8° CONGRESO ARGENTINO DE NEUMONOLOGÍA PEDIÁTRICA
JORNADA DE KINESIOLOGÍA PEDIÁTRICA - JORNADA DE ENFERMERÍA EN ENFERMEDADES RESPIRATORIAS PEDIÁTRICAS

Hospital de Pediatría Garrahan

Por un niño sano en un mundo mejor

BRONQUIECTASIAS NO FIBROQUÍSTICAS
ABORDAJE Y DIAGNÓSTICO INICIAL

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Servicio de Neumonología-Hospital Garrahan
Abril 2018

BRONQUIECTASIAS NO ASOCIADAS A FQ

"Esta afección de los bronquios se produce siempre por catarro crónico, o por alguna otra enfermedad que produce a menudo, violentos y repetidos ataques de tos"

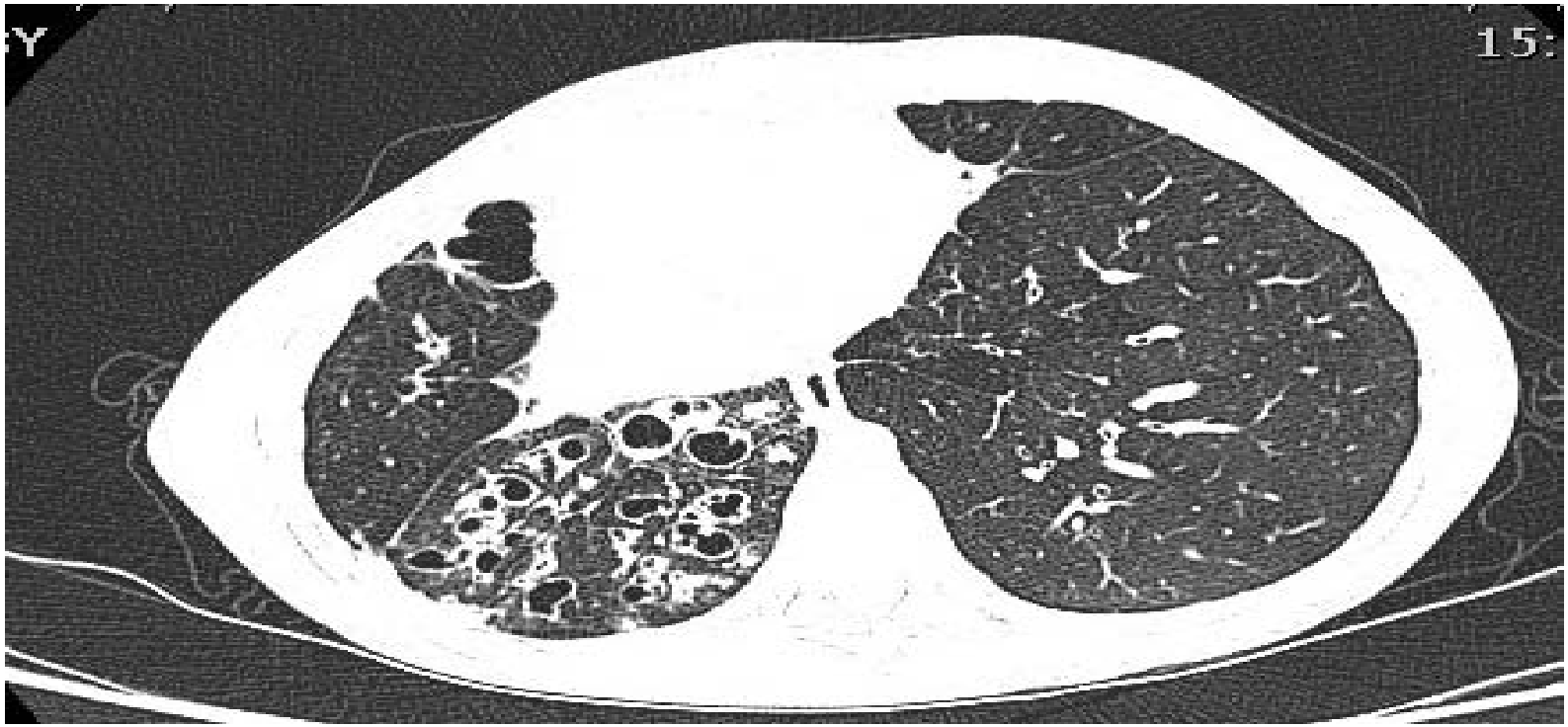
René Laënnec, 1819

Rene Theophile Hyacinthe Laënnec (1781-1826):

BRONQUIECTASIAS NO ASOCIADAS A FQ

- Definición-Epidemiología
- Síntomas
- Etiopatogenia
- Diagnóstico
- Severidad
- Función pulmonar/Evolución
- Conclusiones

BRONQUIECTASIAS NO ASOCIADAS A FQ
DEFINICIÓN



Dilatación anormal de las vías aéreas asociada a la presencia de supuración en su interior.

