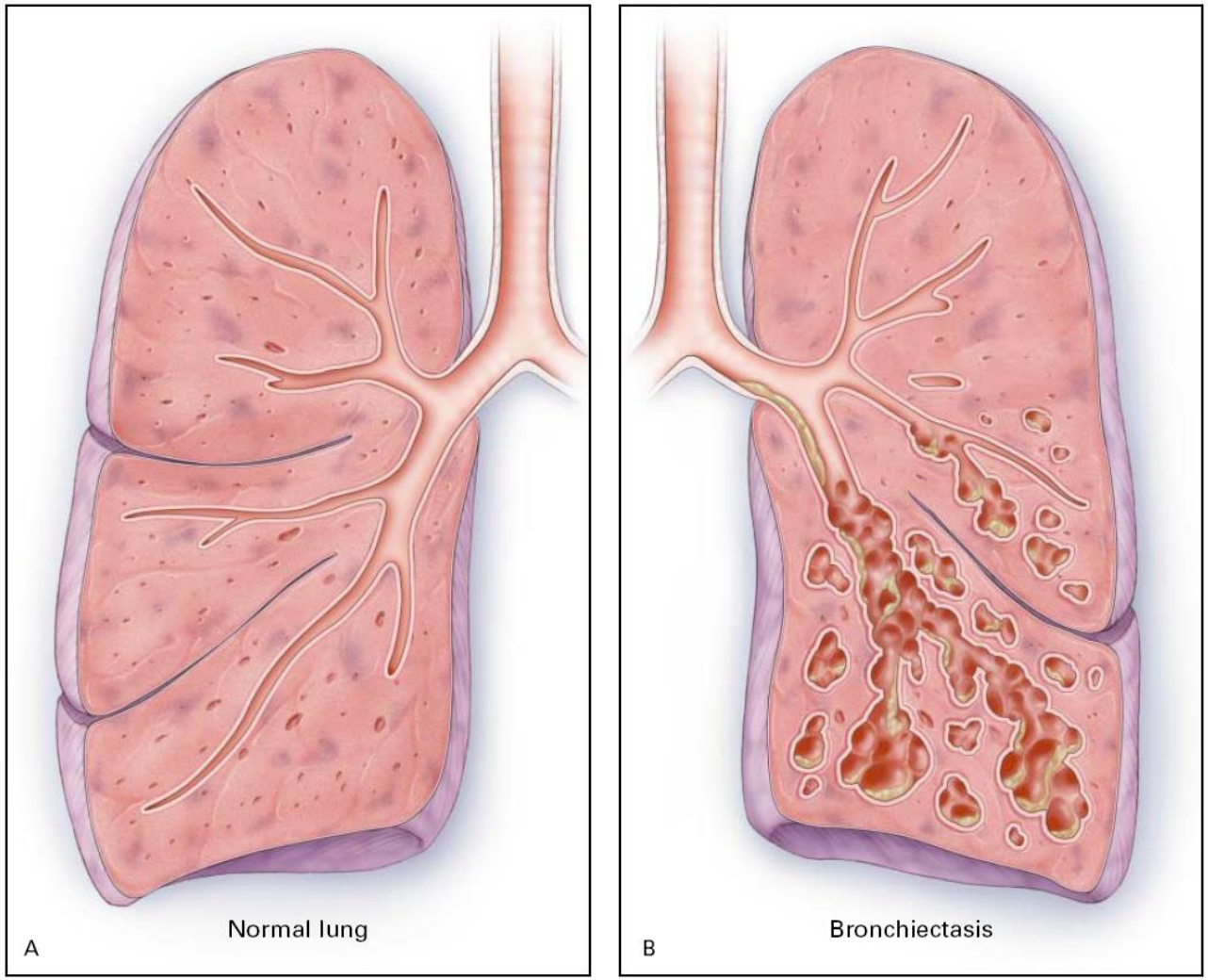


Figure 2. Normal Lung and Airways (Panel A) and the Lung of a Patient with Bronchiectasis (Panel B).
In Panel B, bronchiectasis is primarily in the lower lobe, which is the most common distribution. The saccular dilatations and grape-like clusters with pools of mucus are signs of severe bronchiectasis.

Barker, N Engl J Med, Vol. 346, No. 18 May 2, 2002

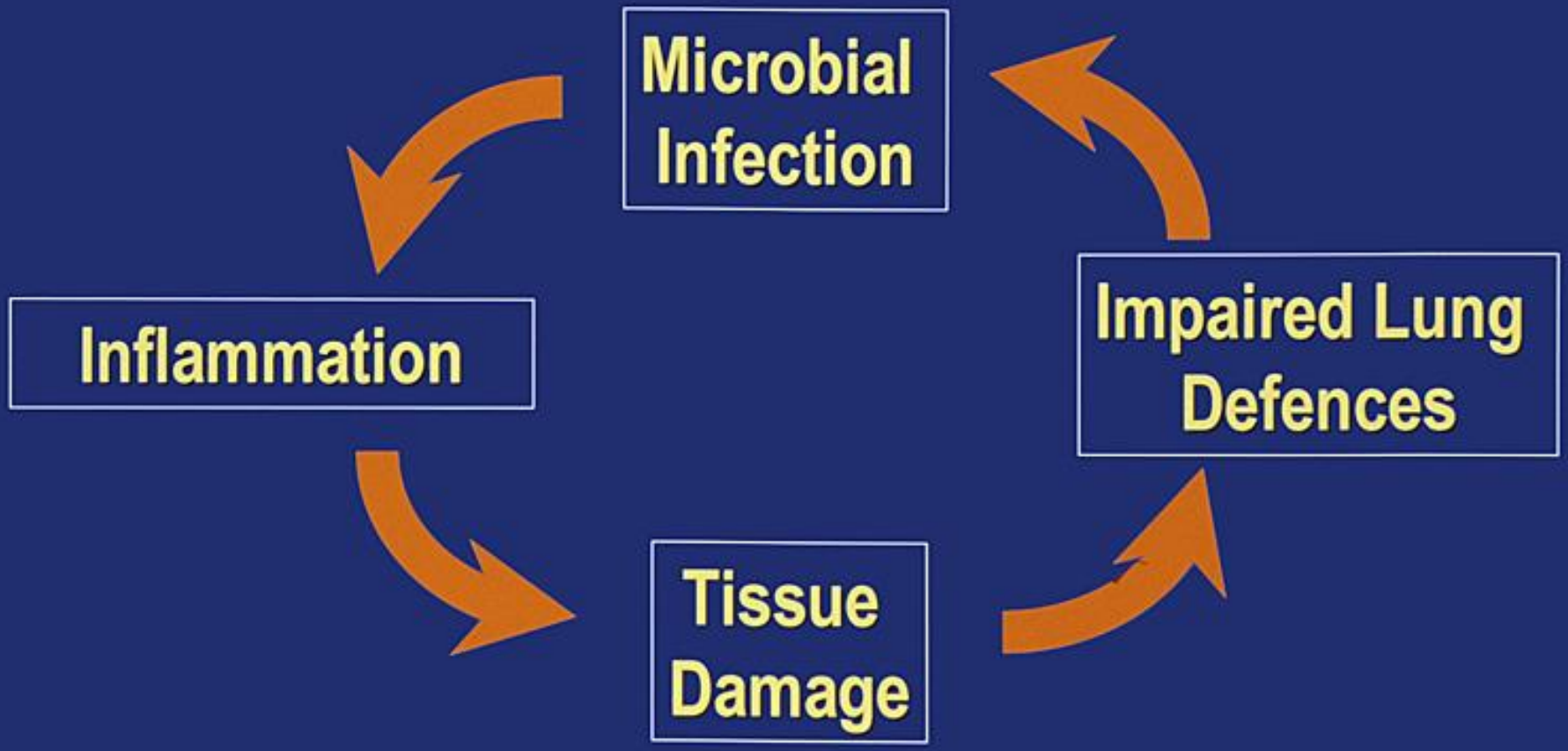
bronchiëctasieën

- definitie
- ontstaan
- symptomatologie
- radiologie
- sputumkweek
- aanvullend onderzoek
- behandeling

Definities van bronchiëctasieën

- **Pathological:** abnormal irreversible dilatation of the bronchi, periphere from segmental bronchi *(Thurlbeck 1995)*
- **Clinical:** chronic purulent sputum production, ?amount, with or without exacerbations
- **HRCT:** Abnormal bronchial dilatation (compared with accompanying pulmonary artery), with or without bronchial wall thickening *(Naidich 1982)*
- Most cases currently diagnosed radiologically.
- Many causes: Post infectious, cystic fibrosis, ciliary dyskinesia, collagen vascular diseases and many others

A VICIOUS CYCLE OF INFECTION AND INFLAMMATION



symptomatologie

- hoesten
- sputum: taai,dik
- haemoptoë
- dyspneu en wheezing
- thoracale pijn door prikkeling pleura visceralis
- bij lich. onderzoek wheezing, crepitaties, rhonchi en clubbing

TABLE 2. COMPARISON OF BRONCHIECTASIS AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

VARIABLE	CHRONIC OBSTRUCTIVE PULMONARY DISEASE	BRONCHIECTASIS
Cause	Cigarette smoking	Infection or genetic or immune defect
Role of infection	Secondary	Primary
Predominant organism in sputum	*Streptococcus pneumoniae, Haemophilus influenzae*	*H. influenzae, Pseudomonas aeruginosa*
Airflow obstruction and hyperresponsiveness	Present	Present
Findings on chest imaging	Hyperlucency, hyperinflation, airway dilatation	Airway dilatation and thickening, mucous plugs
Quality of sputum (in the steady state)	Mucoid, clear	Purulent, three-layered

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TABLE 1. CONDITIONS ASSOCIATED WITH BRONCHIECTASIS.

- Postinfectious conditions
  - Bacteria (pseudomonas, haemophilus)
  - Mycobacterium tuberculosis
  - Aspergillus species
  - Virus (adenovirus, measles virus, influenzavirus, human immunodeficiency virus)
- Congenital conditions
  - Primary ciliary dyskinesia
  - $Alpha_1$-antitrypsin deficiency
  - Cystic fibrosis
  - Tracheobronchomegaly (Mounier–Kuhn syndrome)
  - Cartilage deficiency (Williams–Campbell syndrome)
  - Pulmonary sequestration
  - Marfan's syndrome
- Immunodeficiency
  - Primary
    - Hypogammaglobulinemia
  - Secondary
    - Caused by cancer (chronic lymphatic leukemia), chemotherapy, or immune modulation (after transplantation)
- Sequelae of toxic inhalation or aspiration
  - Chlorine
  - Overdose (heroin)
  - Foreign body
- Rheumatic conditions
  - Rheumatoid arthritis
  - Systemic lupus erythematosus
  - Sjögren's syndrome
  - Relapsing polychondritis
- Other
  - Inflammatory bowel disease (chronic ulcerative colitis or Crohn's disease)
  - Young's syndrome (secondary ciliary dyskinesia)
  - Yellow nail syndrome (yellow nails and lymphedema)

Barker, N Engl J Med, Vol. 346, No. 18 May 2, 2002

TABLE 3. DIAGNOSTIC TESTING FOR BRONCHIECTASIS.*

LEVEL OF TESTING	APPROPRIATE TESTS		
	BLOOD	IMAGING	OTHER
Primary	Complete and differential blood count, IgG, IgA, IgM	High-resolution CT	Spirometry or bronchodilator test
Secondary	Rheumatoid factor; IgE, aspergillus precipitins (ABPA); IgG subclasses; $alpha_1$-antitrypsin level	Sinus CT	Sputum bacterial, mycobacterial, fungal culture and sensitivity; bronchoscopy with mucosal biopsy, cultures (for focal obstruction, infection, primary ciliary dyskinesia); sweat chloride test analysis (for cystic fibrosis)

*The causes for suspicion of bronchiectasis are chronic cough, daily production of mucopurulent sputum, and persistent focal infiltrate on radiography. CT denotes computed tomography, and ABPA allergic bronchopulmonary aspergillosis.

Barker, N Engl J Med, Vol. 346, No. 18 May 2, 2002

The occurrence of CFTR mutations in patients with bronchiectasis

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Registration number R007

Introduction

Homozygosity or compound heterozygosity for mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene causes cystic fibrosis. Carriership of such mutations is known to be harmless or even advantageous, giving protection against infections. However, CFTR mutation carriership has been shown to have health implications in later life, especially concerning lung function and chronicity of lung infections.

Contradictory results have been published on the occurrence of CFTR mutations in patients with bronchiectasis. Several papers have shown that an increase of mutations was found, up to 60%, while others find 0 to 4% mutation carriers (which does not deviate from the expected population frequency). We have started a study investigating 36 CFTR mutations and the polythymidine tract variation in patients with bronchiectasis.

Methods

Selection of patients with bronchiectasis and CFTR mutation analysis using LightCycler (Roche) and Inno-Lipa (Innogenetics).

Mutations on InnoLipa CFTR19 en CFTR17 + Tn update strips with frequencies (%) in specified Dutch populations*

		cystic fibrosis patients**	bronchiectasis patients (n=22)	general population***
dF508	exon 10	73.6		
A455E	exon 9	3.3 - 3.5		
G542X	exon 11	1.3 - 2		
1717-1G/A	intron 10	1.5 - 1.8		
R553X	exon 11	1.2		
R1162X	exon 19	**1.1**	**9.1 (2)**	**0.03**
N1303K	exon 21	1		
S1251N	exon 20	0.5		
W1282X	exon 20	0.5		
R117H	exon 4	**0.4**	**4.5 (1)**	**0.01**
3659delC	exon 19	0.3		
R347P	exon 7	0.1		
D1507	exon 10	0.1		
G551D	exon 11	0.1		

*) The remaining 22 mutations on the InnoLipa strips are not present or present in lower frequencies.
**) see references 2
***) based on detection of 88.4% of CFTR mutations using InnoLipa strips with expected detection in Dutch population of 2.9% (Dutch carriership 1/30)

Results

- So far, in 22 patients with bronchiectasis 3 mutations (13.6%) have been found.
- The difference with the expected population frequency of CF mutations (3.3%) that can be detected with the assay (2.9%) is significant (Fisher exact $p<0.05$).
- One patient carried the R117H mutation and two patients carried the R1162X mutation. Both these mutations have [illegible] esp.) and CF patients (0.4 and 1.1, resp.).

Plaatje bronchiectasis

Chest CT?

Bronchiectasis:

abnormal stretching and enlarging of respiratory passages

50% of all cases result from cystic fibrosis

Pathogenesis:

blockage and accompanying infection may

weakening and widening of passages

scarring and deformation
infection and blocked airways

Etiology:

- cystic fibrosis
- lung infections
- abnormal host defense
- localized airway obstruction
- inflammation (granulomatous lung diseases, allergic aspergillosis)

Conclusion

Mutations in the CFTR gene predispose to the development of bronchiectasis. Enlargement of the patient population in the future should unveil whether this is primarily due to specific, rare CFTR mutations.

Acknowledgements

DNA diagnostics team: Marit Goossens-Geerdink, Robert van der Laan, Ati van der Lugt, Rik Temmink and Annette van der Vis

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2. Dequeker E, Cuppens H, Dodge J, Estivill X, Goossens M, Pignatti PF, Scheffer H, Schwartz M, Schwarz M, Tummler B, Cassiman JJ. Recommendations for quality improvement in genetic testing for cystic fibrosis, European concerted action on cystic fibrosis. Eur J Hum Genet 2000;8(Suppl 2):S2-24.
3. Van den Bergh HAJTM, Martens A. Diagnostiek van cystische fibrose; liever eenvoudige genotypering om de ziekte uit te sluiten dan starten met de zweettest. NTVG 2003 24 mei; 147(21):1001-5.

