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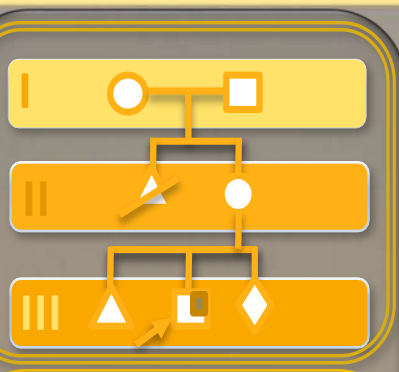

From the desk of Editor

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.

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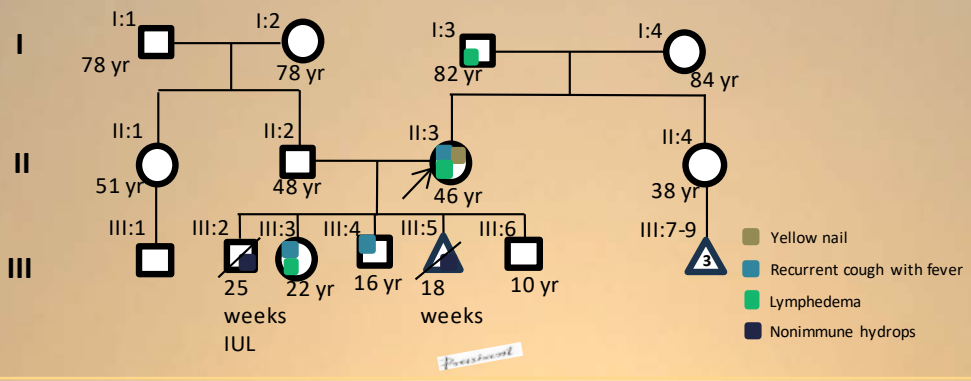
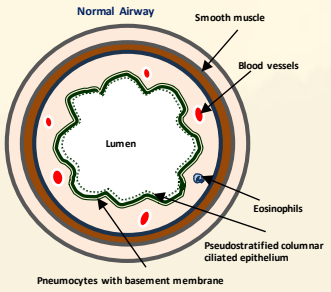
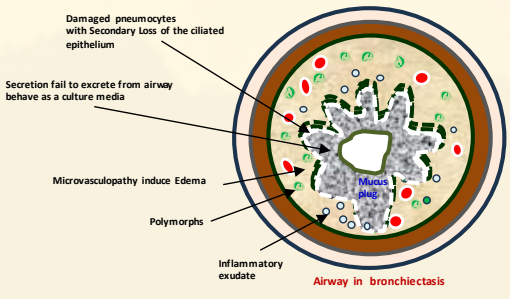
Pulmogenetics-X / Hereditary Bronchiectasis / Yellow nail syndrome (YNS)



Impact on airways due to microvascular pathology

Yellow nail

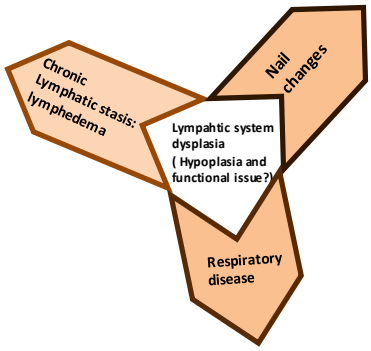




Insight:

1. What is the yellow nail syndrome?
2. How to approach a case with yellow nail syndrome?
3. What are the meanings of symbols marked before a MIM number?
4. What is the possible phenotype of III: 6?

Triad of Yellow nail syndrome



Plausible tenets: Yellow nail syndrome

- **First reported in early 19th century**
- **The first series discussed in 1964 by Samman & White**

- **Diagnostic criteria**: yellow nail PLUS presence of any of these two features: lymphedema or respiratory tract involvement upper (rhinosinusitis), or lower (bronchiectasis, pleural effusion).
- Triad is present in only **one-third of cases, and** lymphedema might be the first sign **in one-third of cases.**
- **Onset after 18 years of age, presenting** clinical feature could be **any of the three.**

Key features among MIM entries with "Yellow nail":

Syndrome with yellow nail/ Features	Yellow nail syndrome (YNS)	Lymphedema-distichiasis syndrome	Lymphatic Malformation 5; LMPHM5(Meige disease) *Lymphatic malformation - PS153100 - 14 Entries*
Gene/ MOI	Not known / AD	FOXC2 (16q24.1)/ AD	Not Mapped / AD
Age dependence penetrance	Middle age onset (complete by 65 years)	Pubertal onset of lymphedema (complete by 40 years)	Birth or early childhood with variable severity (completed by 20-30 years)
Chronicity	Yes	Yes	Yes
Lymphography	Hypoplasia, and defective lymphatic transport, Lower limb > upper limb	'Bilateral hyperplasia' lymphedema, Lower limb >> upper limb	Scarcity or lack of lymph nodes , Lower limb >> upper limb
Particular presentation	Any or combination – respiratory or / lymphedema or /respiratory	Distichiasis(94%): double rows of eyelashes –corneal ulceration (ophthalmologist)	Lymphedema
Other system	Microvasculopathy	Cardiac defects(6.8%), spinal extradural cysts, ptosis(31%), Varicose veins	Swelling in other body part, cleft palate
Nail	Characteristic but not prime onset in all	Sometime observed	Sometime observed
Nailfold capillaroscopy	convoluted capillaries	No	No

Characteristic findings with YNS:

Nail changes: thickened nail plate, pale yellow to dark greenish, over-curvature, scleronychia, hyperkeratosis, paronychia, progressive onycholysis.
Upper respiratory: rhinitis and chronic and recurrent sinusitis**.**
Lower respiratory tract: pleural effusion (chylothorax > empyema), bronchiectasis (44% cases, no specific bacterial culture or histopathological report of lung tissue), recurrent pneumonias.

Symbols meaning preceding a MIM number

Symbol	Meaning	OMIM entries
*	A gene	17,396
#	A mendelian phenotype with known gene	6,913
+	Description of a gene & phenotype	14
%	A mendelian phenotype unknown gene	1,498
None	A doubtful mendelian phenotype	9
^	Entry has been removed	1367

The possible phenotype of III: Six- Theoretically, there is a 50% risk to have an YNS, but without a confirmatory test, concealed disease status cannot be recognized. YNS could be present with any of the triad features, which could evolve over time.

Thought Riveting:

- ***What is the mechanism of non-immune hydrops in YNS?***
- ***Is YNS a mild form or mosaic disease of the FOXC2 gene?***
- ***Is there any role of early intervention for preventing progressive pulmonary disease in YNS by the immunomodulators?***
- ***Distichiasis is a unique phenotype (only sixteen clinical synopses entries in MIM). Is there a rational pleiotropy of distichiasis reported with FOXC2-related disorders?***
- ***Is YNS an environmental toxins-induced disease (especially very heavy metal) with an unknown genetic susceptibility (just like Indian childhood cirrhosis)?***