Es una condición heterogénea resultante de una variedad de desórdenes que causan injuria pulmonar

Es una enfermedad adquirida en la mayoría de los casos.

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BRONQUIECTASIAS NO ASOCIADAS A FQ
EPIDEMIOLOGÍA

- Prevalencia : es variable según las características étnicas de cada población y su nivel socioeconómico

- Disminuyó con respecto a primeros años del siglo pasado. Aumentó en las últimas dos décadas

- 0,5-100000 niños/año FINLANDIA
- 3,7-100000 niños/año Nueva Zelanda.

- Aumenta considerablemente en poblaciones aborígenes(Australia – Alaska).

- EEUU: aprox. 30000 enfermos con FQ VS 110000 Bronquiectasias no FQ.

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Chang A.Expert Opin. Emerging Drugs (2015) 20(2)

BRONQUIECTASIAS NO ASOCIADAS A FQ EPIDEMIOLOGÍA

- Frecuencia mayor en niños varones , la relación se invierte en la adultez prevaleciendo en el sexo femenino.

- 60-80 % de los adultos diagnosticados refieren síntomas que se iniciaron en la infancia.

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Chang et al Expert Opin Emerg Drugs 2015

BRONQUIECTASIAS NO ASOCIADAS A FQ
EPIDEMIOLOGÍA

- Mortalidad : variable según la población analizada
- 5745 muertes atribuídas a bronquiectasias en Inglaterra/Gales e/2001-2007 solo 12 pertenecían al grupo 0-14 años
- 120 indígenas adultos (50% diagnosticados de niños), 34% murieron en el período 2000-2006 .mediana edad 42,5 años

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Goyal et al ;Ped Pulmonology-51:450-469(2016)

MANIFESTACIONES CLINICAS

Tos productiva, prolongada, recurrente

Signos y Síntomas

- Dolor torácico
- Hiperreactividad bronquial
- Fatiga
- Hemoptisis
- Fiebre
- Infecciones recurrentes
- Fallo en el crecimiento
- Deformidad torácica
- Hipocratismo digital

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SÍNTOMAS

Box-1

Recurrent (≥3 episodes) wet or productive cough, each lasting for >4-weeks, with or without other features, e.g. exertional dyspnoea,

- symptoms of airway hyper-responsiveness,
- recurrent chest infections,
- growth failure,
- clubbing,
- hyperinflation or chest wall deformity.

In children, triggers for referral to a specialist include one or more of the following:

(i) persistent wet cough not responding to 4-weeks of antibiotics,

(ii) ≥3 episodes of chronic (>4-weeks) wet cough per year responding to antibiotics,

(iii) a chest radiograph abnormality persisting >6-weeks after appropriate therapy.