Genetic studies implicate altered regulation of natural killer (NK) cells in idiopathic bronchiectasis

- HLA-Cw*03 and HLA-C group 1 homozygosity associated with idiopathic bronchiectasis
- Analysis of relationship between HLA-C and KIR genes suggest a shift to activated NK cell activity

HLA-C and killer cell immunoglobulin-like receptor genes in idiopathic bronchiectasis. Boyton et al 2006 Am J Respir Crit Care Med 173, 327-333

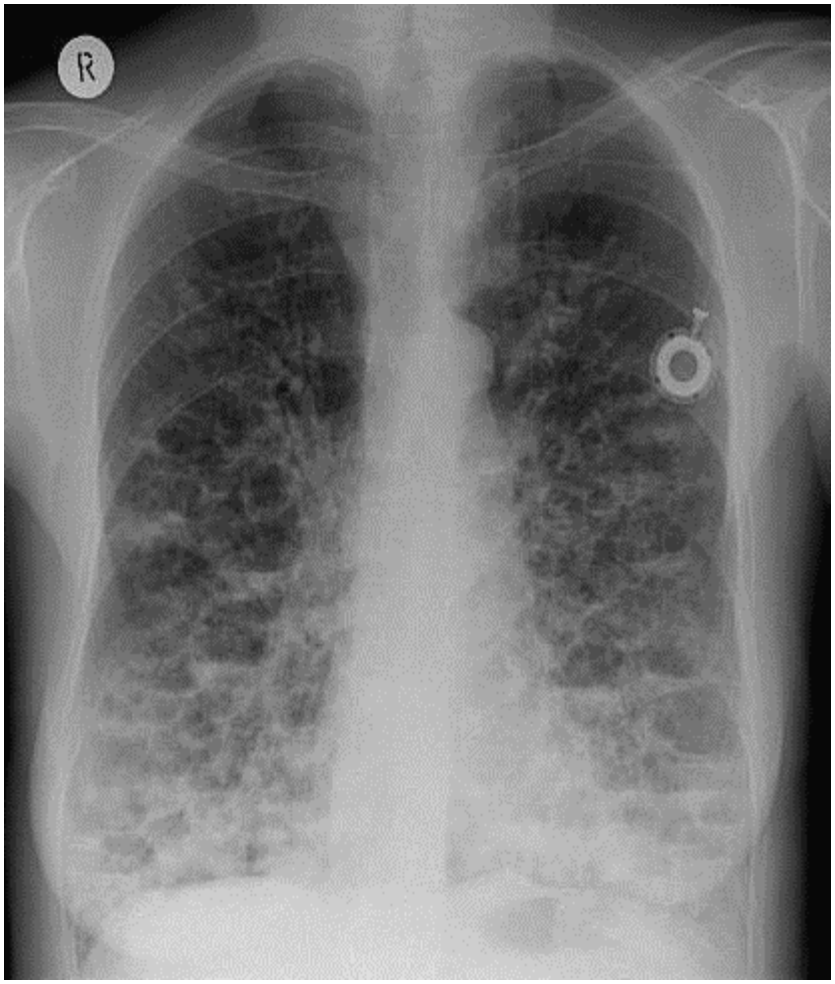
MRC Medical Research Council

Ziekteverwekker	**Aandoening**
Haemophilus influenzae *Staphylococcus aureus* (mucoïde) *Pseudomonas aeruginosa* *Burkholderia cepacia*	Cystic Fibrosis
Haemophilus influenzae *Staphylococcus aureus* *Pseudomonas-spp.*	Bronchiëctasieën
Haemophilus influenzae *Streptococcus pneumoniae* *Moraxella catarrhalis*	B-cel-deficiëntie
Pneumocystis jiroveci (voorheen *carinii*) herpesvirussen, respiratoir syncytieel-virus Candida, *Aspergillus* *Mycobacterium*-spp.	T-cel-deficiëntie
Staphylococcus aureus *Klebsiella pneumoniae* *E. coli* Candida, *Aspergillus*	Fagocytendisfunctie
Streptococcus pneumoniae *Haemophilus influenzae*	Complementdeficiënties

Radiographic diagnosis of bronchiectasis

"The diagnosis of bronchiectasis on the basis of CXR alone is uncertain unless the disease is extensive and severe…"

- CXR sensitivity 88%, specificity 75%
  - "A normal CXR almost always excludes relevant bronc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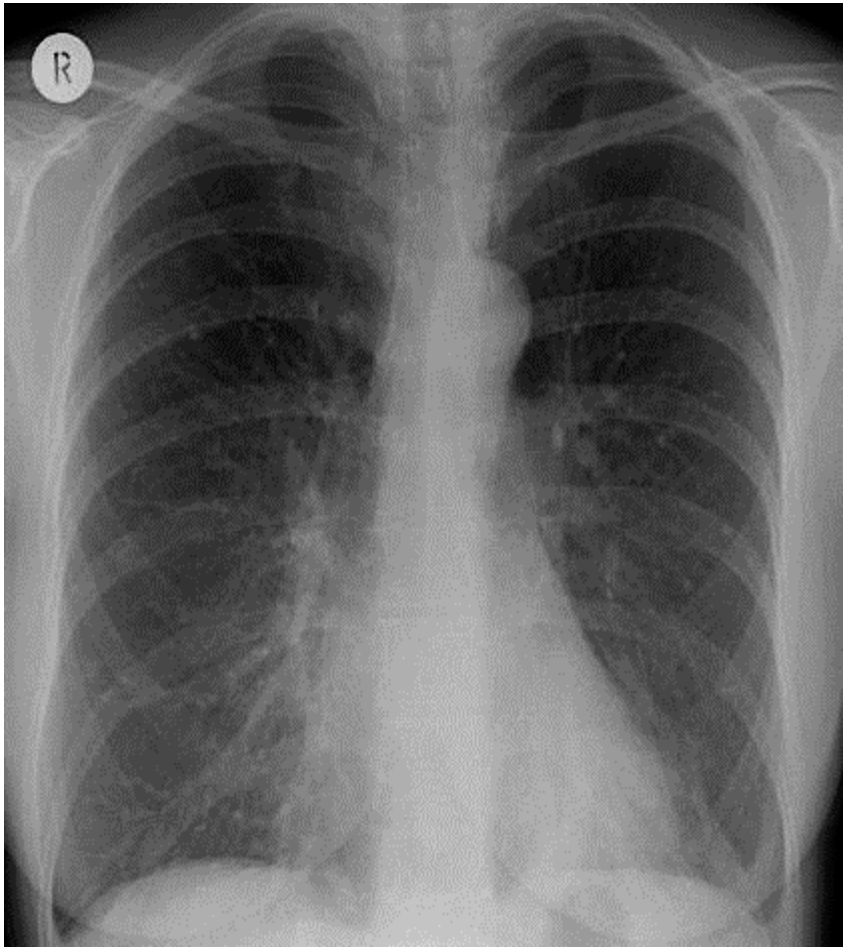

R

bronchiëctasieën

radiologische indeling:

- cylindrisch
- cystisch
- variceus

Reid LM. Reduction in bronchial subdivision in bronchiectasis. Thorax 1950;5:233-47

indeling

- **cylindrisch** oedeem en ontsteking, soms reversibel, intacte pulmonale circulatie
- **variceus** verwijd en met insnoeringen, pulm. circulatie kan ontbreken,bronchiale circulatie al meer op de voorgrond
- **sacculair/cystisch** zakvormig verwijd, ulceratie: bronchiale circulatie heeft pulmonale circulatie verdrongen
- tractiebronchiëctasieën bij fibrose

indeling

bronchial dilatation as compared with the diameter of the adjacent pulmonary artery is divided into three categories

- **normal: < 110 %**
- **mild: 110-150%**
- **severe: > 150 %.**

The luminal diameter of the bronchus as compared with the total diameter of the bronchus is also divided in three categories:

- **normal > 80 %**
- **mild 80 -50%**
- **severe <50 %**

HRCT criteria for bronchiectasis

MAJOR

- Lack of tapering or flaring (long axis)
- “Signet ring” sign (short axis)

MINOR

- Bronchi visible in outer third of lung
- Crowding of bronchi
- Mucus plugging (large or small airways)
- Areas of decreased attenuation (mosaicism)

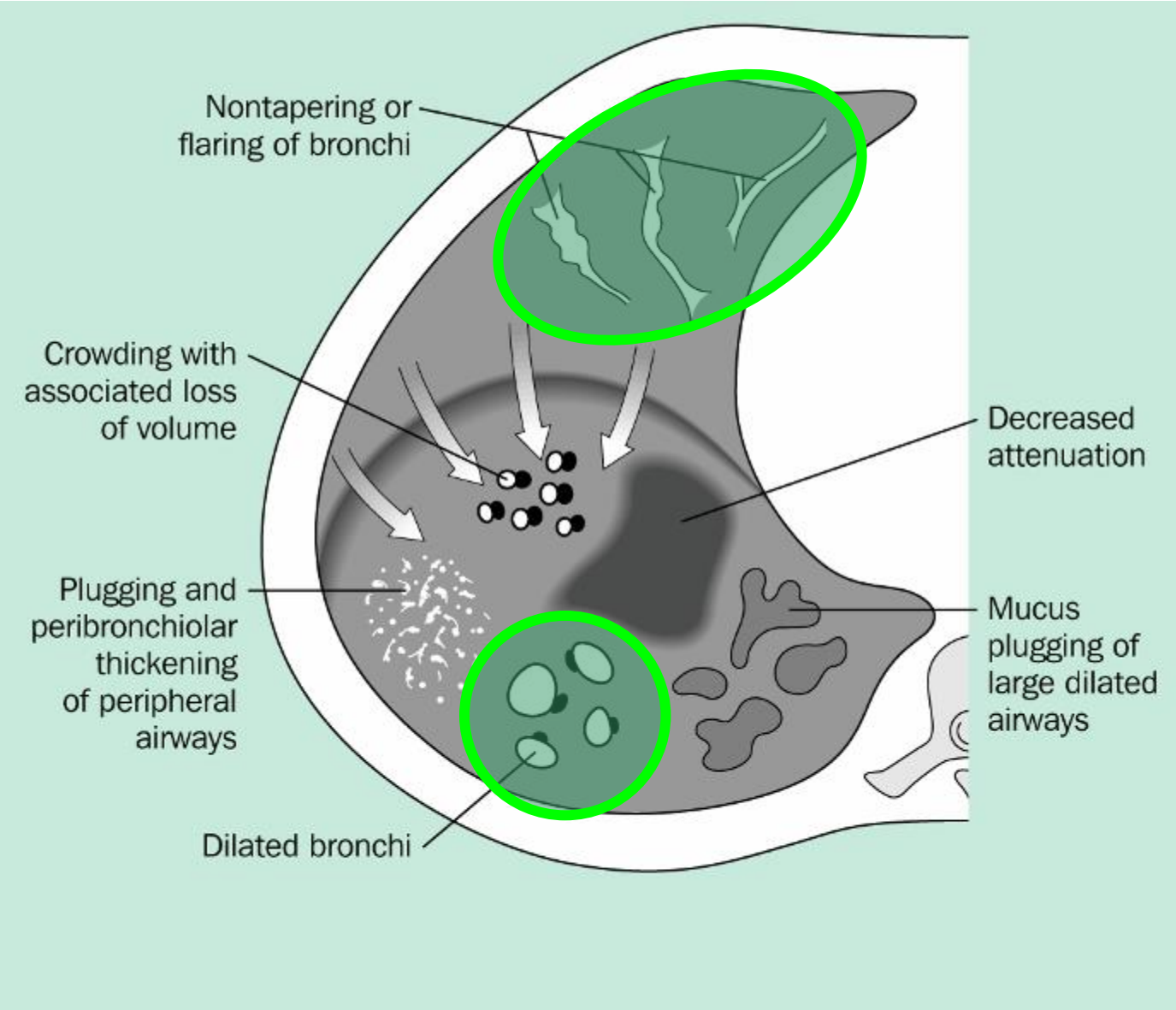
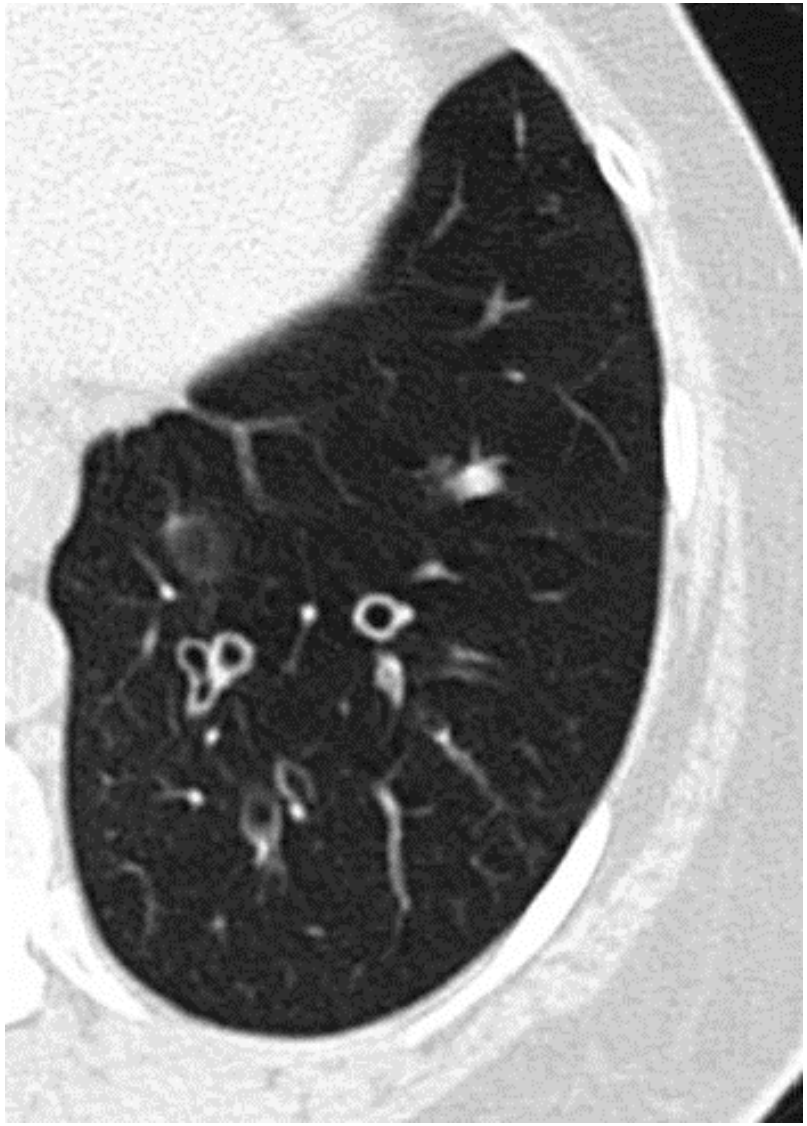
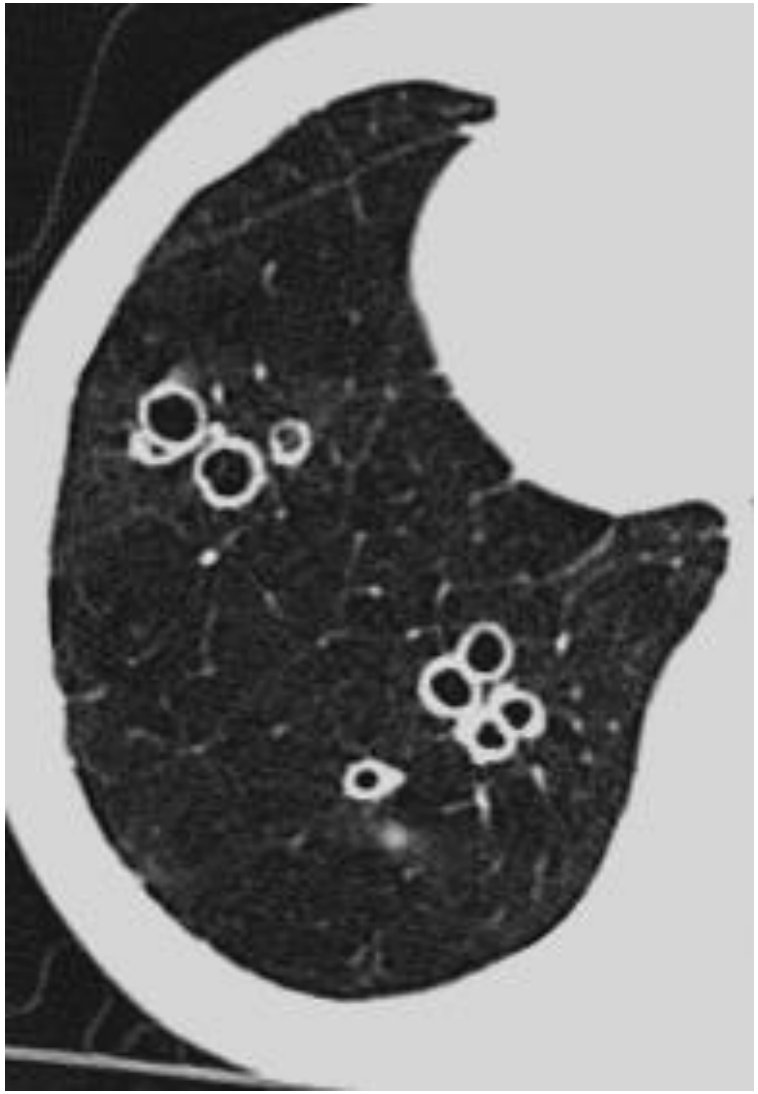

