. What are the newer supportive tests for PCD?
4. What is the role of an anomaly scan in genetic counselling for case IV: 5?

Cilia dyskinesia (primary or secondary) fail to remove various alien particles



Essential components for normal functioning ciliary machinery

Plausible tenets:

Primary CILiary Dyskinesia (PCD or CILD)

- Clinical diagnosis: **≥ 2 features**: **1. Changes in situs normalis; 2. Idiopathic Respiratory distress; 3. unexplained chronic wet cough (LRTI); 4. Unexplained chronic nasal congestion (URTI).**
- Most crucial physical function as cellular wiper, and transporter
- Situs inversus (viscera positioned in mirror image only), usually a nonlethal condition, is not mandatory to be present (only detected in around 50% cases), while Heterotaxy ('other' + 'arrangement'), lethal from a cardiac perspective, is reported up to 12% cases of PCD.
- Around **two-third cases present in neonatal age** with **RDS**, and later in childhood present as sputum-positive chronic cough progress to bronchiectasis, broncholithiasis with or without lithoptysis over a time period.
- Frequent upper airway congestion and Infections with its sequelae as otitis media.
- Loss of cellular motility in sperm leads to infertility.
- Electron microscopy phenotyping of ciliary body helps in genotyping to a certain extent.
- Clinical diagnosis should be supported by a low airway NO level, and abnormal cilia under transmission electron microscopy (**30 % cases)**- normal ultrastructural
- Confirmation done by molecular genetic testing (**30% cases**: failed to get a variant by NGS, might be new genes or not replicable genomic areas)

Phenotypic Series: PS244400, 52 Entries:

- Type 1 to Type 53, and **Missing Entry for CILD Type 31**
- In all entries, the mode of inheritance is AR, except CILD, 36, X-linked, and XLR and CILD, 43 AD
- The most Common PCD: **Type 3 (15%-29%),** Type 1 (2-10 %), & Type 7(6%-9%) ≈ Type 14

Role of Nasal Nitric Oxide: low in PCD

Need child cooperation for palate closure maneuvers **(usually feasible with > 5 years of age)** cut-off value **77 nL/min (98% sensitive and 99% specific).**

Prerequisite: no acute viral infections, no cystic fibrosis (**negative sweat chloride or CFTR gene testing**), and no local bleeding (**reason**: damaged mucosal surface, which leads to a false positive result). * **allergic rhinitis increased NO values.**

Newer under evaluation Supportive Tests for PCD:

Newer test	Issues besides equipment and facilities
High-speed videomicroscopy of ciliary motility	need biopsies, need to do in first 3 hours, exam multiple videos, need more data
Mucociliary clearance analysis of radiolabeled particles	Radiation exposure, more data
Immunofluorescent staining of the ciliary biopsy	Functional defects or partial defects can be missed; low sensitivity
Semen analysis	Not feasible for the pediatric age group

Role of anomaly scan in genetic counselling for case IV: 5- The presence of situs inversus helps in genetic counselling, however, its absence could not rule out the genotype or other associated phenotypes.

Thought Riveting:

- ***What could be the most useful management for Lithoptysis with PCD?***
- ***What are evolutionary reasons for embryonic development as Situs solitus and not Situs inversus?***
- ***What could be the other possible effects on the nervous system due to PCD besides hydrocephalus?***
- ***What is the underlying molecular mechanism for the low nasal NO level (approx. < 1/10 of the control value) in the airways of a PCD case? Why are those changes not happening with RSPH1 mutations?***
- ***What are the phylogenetic differences between proteins related to ciliopathies with and without ciliary dyskinesia?***