ETIOLOGÍA

Condition (reference)	Description	Diseases	Comment
Primary ciliary dyskinesia[29]	Causes impaired mucociliary clearance by structural or functional defects of motile cilia in the airway. Can be associated with infertility and organ laterality defects.	PCD, Kartagener syndrome.	Genetics does not identify all the patients with a PCD phenotype, but 90% of patients with ultrastructural abnormalities have dynein arm defects.
Impaired immune function	Primary immune-deficiencies have been discussed elsewhere.[187]	XLA,[188] CVID,[189,190] HIES or STAT3 deficiency.[191]	Disruption of B cell differentiation causes recurrent pyogenic sinopulmonary infections and may lead to bronchiectasis in XLA. Recurrent sinopulmonary infections in CVID. Eczema, recurrent lung and skin infections, skeletal anomalies and coarse facial features seen in HIES.
CFTR abnormalities[192–194]	Two genes or homozygous state produces CF genotype.	Almost 2,000 mutations in the CFTR gene have been identified in people with CF.	Bronchiectasis patients with CFTR mutation have more severe disease.
Clinical syndromes	Triad of obstructive azoospermia, sinusitis, and bronchitis or bronchiectasis, possibly related to mercury exposure.	Young's syndrome.[195]	The ciliary impairment is thought to be secondary to mucus secretion rather than vice-versa.
	Triad of yellow and thickened nails, lymphedema and respiratory manifestations.	Yellow nail lymphedema syndrome.[196,197]	Impaired lymphatic drainage at the microcirculation level may delay bacterial clearance and promote microbial proliferation. Vasculopathy and B & T cell deficiency has also been described.
	Disorder of connective tissue caused by the mutation of gene encoding the extracellular matrix protein fibrillin-1.	Marfan syndrome.[198]	Bronchiectasis reported in 28% adult patients with Marfan syndrome in a single study.
	Sensorineural hearing loss, respiratory symptoms with visual loss due retinitis pigmentosa.	Usher syndrome.[199]	A ciliopathy where mean ciliary beat frequency is slightly lower, but the ultrastructural is normal.
Local bronchiectasis[200]	Following obstruction, which leads to impaired clearance, repeated infection and airway injury.	Inhaled foreign body, tumor.	Bronchiectasis found in up to 25% of patients foreign body missed for >30-days.
Congenital Tracheo-bronchomegaly[201,202]		Mounier–Kuhn syndrome. William–Campbell syndrome.	Atrophy of smooth muscles and elastic tissue in the trachea and main bronchi causes tracheobronchomegaly, can be associated with tracheal and bronchial diverticuli.
Associated conditions[203–205]			
Aspiration[27,76]	Conditions associated with bronchiectasis based upon epidemiological data.	Aspiration secondary to neuromuscular disorders. Tracheo-esophageal fistula or gastro-esophageal reflux.	Reflux is seen in 10–18% of children with bronchiectasis.
Previous infection[6,22,206]		Previous pneumonia.	Previous hospitalization for severe pneumonia is associated with increased bronchiectasis risk in children.
		Recurrent respiratory tract infections ABPA.	ABPA is associated with bronchiectasis in adults.
Structural/developmental		Bronchopulmonary dysplasia.	
Inflammatory conditions[207–209]		Rheumatoid arthritis. Inflammatory bowel disease. Coeliac disease	Bronchiectasis is seen in up to 30% patients with RA and associated with increased mortality. Bronchiectasis seen in up to two third of adult patients with IBD

continued

ETIOLOGÍA

TABLE 1—(*Continued*)

Condition (reference)	Description	Diseases	Comment
Proposed associations where more data are needed			
MBL deficiency[210–212]	MBL recognizes a wide array of pathogens independently of specific antibody, and initiates the lectin pathway of complement activation functioning as an opsonin.	—	Conflicting evidence, where a prospective study showed that MBL deficient genotype was associated with more bronchiectasis, whereas a retrospective study found no difference in severity
Fecolin-2 deficiency[213–215]	Activates the lectin pathway of complement, also binds to the DNA at surface of apoptotic cells and increases clearance.	—	Low levels of fecolin 2 have been associated with bronchiectasis and disease severity.
MMP expression[216]	MMPs are a group of more than 20 zinc dependent proteolytic enzymes. Increased MMP-1 (interstitial collagenase) activity is associated with post-inflammatory lung destruction and fibrogenesis. align="6pt 0cm 0.0001pt; text-align: left" align="6pt 0cm 0.0001pt; text-align: left"	—	Serum levels of MMP-1 and TGF-β1 higher in patients with 1G/2G and 1G/1G genotype. Frequency of MMP-1(-1,607G) polymorphism associated with greater extent of disease and more lung destruction in patients with bronchiectasis.

Pediatric Pulmonology 51:450–469 (2016)

Post-infectious bronchiolitis obliterans and mannose-binding lectin insufficiency in Argentinean children