Nontapering or flaring of bronchi
Crowding with associated loss of volume
Plugging and peribronchiolar thickening of peripheral airways
Dilated bronchi
Decreased attenuation
Mucus plugging of large dilated airways

Table 2
Bronchiectasis based on distribution

Location	Disease
Focal	Congenital bronchial atresia
	Foreign body
	Broncholithiasis
	Endobronchial neoplasm
Diffuse	
Upper lung	Cystic fibrosis
	Sarcoidosis
	Progressive massive fibrosis of pneumoconiosis
	Radiation fibrosis
Central lung	Allergic bronchopulmonary aspergillosis
	End-stage hypersensitivity pneumonitis (also upper lobes)
	Mounier-Kuhn (also lower lobes if repeated infections)
Lower lung	Usual interstitial pneumonia (IPF)
	Nonspecific interstitial pneumonitis
	Hypogammaglobulinemia
	Lung and bone transplantation
	Chronic aspiration
	Idiopathic
Right middle lobe and lingula	Atypical mycobacterial infection
	Immotile cilia syndrome (PCD) (also lower lobes)





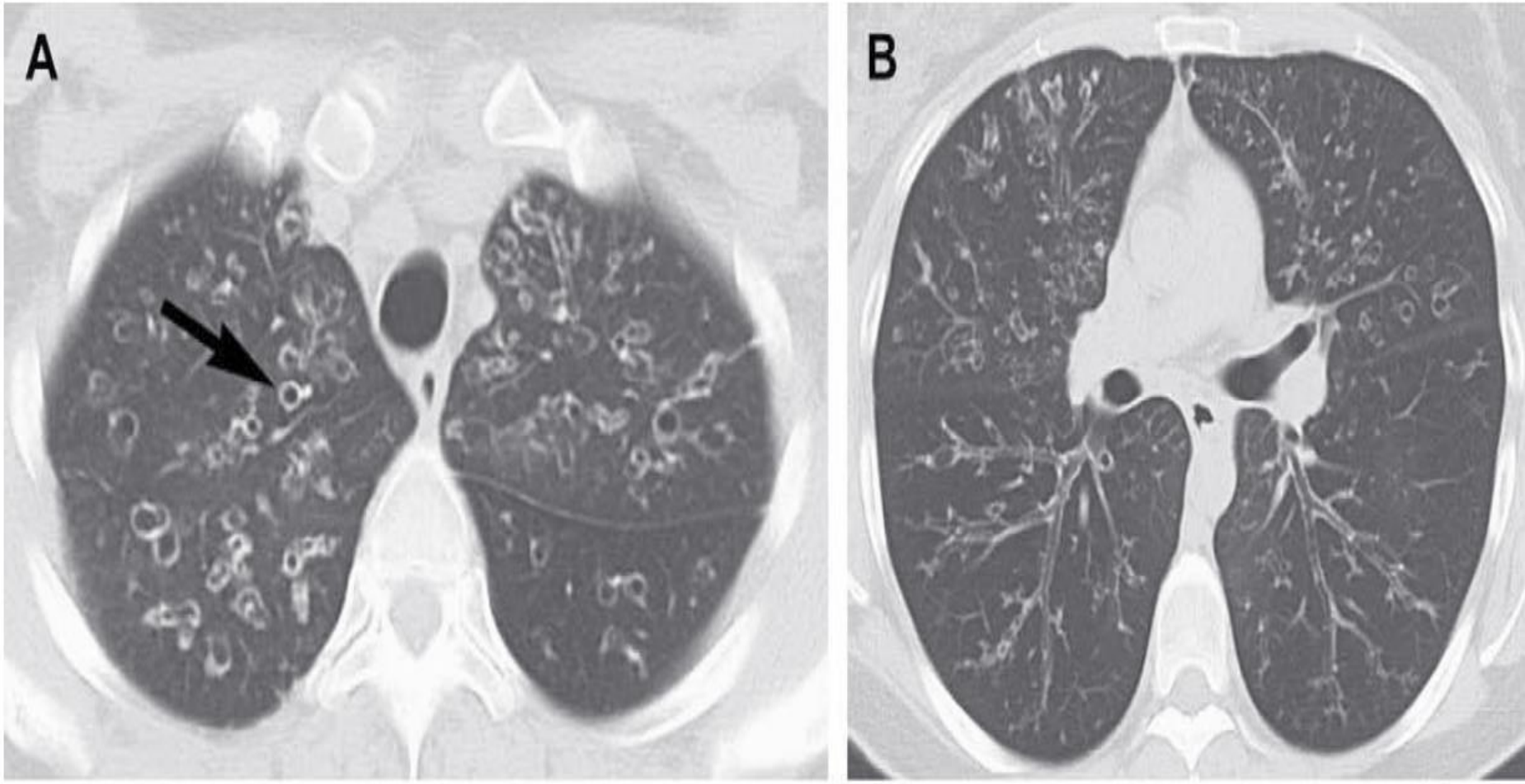


Fig. 7. CT findings of diffuse bronchiectasis in a 27-year-old woman with cystic fibrosis. Transaxial images show the dilated bronchus and adjacent arteriole, seen along their short axis, creating the signet ring sign (*arrow*) (*A*). When the bronchi are visualized along their course, the lack of normal tapering and smooth bronchial wall thickening can be appreciated (*B*). In cystic fibrosis the fatty attenuation of the pancreas is indicative of the pancreatic insufficiency (*C*).

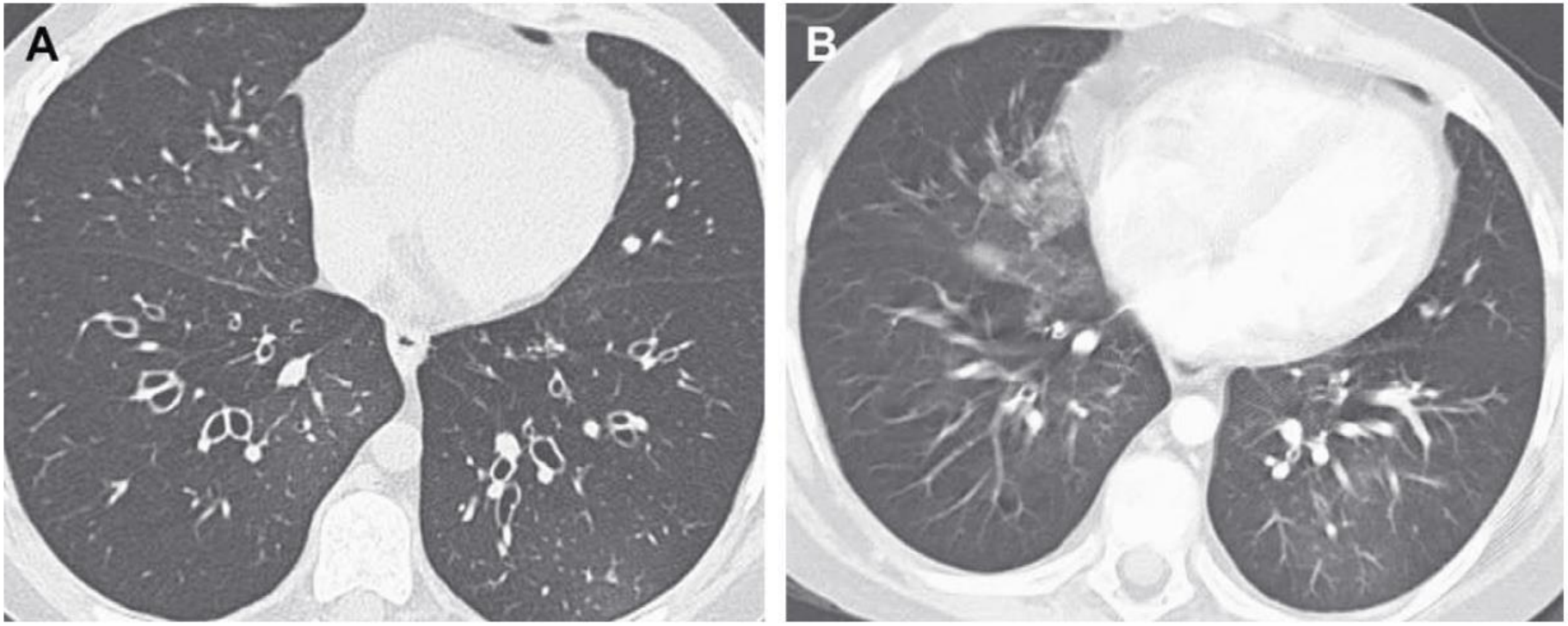
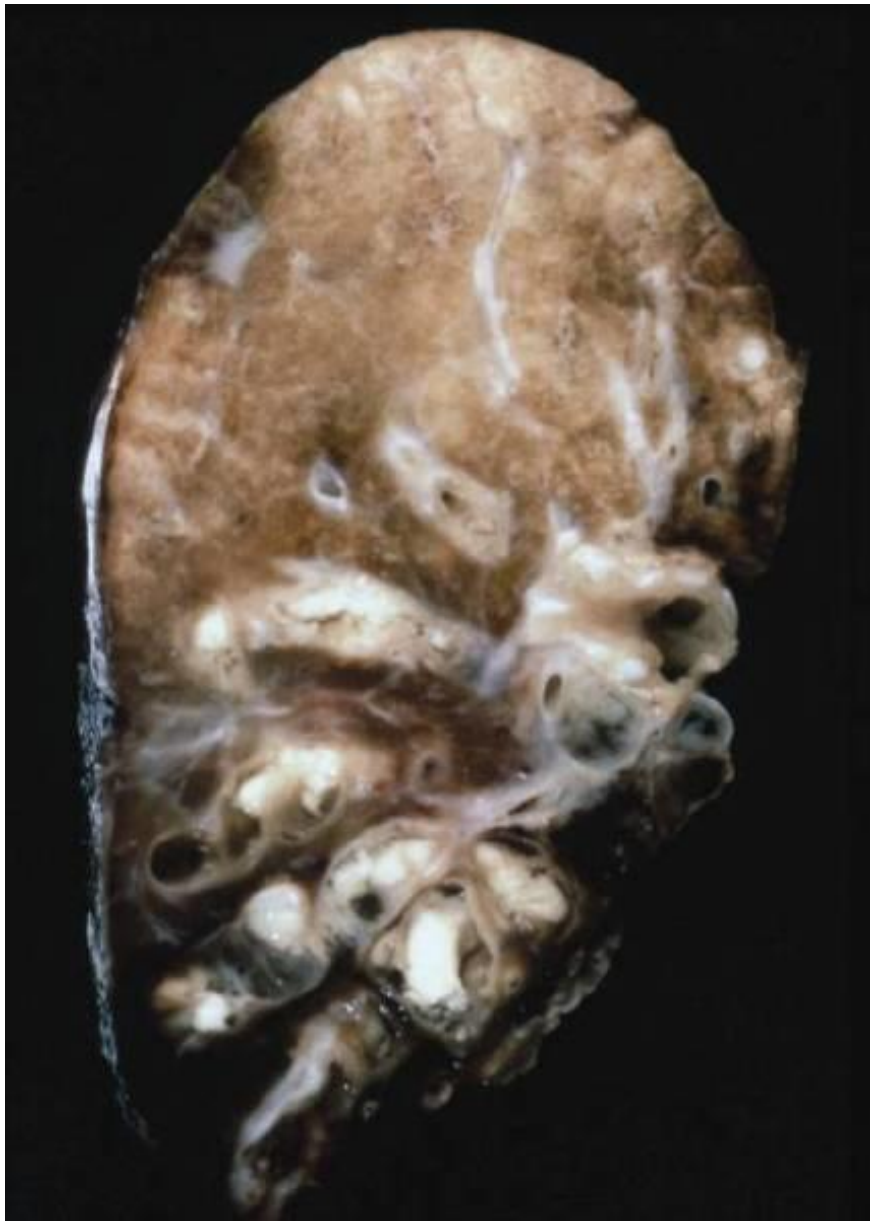
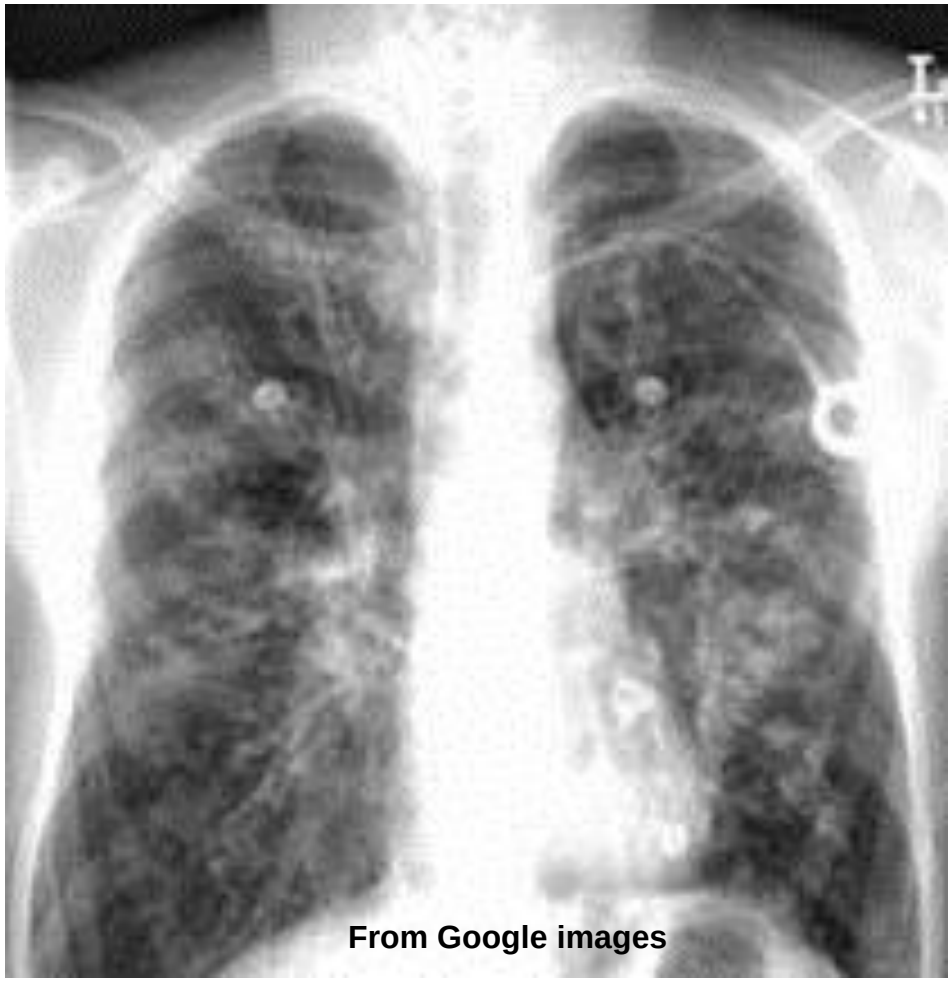


Fig. 1. Reversible lower lobe bronchial dilatation due to pneumonia. Initial CT (*A*) in this 12-year-old girl with hypogammaglobulinemia and pneumonia showed bilateral dilated lower lobe bronchi. Subsequent CT (*B*) performed 6 months later showed resolution of the bronchial dilatation, although it revealed a right middle lobe pneumonia. Because this dilatation is reversible, it would not qualify as bronchiectasis.

CYSTIC FIBROSIS





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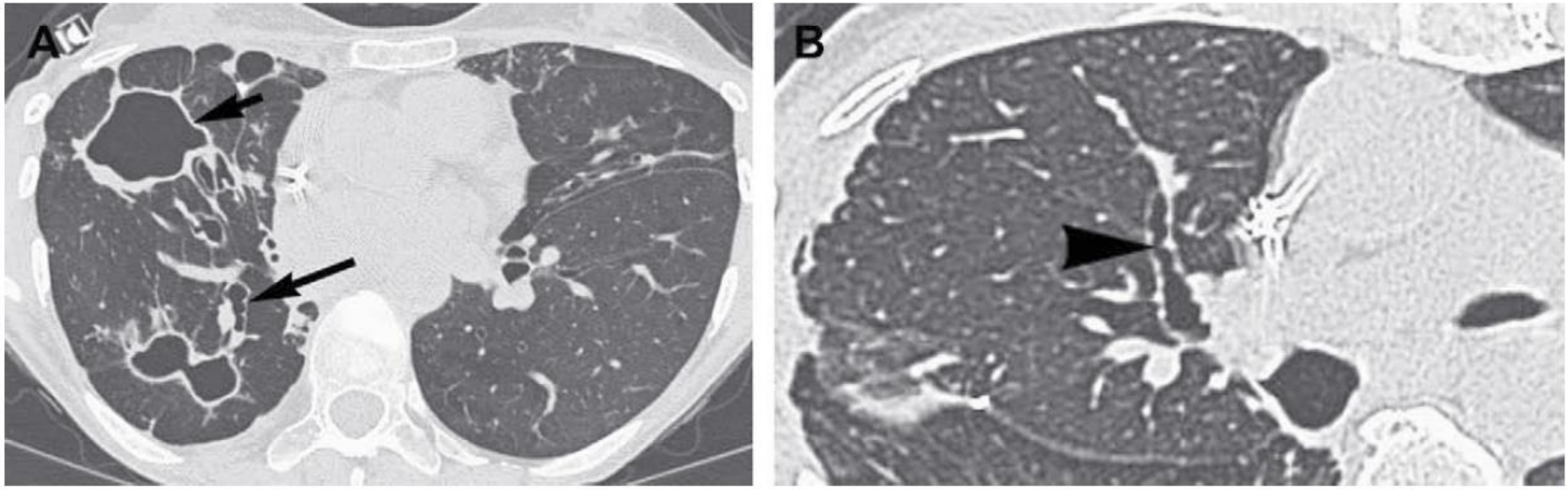


Fig. 8. CT findings of varicose and cystic bronchiectasis. CT images from the same patient as in **Fig. 6** show a more severe form of bronchiectasis, where both varicose (*long arrow*) and cystic (*short arrow*) bronchiectasis is present (*A*). In varicose bronchiectasis, the bronchial lumen has a beaded appearance and nodular wall thickening is seen (*arrowhead*) (*B*).

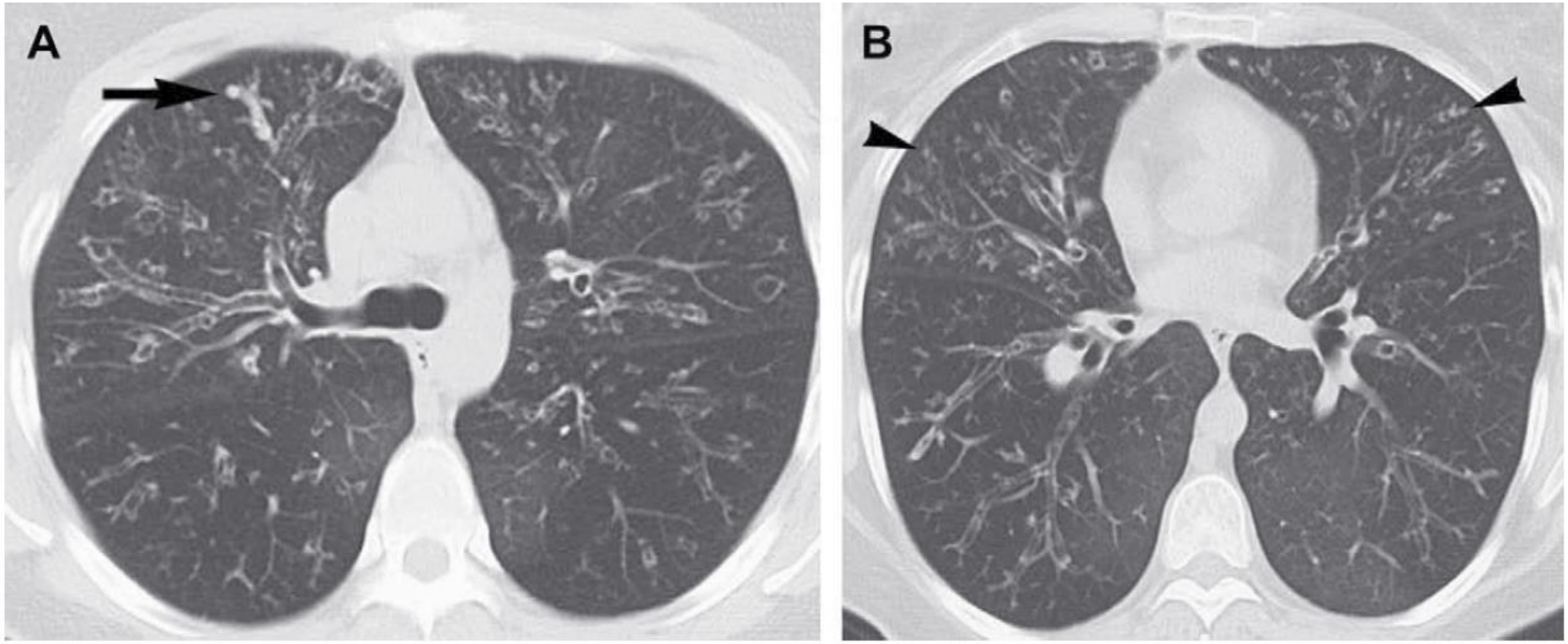
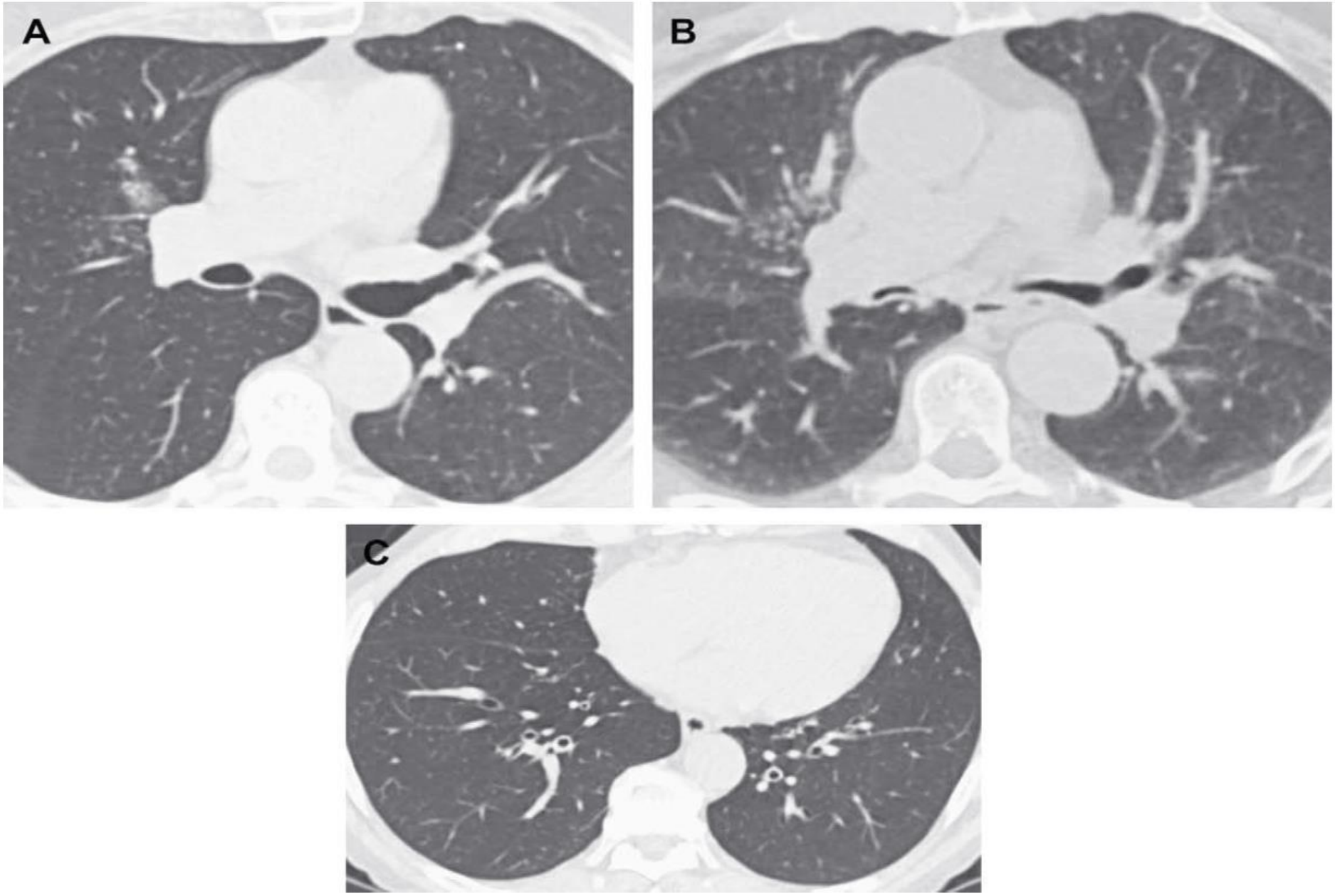


Fig. 11. Mucus plugging on CT. On transaxial images, the filling of bronchiectasis by mucus appears as tubular and branching opacities, with club-like, rounded ends (*arrow*) (*A*). The mucus-filled smaller branching bronchi and bronchioles appear as tree-in-bud opacities (*arrowheads*) (*B*). The mosaic attenuation of the surrounding lung is due to air trapping. In this case, the bronchiectasis was from cystic fibrosis.



ig. 12. Bronchomalacia and bronchiectasis: a 68-year-old man with a reported history of asthma nonresponsive to teroid therapy. CT images show a normal caliber of the central bronchi (*A*), and marked collapse of their lumina when imaged during forced exhalation (*B*), consistent with bronchomalacia. The distal bronchi are diffusely ilated and have smooth wall thickening, consistent with mi

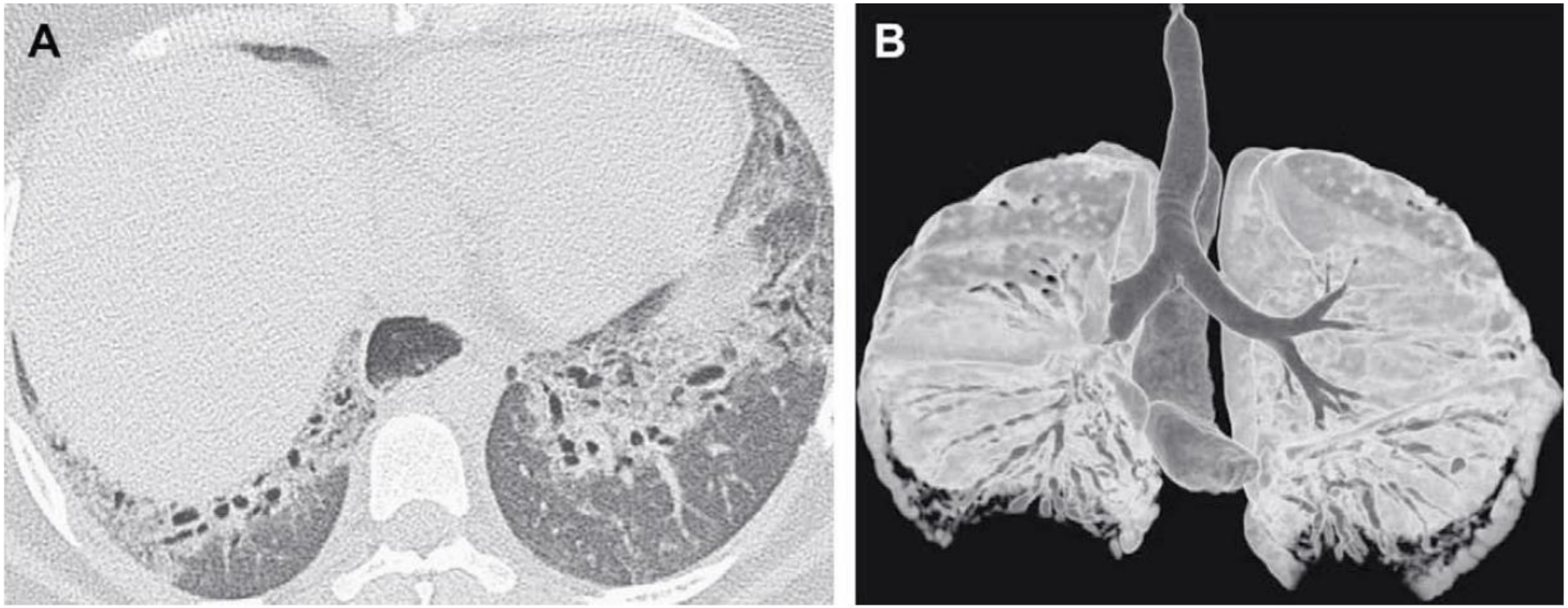


Fig. 13. Bronchiectasis out of proportion of surrounding fibrosis. Transaxial CT of the chest of a 34-year-old woma with scleroderma shows a dilated esophagus, basilar pulmonary fibrosis, and significant bronchiectasis withou evidence of honeycombing (*A*). The volume-rendered image demonstrates the extent of the bronchiectasis (*B* and the markedly dilated esophagus.

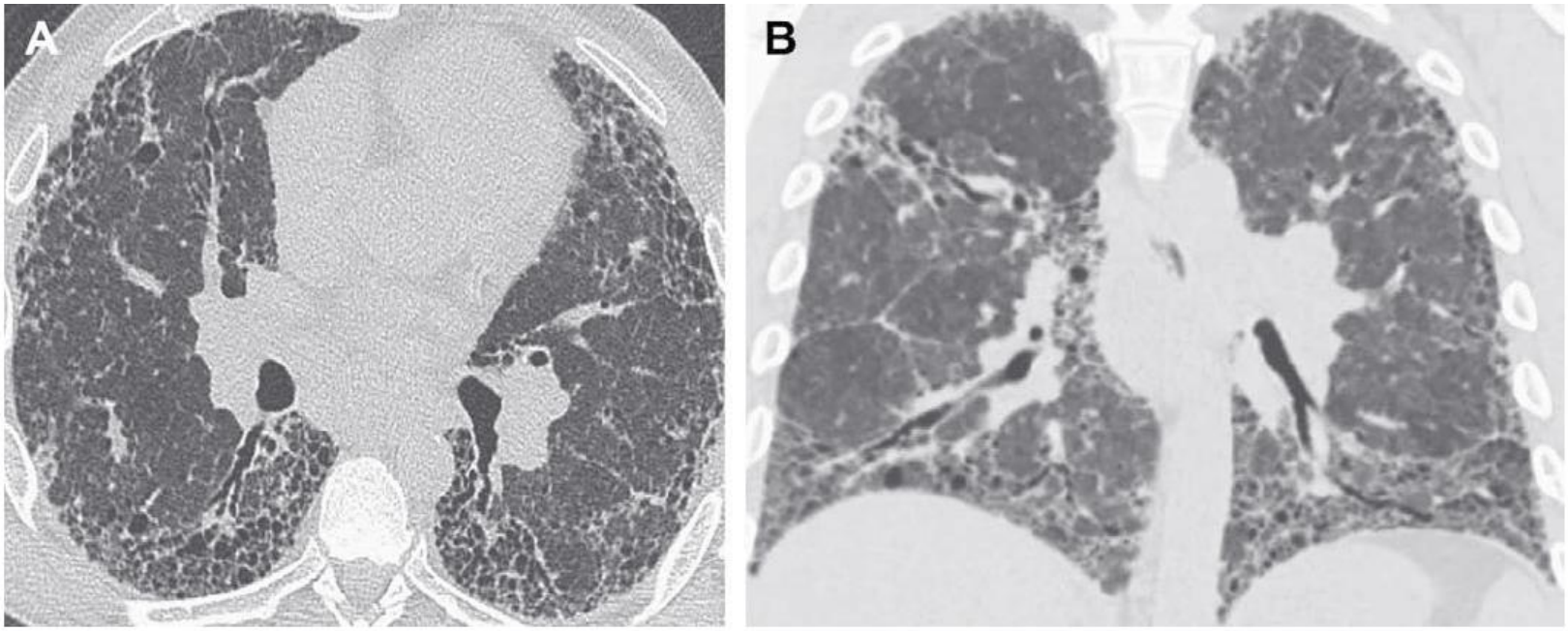


Fig. 4. Lower lobe traction bronchiectasis from usual interstitial pneumonitis. Transaxial image at the level of the superior segmental bronchi (*A*) demonstrates traction bronchiectasis, within peripheral-dominant honeycombing in this 52-year-old man with idiopathic pulmonary fibrosis. Coronal reformatted image (*B*) shows that the basilar and peripheral bronchiectasis follows the distribution of the fibrosis.