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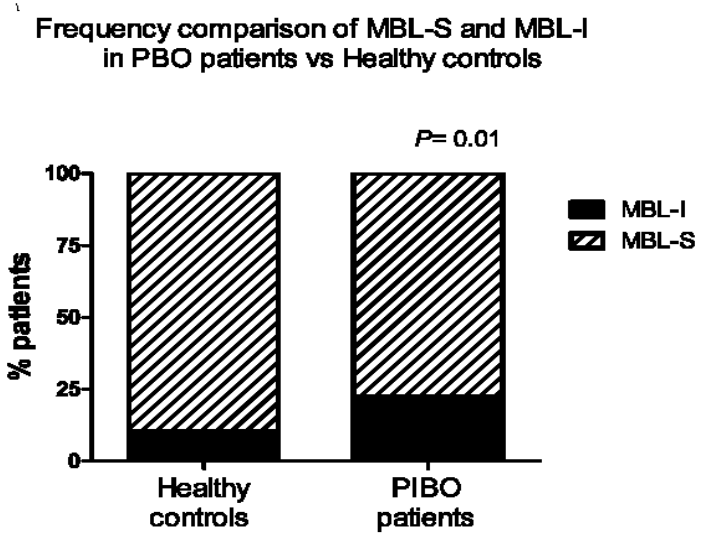

Conclusions: **Insufficiency of *MBL* was more common in PIBO children than in healthy controls. This genetic condition was significantly associated with more severe initial disease, illustrating the relevance of innate immune defence factors prior to the maturation of the adaptative immune system.**

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 Respirology (2015) **20**, 982–986
doi: 10.1111/resp.12547

The etiologies of non-CF bronchiectasis in childhood: a systematic review of 989 subjects

Kelly S Brower[1], Michael T Del Vecchio[1,2] and Stephen C Aronoff[1,2*]

BMC Pediatrics

Table 2 Etiology of non-CF Bronchiectasis in childhood by study

	Primary immuno-deficiency N/%	Ciliary dyskinesia N/%	Infection N/%	Aspiration N/%	Idiopathic N/%	Congenital malformation N/%	Secondary immuno-deficiency N/%	Asthma N/%	Skeletal diseases N/%	Bronchiolitis obliterans N/%	Other N/%
Kapur et. al [9]	13	2	14	10	62	4	5	-	-	3	-
	11.50%	2%	12%	9%	55%	3.50%	4%			3%	
Zaid et. al [17]	20	8	16	17	29	1	-	-	-	1	-
	22%	9%	17%	18%	32%	1%				1%	
Karakoc et. al [11]	2	1	9	-	6	-	-	4	-	-	-
	9.10%	4.50%	41%		27.20%			18.20%			
Banjar et.al [6].	27	21	6	19	60	11	2	-	10	-	-
	17.31%	13.46%	3.85%	12.18%	38.46%	7.05%	1.28%		6.41%		
Li et. al [13]	40	20	5	25	35	5	6	-	-	-	-
	29.40%	14.70%	3.70%	18.40%	25.70%	3.70%	4.40%				
Karadag et. al [10]	17	7	33	4	42	3	-	5	-	-	-
	15.30%	6.30%	29.70%	3.60%	37.80%	2.70%		4.50%			
Eastham et. al [7]	18	1	28	3	17	7	6	-	-	8	5
	19.35%	1.10%	30.10%	3.20%	18.30%	7.50%	6.45%			8.60%	5.40%
Munro et. al [14]	8	-	21	9	41	-	10	-	1	-	1
	9%		23%	10%	45%		11%		1%		1%
Singleton et.al [16]	-	-	26	2	-	-	-	-	-	-	-
			93%	7%							
Gaillard et.al [8]	4	-	2	2	3	3	-	7	-	-	1
	18.20%		9.10%	9.10%	13.60%	13.60%		31.80%			4.60%
Koh et. al [12]	-	6	6	-	13	-	-	-	-	-	-
		24%	24%		52%						
Santamaria et. al [15]	11	25	7	4	58	-	-	-	-	-	-
	10.5%	23.8%	8.7%	3.8%	55.2%						

Table 3 Summary of associations with non-CF bronchiectasis of childhood by disease category (989 patients with 994 associations)

	Total number	% of total
No association	308	31%
Infectious	174	19%
Primary immunodeficiency	158	17%
Aspiration/foreign body	91	10%
Primary ciliary dyskinesia	66	7%
Congenital malformation	34	4%
Secondary immunodeficiency	29	3%
Asthma	16	2%
Bronchiolitis obliterans	12	1%
Skeletal diseases	11	1%
Others	7	1%

Table 4 Infectious diseases associated with non-CF bronchiectasis of childhood (n = 108)

	Total number	% of total
Pneumonia*	66	61%
Measles	15	14%
Tuberculosis	12	11%
Interstitial pneumonia	3	3%
Varicella	3	3%
Neonatal pneumonia**	1	1%
Allergic Bronchopulmonary Aspergillosis (ABPA)	2	2%
Pertussis	5	5%
Adenovirus	1	1%

*Severe viral or bacterial pneumonia.
**Pneumonia at age 6 months or less.

Table 5 Primary immunodeficiencies associated with non-CF bronchiectasis in childhood (n = 131)

	Total number	% of total
B cell disorders	**97**	**74%**
IgG deficiency*	63	48%
IgG subclass deficiency	24	18%
IgA deficiency	9	7%
B cell deficiency NOS	1	1%
T cell disorders	**9**	**7%**
Hyper IgE syndrome	3	2%
Hyper IgM syndrome	2	2%
T Cell deficiency	3	2%
Chronic mucocutaneous candidiasis	1	1%
Combined immunodeficiency	**13**	**10%**
Severe combined immunodeficiency**	9	7%
Ataxia-telangiectasia	2	2%
Wiskott-Aldrich syndrome	2	2%
Chronic granulomatous disease	**7**	5%
Barre lymphocyte syndrome/MHC class II deficiency	**2**	**2%**
Mannose-binding protein deficiency	**1**	**1%**
Other disorders	**2**	**2%**

*Includes patients identified as common variable immunodeficiency (30), IgG deficiency (13), agammaglobulinemia (10) and antibody deficiency or dysfunction (10).
**Not otherwise specified.

Table 6 Congenital malformations associated with non-CF bronchiectasis of childhood

	Total number	% of total
Tracheo-oesophageal fistula	14	52%
Cystic lung disease	5	19%
Bronchogenic cyst	2	7%
Yellow nail syndrome	1	4%
Tracheomalacia	1	4%
Congenital lobar emphysema	1	4%
Pulmonary artery sling	1	4%
Bronchial atresia	1	4%
Bronchomalacia	1	4%
Total	27	

ETIOLOGÍA

Respiratory Medicine

ELSEVIER

Table 1
Aetiologies of bronchiectasis.

Postinfectious
Necrotising pneumonia
Tuberculosis and non-tuberculosis mycobacterium
Viruses (adenovirus, measles and other childhood infections)
Immunodeficiencies
* *Primary:* antibody deficiency, combined immunodeficiency, neutrophil dysfunction, Wiskott-Aldrich syndrome, among others
* *Secondary:* HIV infection, haematological malignancies, chemotherapy, transplant
Hypersensitivity
Allergic bronchopulmonary aspergillosis
Associated with lung diseases
Asthma
COPD
Swyer-James Syndrome
Diseases associated with connective tissue
Rheumatoid Arthritis
Sjögren Syndrome
Other: Ankylosing spondylitis systemic sclerosis, systemic lupus erythematosus, ankylosing spondylitis, relapsing polychondritis, sarcoidosis, Marfan syndrome and Ehlers-Danlos syndrome
Alteration of the mucociliary escalator
Cystic fibrosis
Primary ciliary dyskinesia
Young's syndrome
Inflammatory bowel disease
Ulcerative colitis
Crohn's disease
Inflammatory pneumonitis
Aspiration and gastroesophageal reflux
Toxic inhalation (drugs, gases, etc.)
Congenital defects of the airway
Tracheobronchomegaly (Mounier-Kuhn syndrome)
Cartilage defects (Williams-Campbell syndrome)
Pulmonary sequestration
Tracheobronchomalacia
Bronchial Obstruction
* *Intrinsic:* scar stenosis, broncholithiasis, foreign body, tumour
* *Extrinsic:* lymphadenopathy, tumour, aneurysm
Others
Alpha 1 antitrypsin deficiency
Yellow nail syndrome
Diffuse panbronchiolitis
Idiopathic or unknown aetiology

HIV: human immunodeficiency virus; COPD, chronic obstructive pulmonary disease.

ETIOLOGÍA

Respiratory Medicine

ELSEVIER

Table 2
Distribution of the aetiologies of bronchiectasis in recent studies.