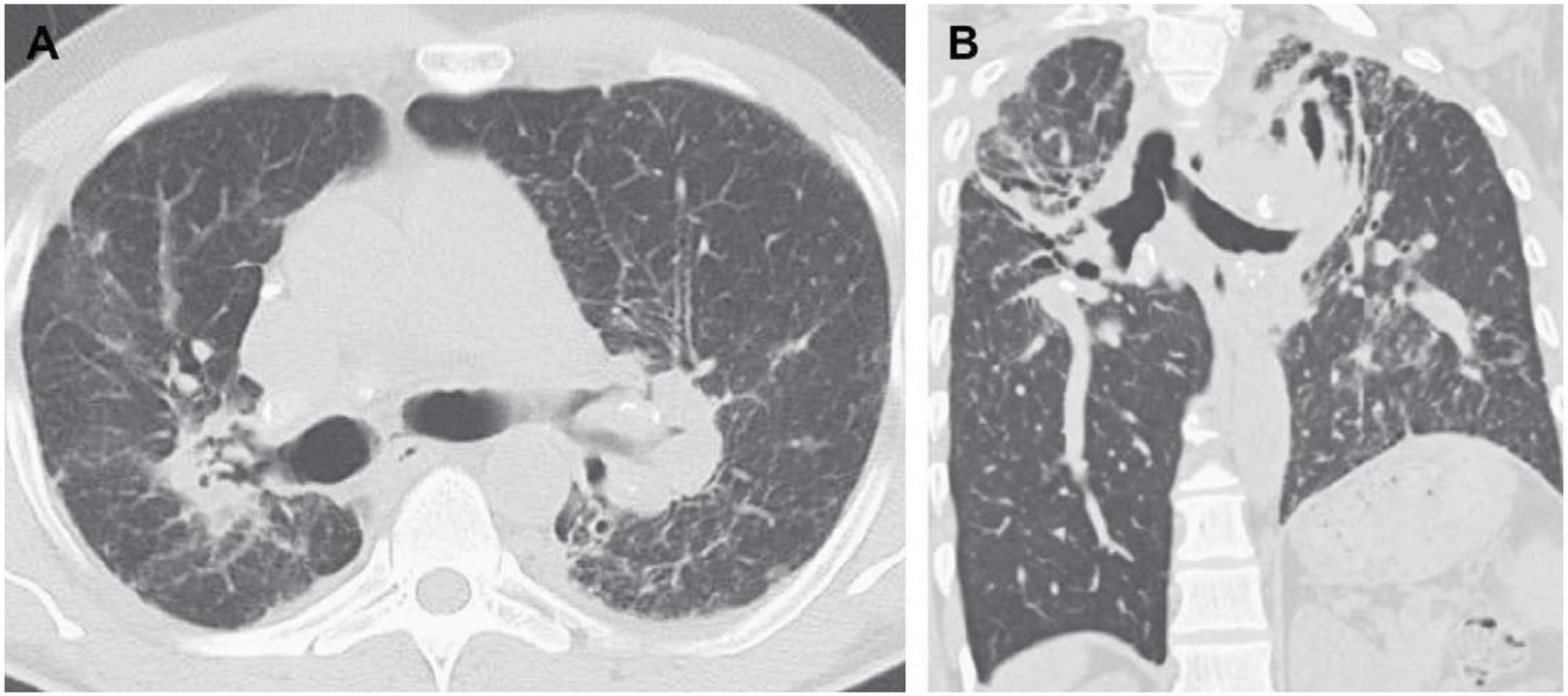


Fig. 3. Upper lobe traction bronchiectasis from end-stage sarcoid. Transaxial image at the level of the carina (*A*) demonstrates tortuous, shortened bronchi amidst upper lobe fibrosis and volume loss. Upper lobe predominance of the bronchiectasis is better appreciated on coronal reconstruction (*B*).

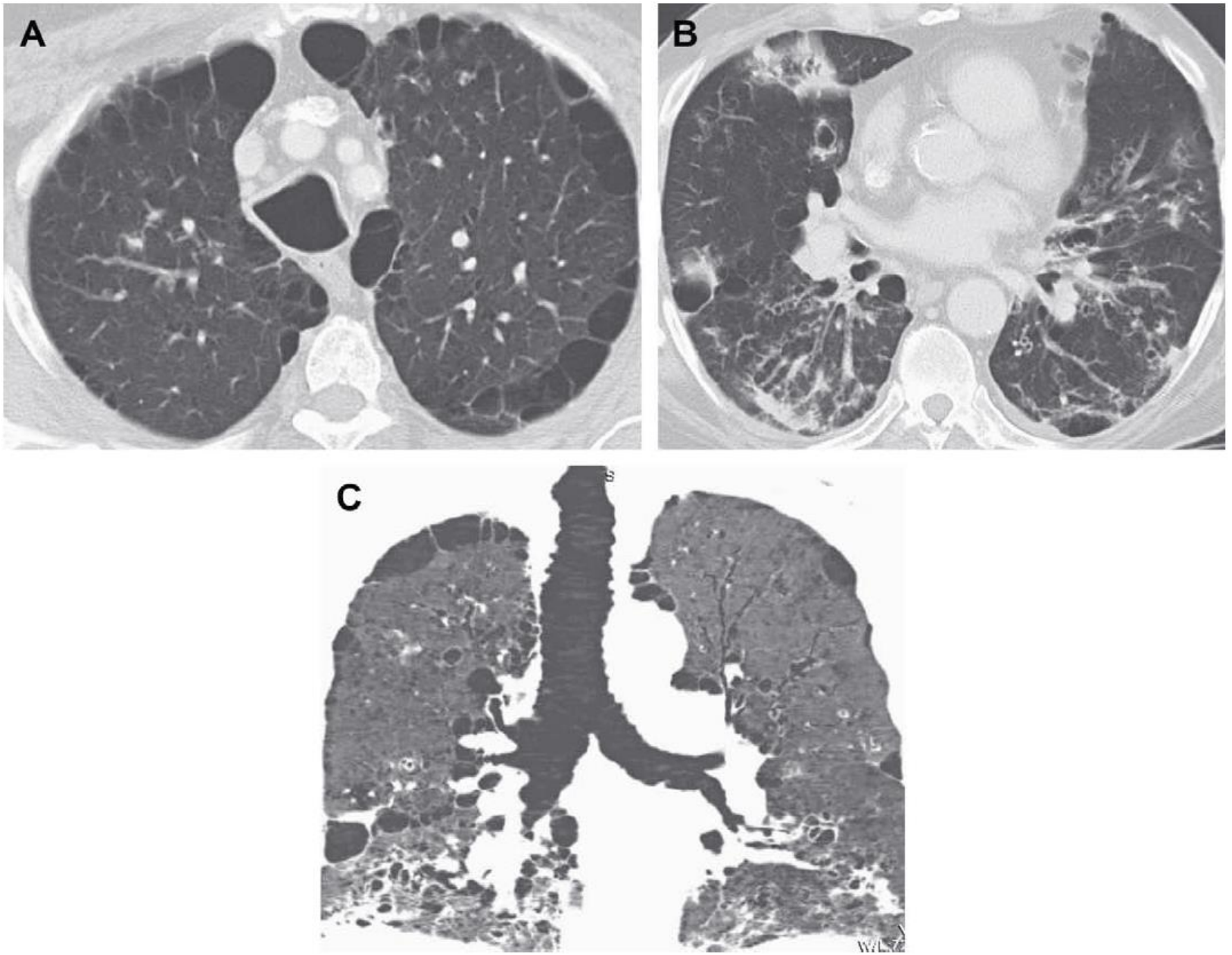


Fig. 14. Mounier-Kuhn Syndrome. Transaxial CT images show tracheomegaly (*A*), and basilar-predominant varicose and cystic bronchiectasis (*B*) seen in Mounier-Kuhn syndrome. The coronal reconstructed image demonstrates the typical corrugated appearance of the tracheal wall (*C*).

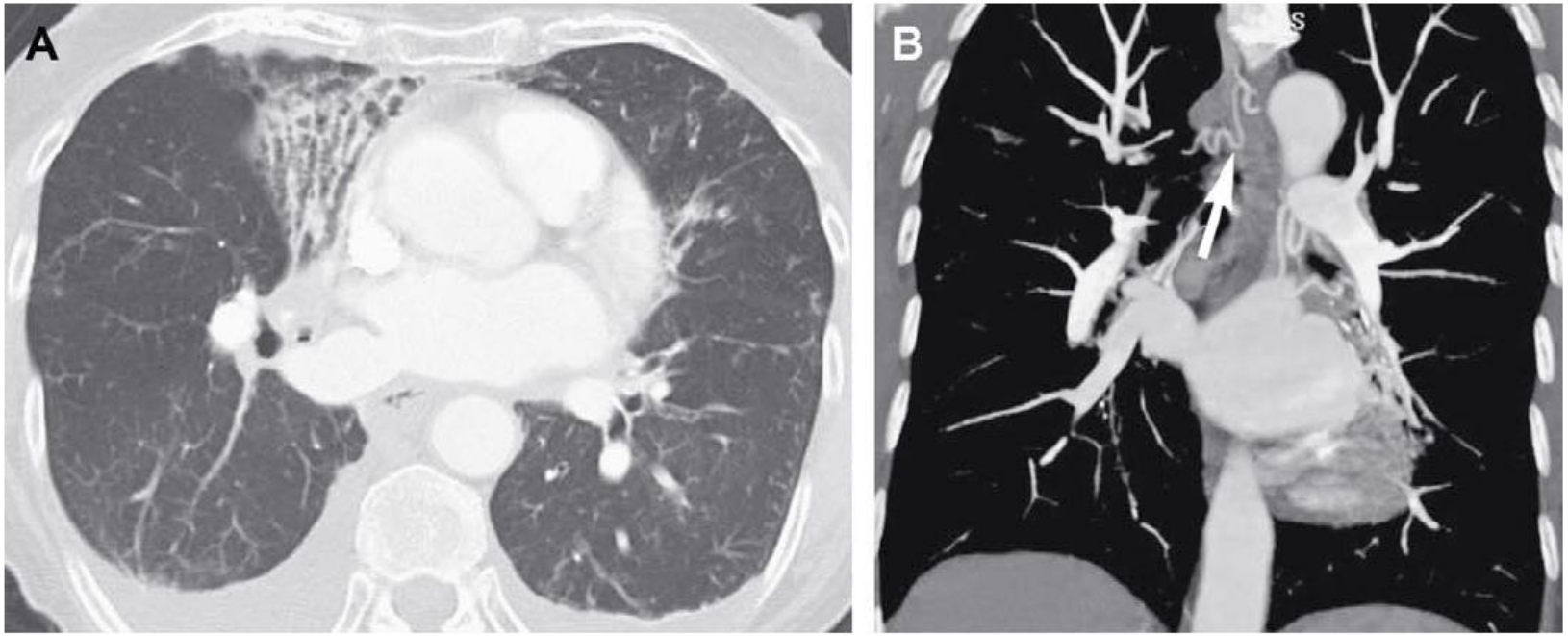


Fig. 18. Bronchial artery collateral formation in bronchiectasis: a 76-year-old woman with chronic productive cough has new-onset of severe, recurrent hemoptysis. CT of chest with intravenous contrast shows severe bronchiectasis and scarring of the right middle lobe (*A*). The dilated bronchial arteries (*white arrow*) providing collateral flow to the lungs are better demonstrated on the coronal thin-MIP (6 mm) reformatted image (*B*).

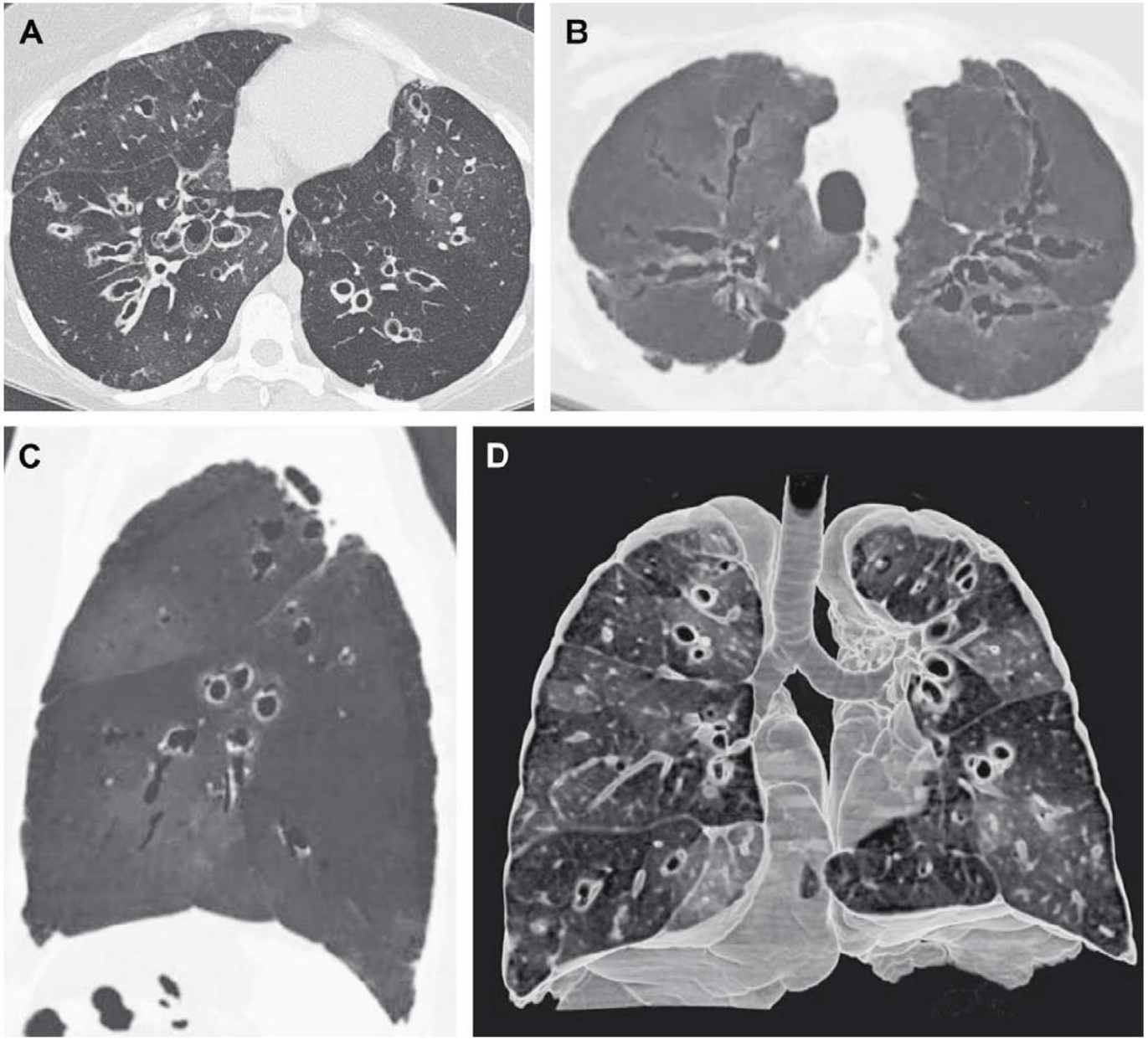


Fig. 21. Primary ciliary dyskinesia: a 37-year-old woman with primary ciliary dyskinesia and chronic pseudomonas aeruginosa infection being evaluated for bilateral lung transplantation. HRCT of chest (*A*) shows mixed tubular, varicose, and cystic bronchiectasis. Minimal intensity reformatted images in axial (*B*) and sagittal (*C*) planes and volume-rendered image (*D*) demonstrate the extent of bronchiectasis and the associated mosaic attenuation.

Behandeling

Een exacerbatie bij een antimicrobiële therapie, waarbij de keuze van het antibioticum afhankelijk is van de verwachte ziekteverwekker en de resistentiegegevens (niveau 4)

Richtlijn Diagnostiek en antimicrobiële behandeling van recidiverende lagereluchtweginfecties, 2005

TABLE 4. SYMPTOMS OF ACUTE EXACERBATION OF BRONCHIECTASIS.*

Change in sputum production
Increased dyspnea
Increased cough
Fever (temperature, >38.0°C)
Increased wheezing
Malaise, fatigue, lethargy, or decreased exercise tolerance
Reduced pulmonary function
Radiographic changes consistent with a new pulmonary process
Changes in chest sounds

*In a study by O'Donnell et al.,[69] a patient with four of these symptoms was defined as having an acute exacerbation.

Prolonged antibiotics for purulent bronchiectasis

- **6 randomised placebo controlled trials from 447 abstracts reviewed**
- **4 weeks or more**
- **2 nebulised, 4 oral**
- **Limited meta analysis**
- **“Response rate” significant for antibiotics**
- **Exacerbation rate and lung function NS**

Cochrane review Evans, Bara, Greenstone 2005

Antibiotic prophylaxis in bronchiectasis

consider if

Management otherwise optimal

3 sputum samples negative for AFB

Frequent oral antibiotics >6/year

and rapid relapse after iv without an explanation

>2 hospital admissions per year

Cochrane review Evans, Bara, Greenstone 2005

INHALED CORTICOSTEROIDS IN BRONCHIECTASIS

Fluticasone 500mg bd versus placebo

No effect on exacerbation frequency or FEV_1

Reduced sputum volume in sub-groups (Pseudomonas)

Fluticasone 500mg bd versus 250mg bd versus no treatment

No effect on exacerbation frequency or FEV_1

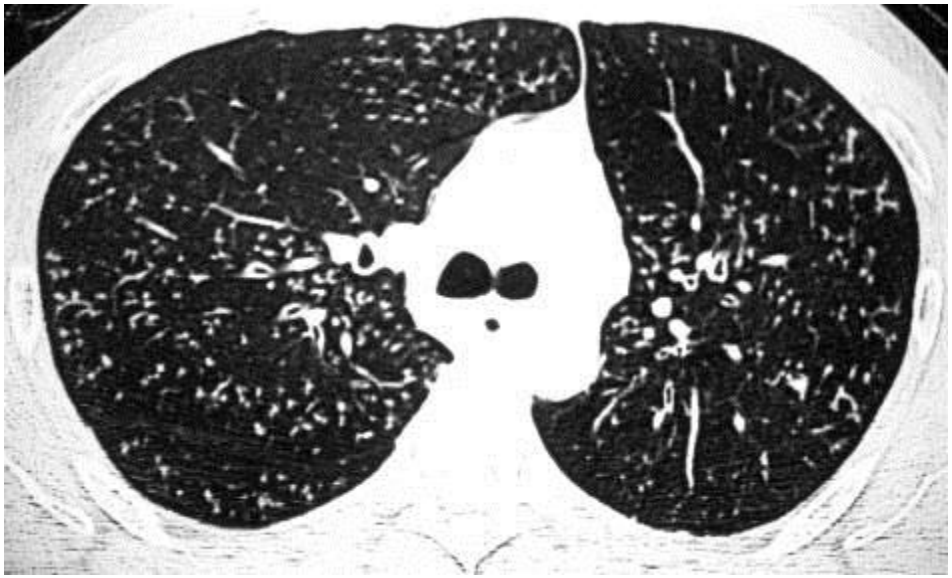
Improved QOL with higher dose

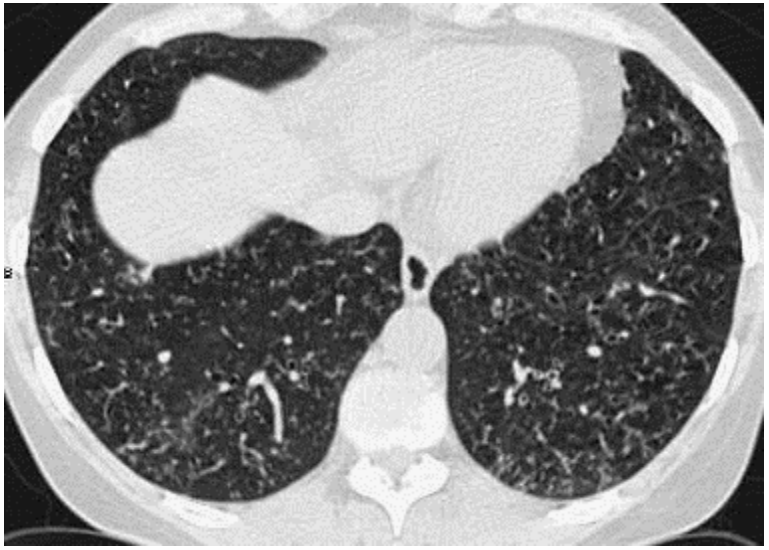
Tsang et al Thorax 2005
Martinez-Garcia et al Resp Med 2006

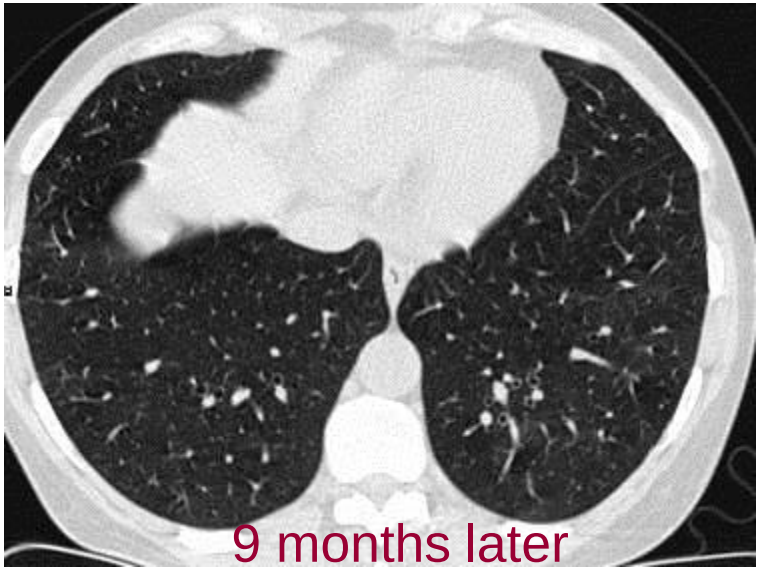
behandeling

- voorafgaand sputumkweek
- gebruikelijke dosering
- 10-14 dagen
- onderhoudsbehandeling bij bronchiëctasieën en Ps. aeruginosa bij voorkeur geïnhaleerde antibiotica
- alleen onderhoudsbehandeling continueren bij afname klachten, verbetering longfunctie
- marolide? geen literatuur alleen bij CF
- alles niveau 4

Richtlijn Diagnostiek en antimicrobiële behandeling van recidiverende lagereluchtweginfecties, 2005







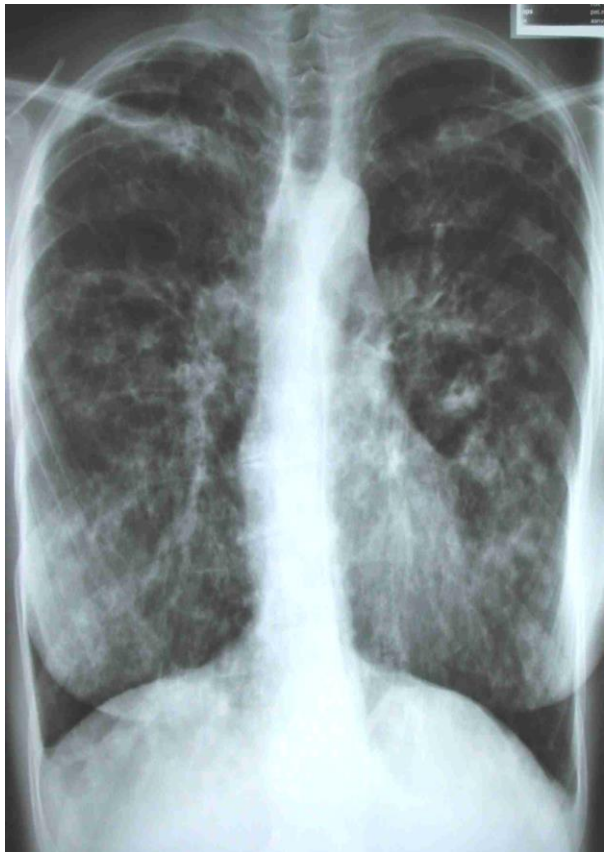
voor en na azithromycine

behandeling

chirurgisch: alleen bij gelokaliseerde afwijkingen

NB voor operatie: beoordeling recidiefkans

casus

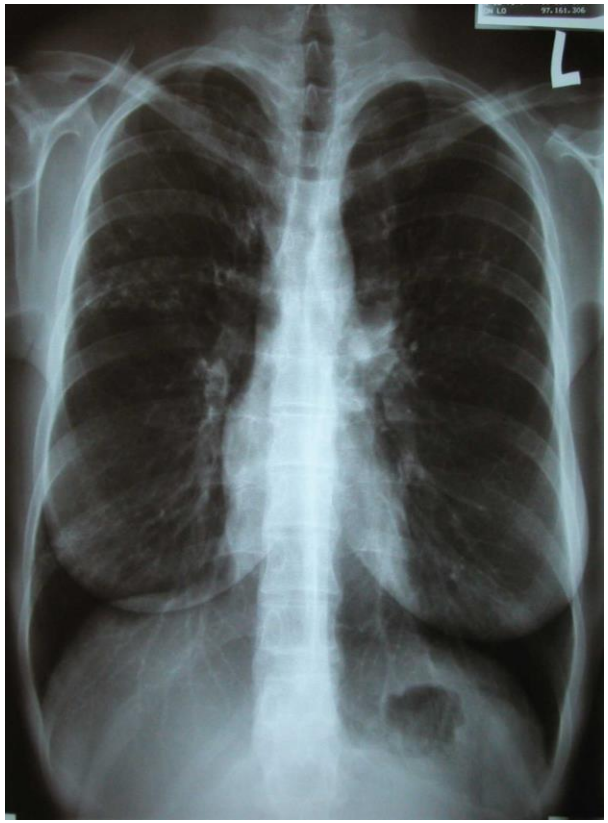


ΔF508/A455E

P.K. 29-9-1972
Diagnosis at 1 year
Malabsorption
Ps.Aeruginosa
P.I. (PEG feeding)
46kg 1.72m
FEV1 : 23 %
Suppl. Oxygen
Waiting for LX

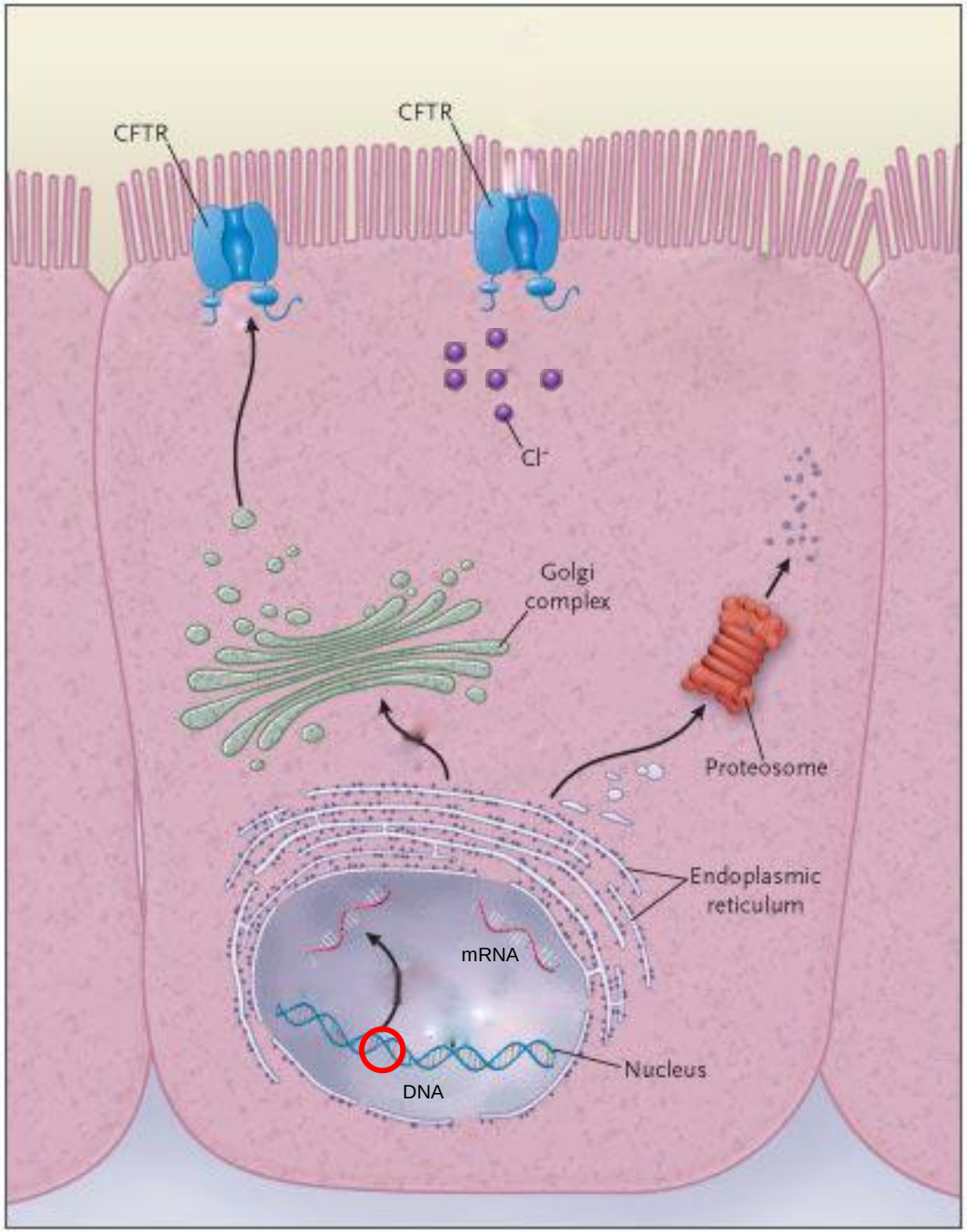
R.L 06-12-1971
Diagnosis at 18yrs
Recurrent pulm infection
Staph aureus
P.S.
70kg 1.76m
FEV1 : 103%