	Pasteur et al. (n = 150)	King et al. (n = 103)	Shoemark et al. (n = 165)	Anwar et al. (n = 189)	Lonni et al. (n = 1258)
Mean age (SD)	52.7 (15.2)	56 (14)	49 (16)	66.1 (11.5)	67 (58–75)[a]
Gender (% M/F)	38/62	37/63	35/65	49/51	40/60
Idiopathic (%)	53	74	26	43	40
Postinfectious (%)	29	10	32	24	20
Immunodeficiencies (%)	8	9	7	2	6
ABPA (%)	7	4	8	4	5
Connective tissue diseases (%)	3	2	2	5	10
COPD (%)	–	–	–	12	15
Asthma (%)	–	–	–	3	3
Inflammatory intestinal disease (%)	1	–	3	2	2
Cystic Fibrosis (%)	3	0	1	<1	0
Ciliary dysfunction (%)	2	1	10	1	2
AAT Deficiency (%)	0	0	0	1	<1
Aspiration/GER (%)	4	0	1	1	<1
Panbronchiolitis (%)	<1	0	2	0	0
Young's Syndrome (%)	3	1	3	<1	0
Yellow nail Syndrome (%)	–	–	2	–	<1
Congenital defect of the airway (%)	<1	0	–	–	<1
Pink's disease (%)	<1	–	–	<1	<1
Other (%)	–	–	Mycobacteria Infection: 2	–	Bronchial obstruction: <1

SD: standard deviation; ABPA: allergic bronchopulmonary aspergillosis; COPD, chronic obstructive pulmonary disease; AAT: Alpha-1 antitrypsin; gastro-oesophageal reflux (GER).

[a] Data presented as median (interquartile range).