ΔF508/ΔF508



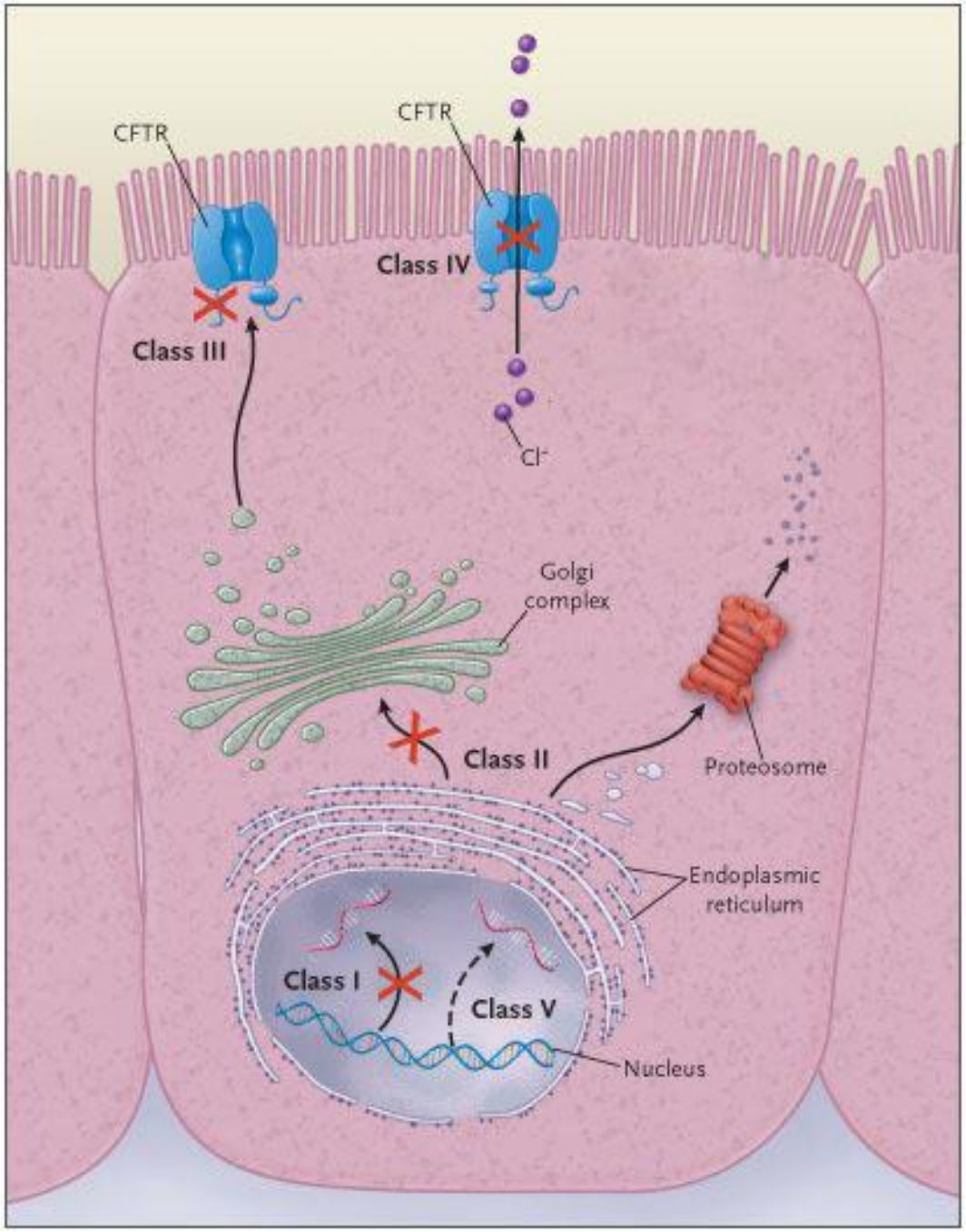
CFTR

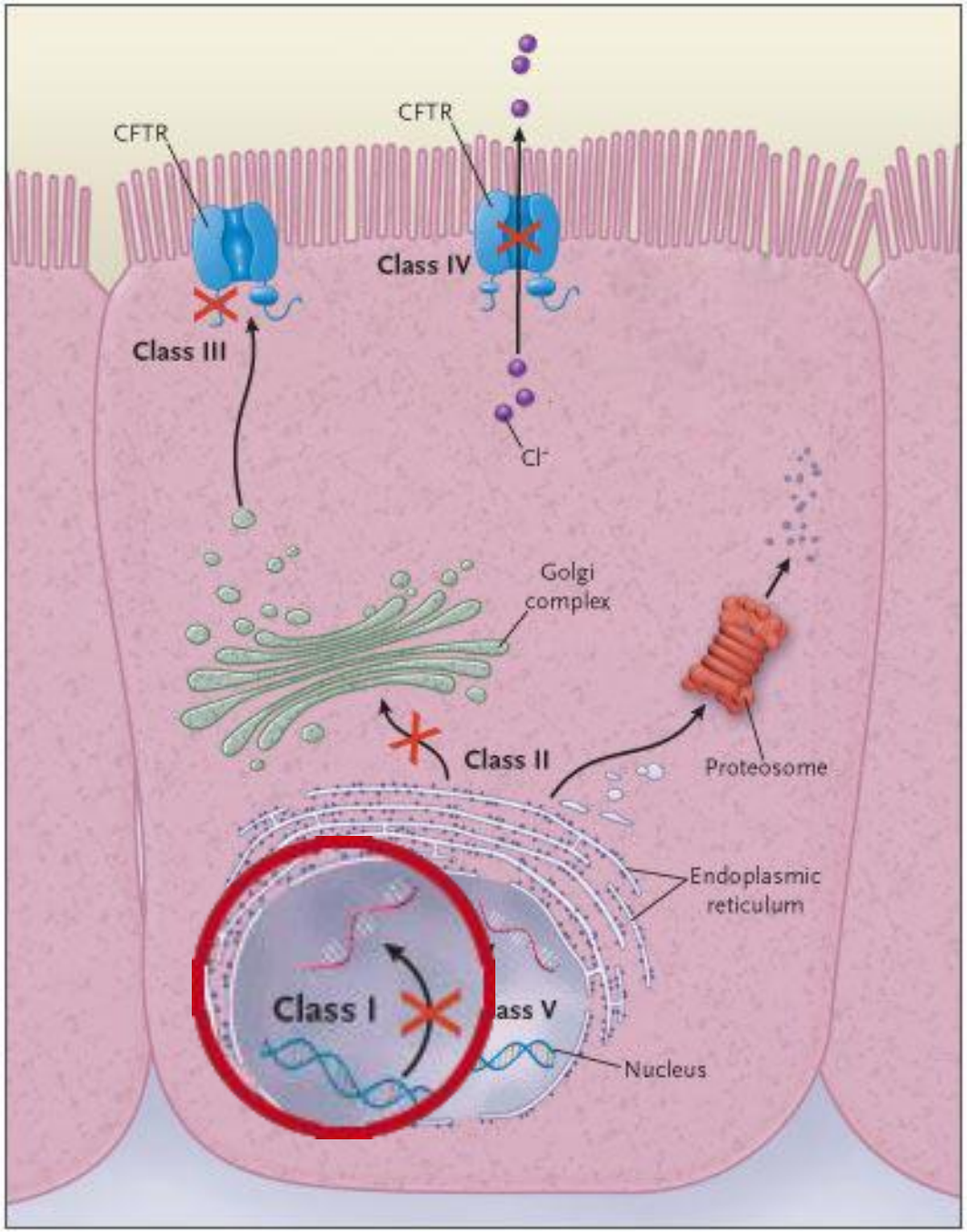
- CFTR= cystic fibrosis transmembrane conductor regulator, chromosoom 7,70% deltaF508
- Regelt transport chloorionen over de celmembraan
- CFTR reguleert chloor-kanaal en andere kanalen
- Stoornis in eiwit folding



Adapted from:

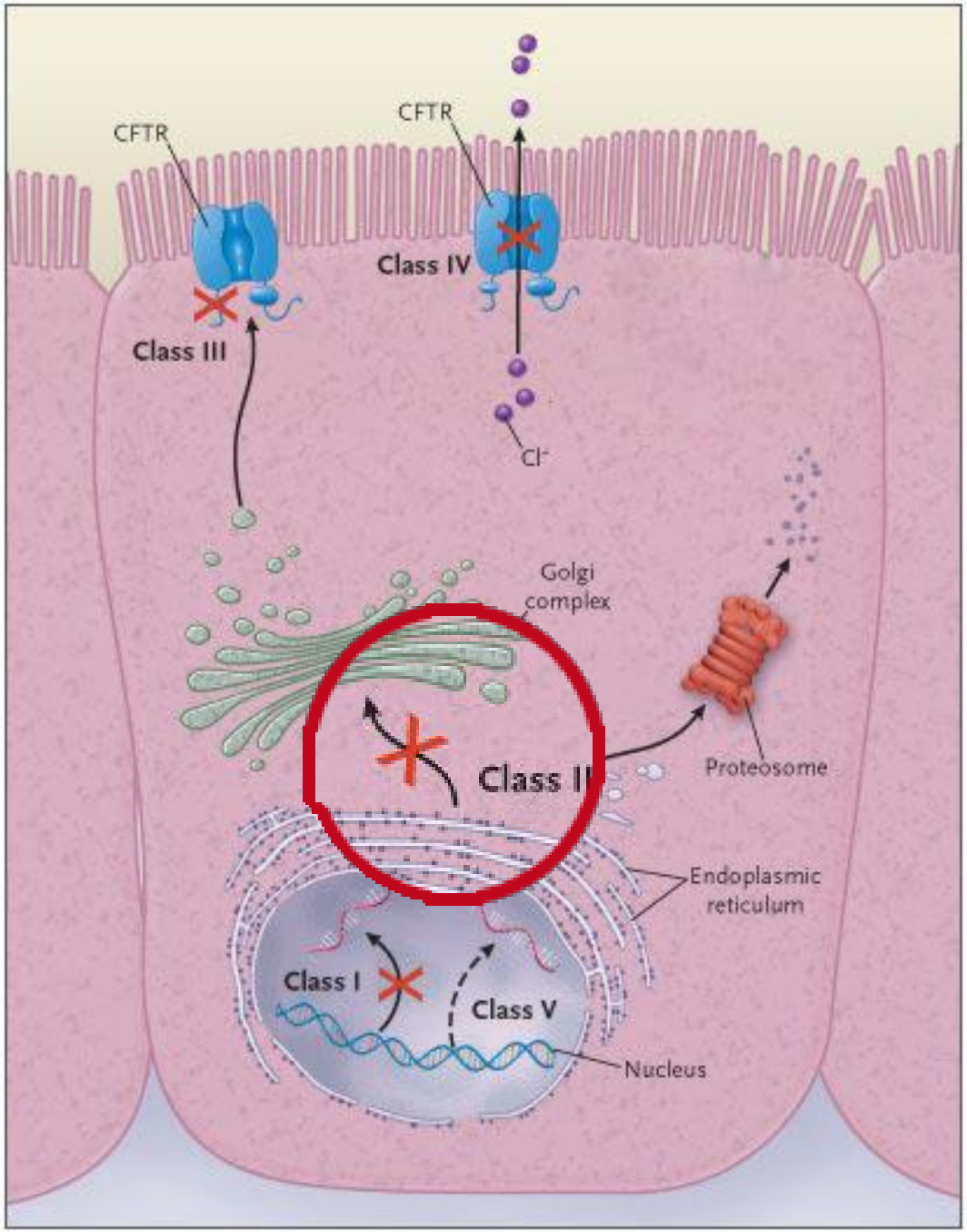
Rowe, N Eng J Med 2005


CFTR
CFTR
Class IV
Class III
Cl⁻
Golgi complex
Class II
Proteosome
Endoplasmic reticulum
Class I
Class V
Nucleus



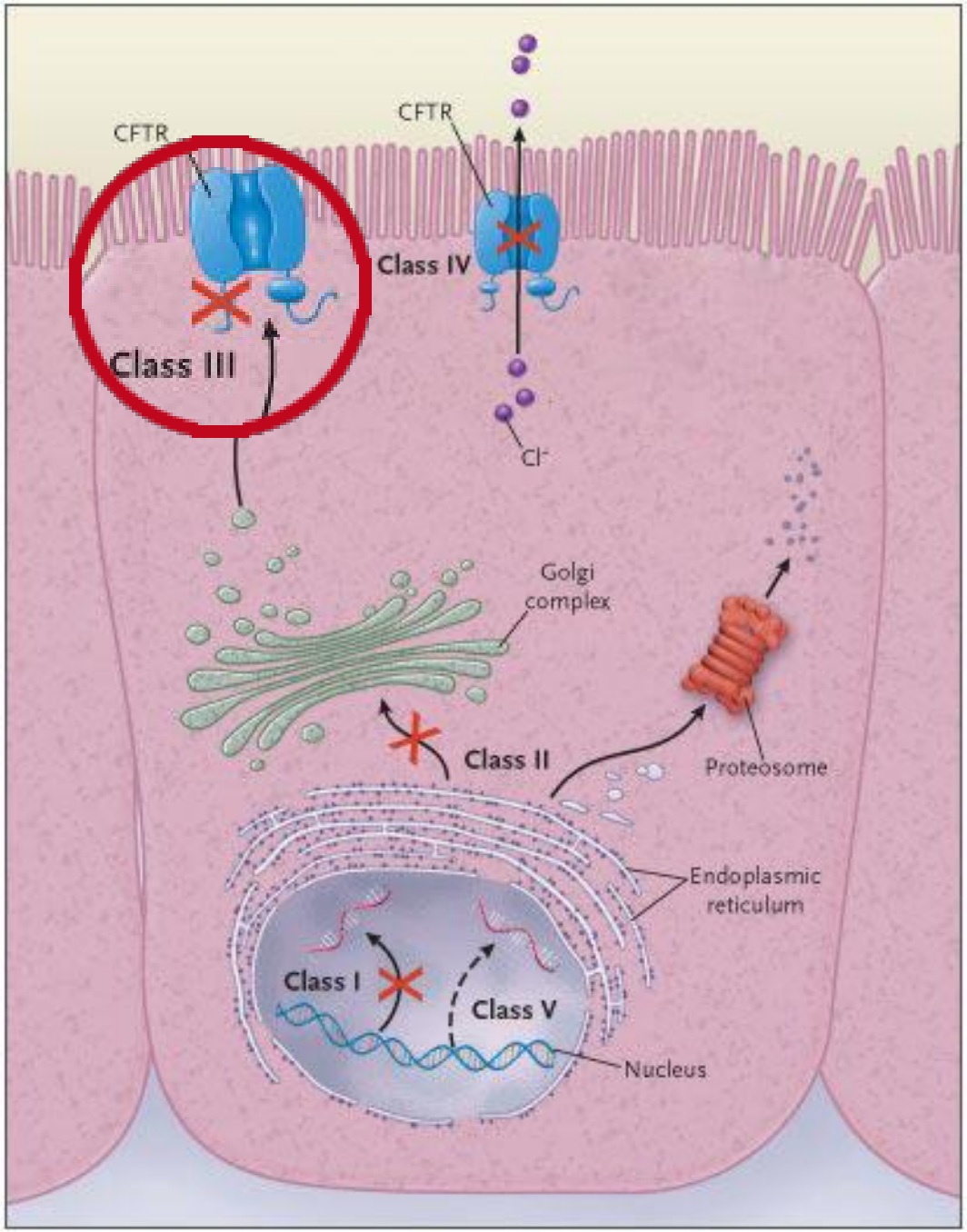
Defective protein production

G542X, 711+1GRT, 1609delCA, R1162X, 1717-8GRA, W1282X, 1782delA, Q890X, 1898+3ARG, CFTRdele19, 936delTA



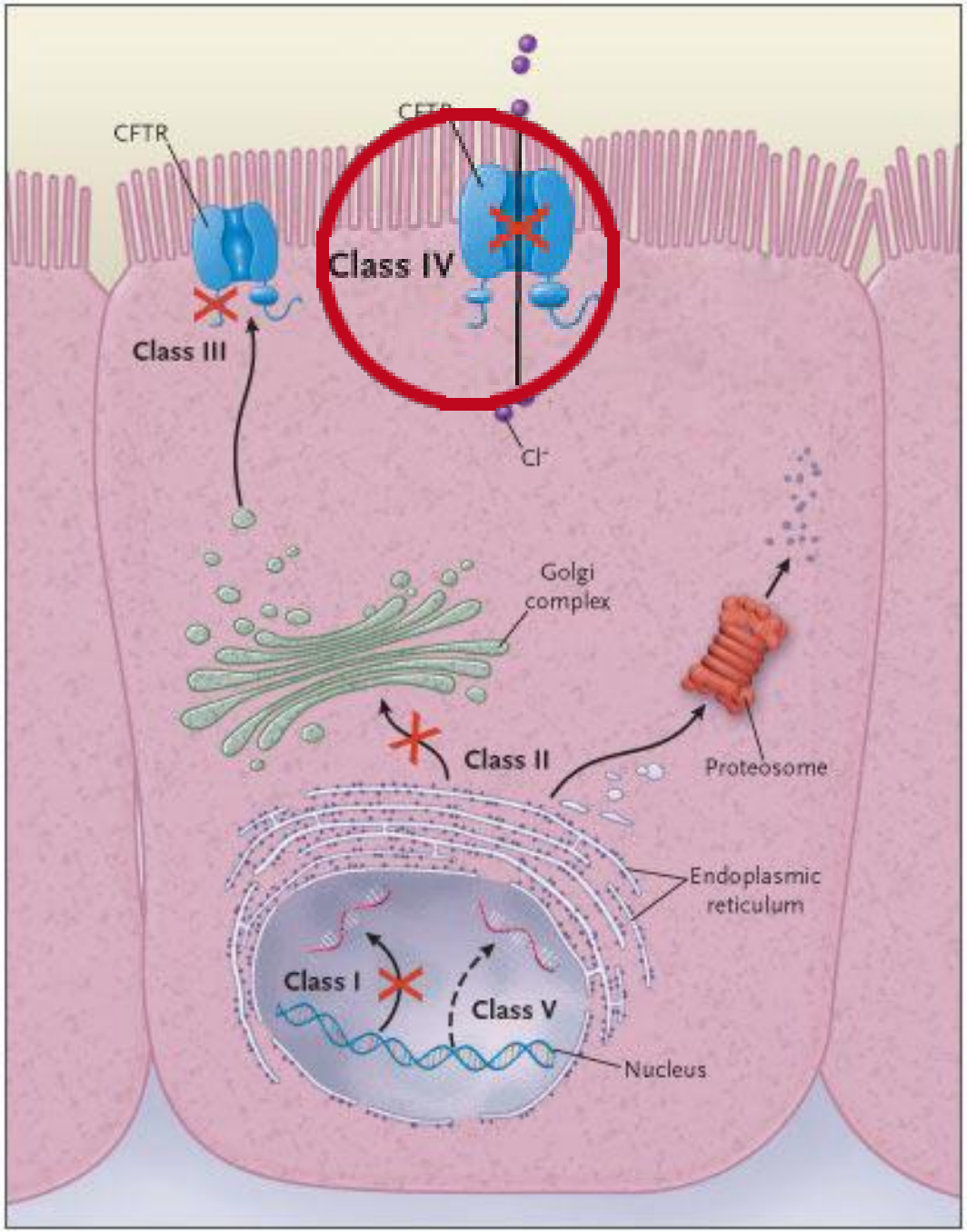
Defective protein processing

F508del, N1303K, I507del, R1066C



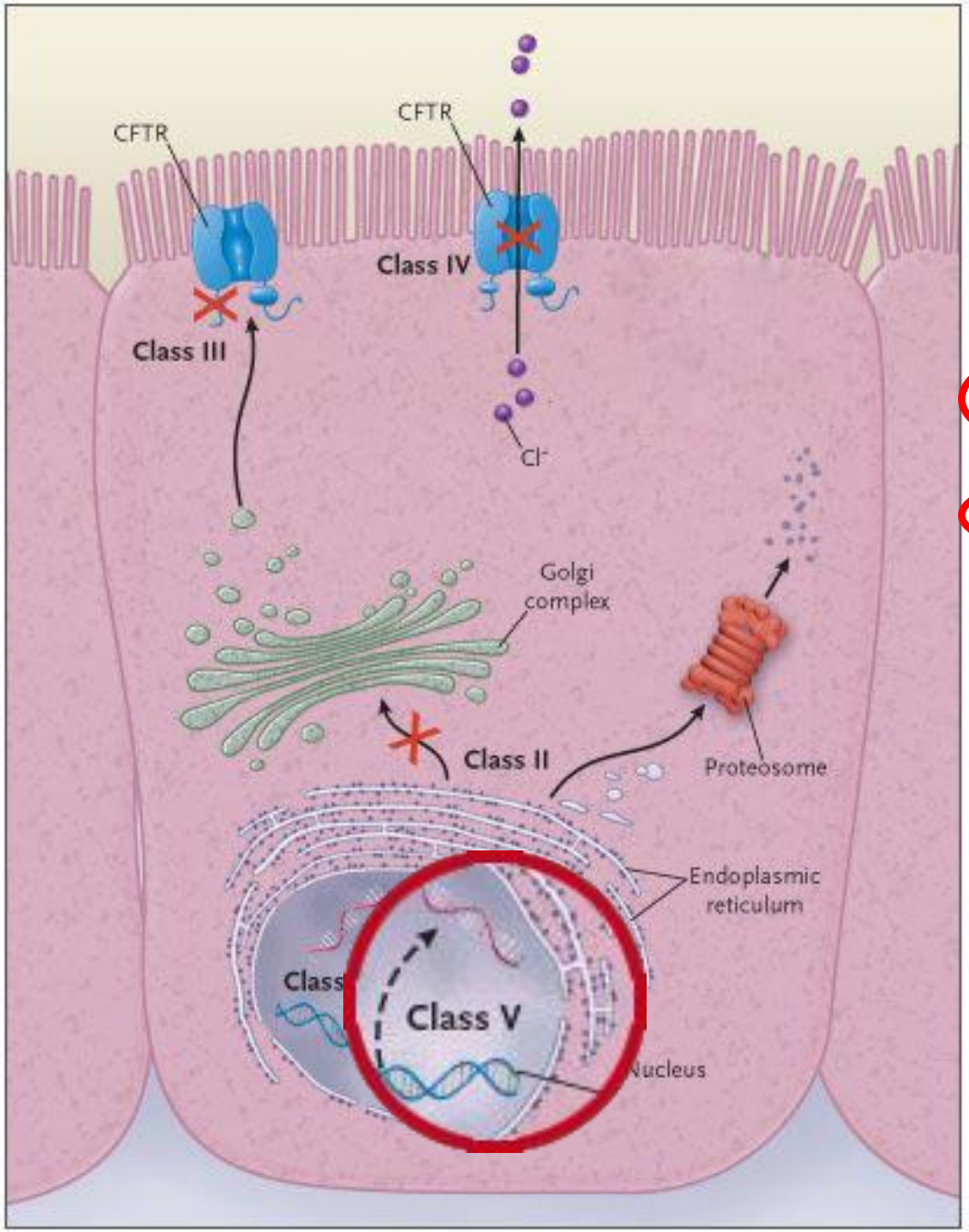
Defective protein regulation

D1270N, G551D



Defective protein conductance

L206W, R334W, R117H, R347H, D836Y, P205S



Partially defective production or processing leading to reduced amounts of functioning CFTR

A455E, 2789+5GRA, 1811+1.6kbARG, 3849+10kbCRT, 3272+26GRA

Clinical Features Associated with a Delayed Diagnosis of Cystic Fibrosis

Table 1. Clinical features of patients diagnosed over the age of 10

Sex	Age in 1996	Age at diagnosis	Mode of presentation	Sweat test chloride mmol/l	Genotype	BMI 1996 kg/m^2	Sputum culture in 1996	FEV1 1996 % predicted	Pancreatic status
M	27	19	pulmonary disease	72	G542X/	22	*B. cepacia*	46	PI
F	15	10	nasal polyps	93	F508/	21	no growth	85	PS
F	36	35	pulmonary disease	88	F508/F508	18	*S. aureus*	38	PI
F	20	18	pulmonary disease	101	R117H/	22	*S. aureus*	69	PS
M	24	16	pulmonary disease	91	F508/R117H	22	*P. aeruginosa*	42	PI
F	14	10	pulmonary disease	92	F508/	22	*H. influenzae*	70	PI
F	14	12	DIOS	122	F508/G551D	21	*P. aeruginosa*	80	PI
M	15	11	nasal polyps	101	F508/6211GT	18	*P. aeruginosa*	78	PI
F	29	13	pulmonary disease	80	F508/	27	no growth	62	PS
M	26	12	pulmonary disease	80	none identified	22	no growth	95	PS
M	20	19	pulmonary disease	131	F508/G551D	19	*P. aeruginosa*	68	PI
F	19	16	atypical mycobacteria infection	101	F508/	19	*S. aureus*	69	PI
M	27	24	hyponatraemic dehydration	102	F508/R117H	26	*H. influenzae*	95	PS
M	31	28	sibling	90	F508/R117H	27	*S. aureus*	82	PS
M	25	23	nasal polyps	81	F508/R117H	24	no growth	85	PS
M	30	19	pulmonary disease	80	F508/F508	20	*P. aeruginosa*	20	PI
M	34	33	pulmonary disease	97	F508/R117H	20	*H. influenzae*	45	PI
F	30	28	pulmonary disease	82	R117H/	22	no growth	93	PS

PI = Pancreatic insufficiency; PS = pancreatic sufficiency; G542X/ = second mutation unidentified.

McCloskey et al Respiration 2000;67:402-7

Table 1. Characteristics of Pairs of *ΔF508* Homozygotes and *A455E* Compound Heterozygotes Matched According to Sex and Age.*

Characteristic	No. of Pairs	*ΔF508* Homozygotes	*A455E* Compound Heterozygotes†	P Value
Sex — no. (%)	33			
Male		16 (49)	16 (49)	NS
Female		17 (51)	17 (51)	
Age — yr	33			
Mean		22.9	23.0	NS
Range		0–40	1–41	
Age at diagnosis — yr	33	3.1±3.9	15.0±10.6	<0.001‡
FEV_1 — % of predicted value	29§	54.3±28.4	73.9±25.5	0.002‡
FVC — % of predicted value	29§	76.3±24.4	88.7±21.1	0.04‡
Pseudomonas colonization — no. (%)	33	20 (60.6)	11 (33.3)	0.02¶
Pancreatic insufficiency — no. (%)	33	31 (93.9)	7 (21.2)	<0.001¶
Diabetes mellitus — no. (%)	33	9 (27.3)	0	0.004¶
Weight — (percentile)‖	33	61.0±29.4	53.4±30.3	NS
Height — (percentile)				
Men	16	21.4±25.0	42.0±27.6	0.03‡
Women	17	38.1±28.2	38.7±29.4	NS

*Plus–minus values are means ±SD. NS denotes not significant.

Gan KH, Veeze HJ, van den Ouweland AMW, Halley DJJ, Scheffer H, van der Hout A, Overbeek SE, de Jongste JC, Bakker W, Heijerman HGM. A CF mutation associated with mild lung disease. N Engl J Med 1995; 333:95-99

Genotype-phenotype correlation for pulmonary function in CF

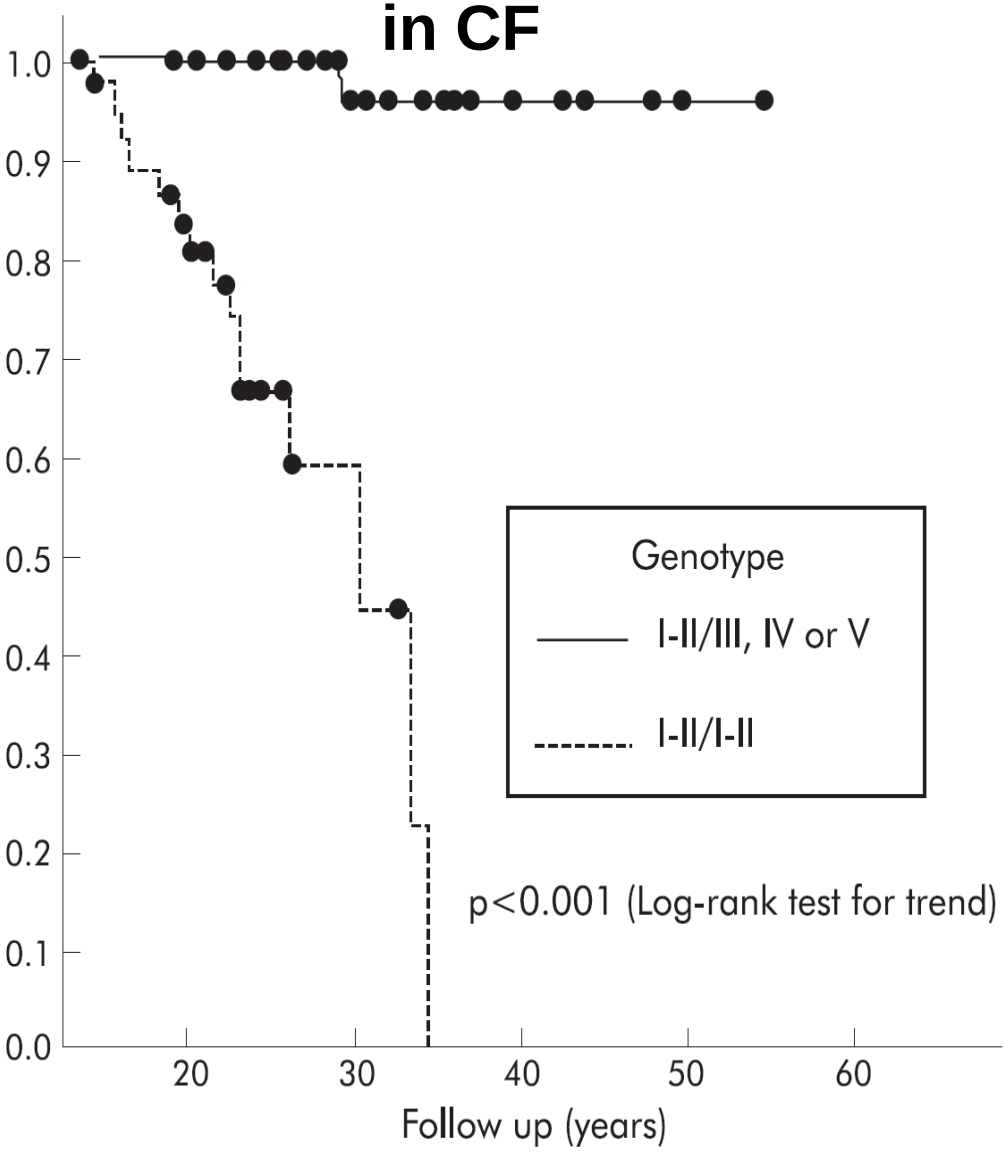
Table 4 Demographic and clinical characteristics of groups according to genotype*

	Genotype I–II/I–II (n = 37)	Genotype I–II/III, IV or V (n = 37)	p value
Sex (no (%) male)	18 (48.6%)	22 (59.5%)	0.484
Mean (SD) age (years)	22.5 (4.9)	30.9 (8.8)	<0.001
Mean (SD) age at diagnosis (years)	4.2 (5.3)	21.9 (13.4)	<0.001
Adult age at diagnosis, n (%)	1 (2.7%)	28 (75.7%)	<0.001
Mean (SD) follow up (years)	3.7 (3.7)	5.3 (1.9)	0.024
Mean (SD) BMI (kg/m^2)	18.4 (2.9)	23 (3)	<0.001
Mean (SD) sweat chloride concentration (mEq/l)	108 (23)	89 (22)	0.001
Digestive symptoms at diagnosis, n (%)	28 (73.7%)	9 (24.3%)	0.010
Pancreatic insufficiency, n (%)	36 (97.3%)	9 (24.3%)	<0.001
Pulmonary symptoms at diagnosis, n (%)	25 (68.4%)	28 (75.7%)	0.439
P aeruginosa colonisation, n (%)	32 (86.5%)	16 (43.2%)	<0.001
S aureus colonisation, n (%)	22 (59.5%)	12 (32.4%)	0.019
End-stage lung disease, n (%)	15 (40.5%)	1 (2.7%)	0.001
Lung transplantation, n (%)	9 (24.3%)	1 (2.7%)	0.010
Dead patients, n (%)	11 (29.7%)	1 (2.4%)	0.012

BMI, body mass index.
*Data obtained at the first visit to adult unit.

Gracia Thorax 2005

Genotype-phenotype correlation for pulmonary function in CF



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Atypisiche CF

- bij bronchiëctasieën
- onverklaard: genetisch onderzoek
- onderzoek naar behandeling afhankelijk defect in CFTR-gen