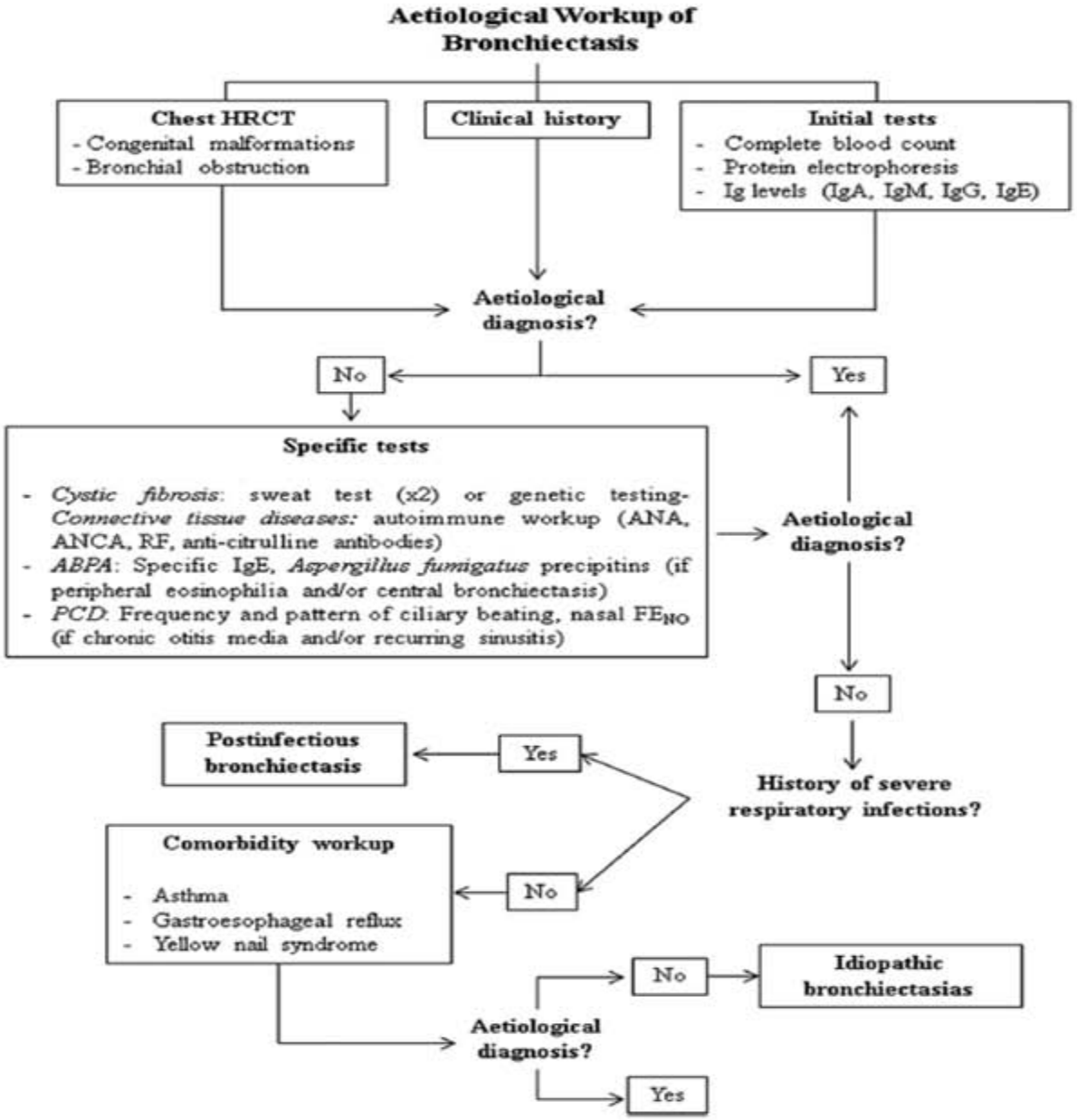


Fig. 1. Proposed algorithm for establishing the aetiologic diagnosis of bronchiectasis. HRCT: high-resolution computed tomography; Ig: Immunoglobulin; Alpha-1-AT: Alpha-1 antitrypsin; ANA: antinuclear antibodies; ANCA: anti neutrophil cytoplasmic antibodies; RF: rheumatoid factor; ABPA: allergic bronchopulmonary aspergillosis; PCD: Primary ciliary dyskinesia; FE_{NO}: Fraction of exhaled nitric oxide, COPD, Chronic obstructive pulmonary disease.

BRONQUIECTASIAS NO ASOCIADAS A FQ

ETIOLOGÍA

Hospital Garrahan, 1988-2002: 687 pacientes

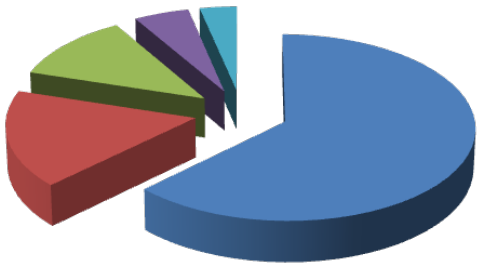


Tabla 1. Clasificación de las bronquiectasias (n: 687)

Grupo I: posinfecciosas
- Infección aguda baja inespecífica: 59%
- Sarampión: 1,3%
- Tuberculosis: 1,2%
- Coqueluche: 0,6%
- Aspergilosis: 0,4%

Grupo II: aspirativas
- Síndrome aspirativo crónico: 4,8%
- Atresia de esófago: 2,3%
- Reflujo gastroesofágico: 1,6%
- Trastornos de deglución: 0,7%
- Fístula broncoesofágica adquirida: 0,1%
- Cuerpos extraños: 0,4%

Grupo III: enfermedades genéticas o congénitas
- Fibrosis quística: 16%
- Inmunodeficiencias primarias: 11%
- Malformaciones pulmonares: 3,2%
- Kartagener: 0,9%
- Mounier-Kuhn: 0,1%
- Marfan: 0,1%
- Sin diagnóstico: 0,2%

Grupo IV: misceláneas
- Neumonitis actínica y/o por drogas: 0,4%
- Sarcoidosis: 0,1%
- Carcinoma mucoepidermoide endobronquial: 0,1%
- Tumor pseudoinflamatorio pulmonar: 0,3%
- Mucopolisacaridosis: 0,1%
- Atresia de vías biliares transplantada: 0,1%

Murtagh P.et al Arch Ped Urug. 2003

BRONQUIECTASIAS NO FQ-GUÍAS BRITÁNICAS ETIOLOGÍA

- Defectos congénitos de la vía aérea
- Síndromes aspirativos y cuerpos extraños
- Historia de infecciones previas
- BAAR (Myc. TBC y no TBC)
- Inmunodeficiencias primarias especialmente anticuerpos
- Aspergilosis broncopulmonar alérgica (IgE , Rast/Cap, precipitinas)
- Asma que no responde al tratamiento.
- Sindrome de panbronquiolitis en raza oriental
- Fibrosis Quística
- Desórdenes del tejido conectivo especialmente artritis reumatoidea
- Desórdenes de la función ciliar (historia neonatal , oma , infertilidad)
- Enfermedad inflamatoria intestinal con tos crónica productiva.

British Thoracic Society guideline for non-CF
Bronchiectasis. Thorax 2010;65:i1ei58. doi:10.1136/thx.2010.136119

PATOGENIA

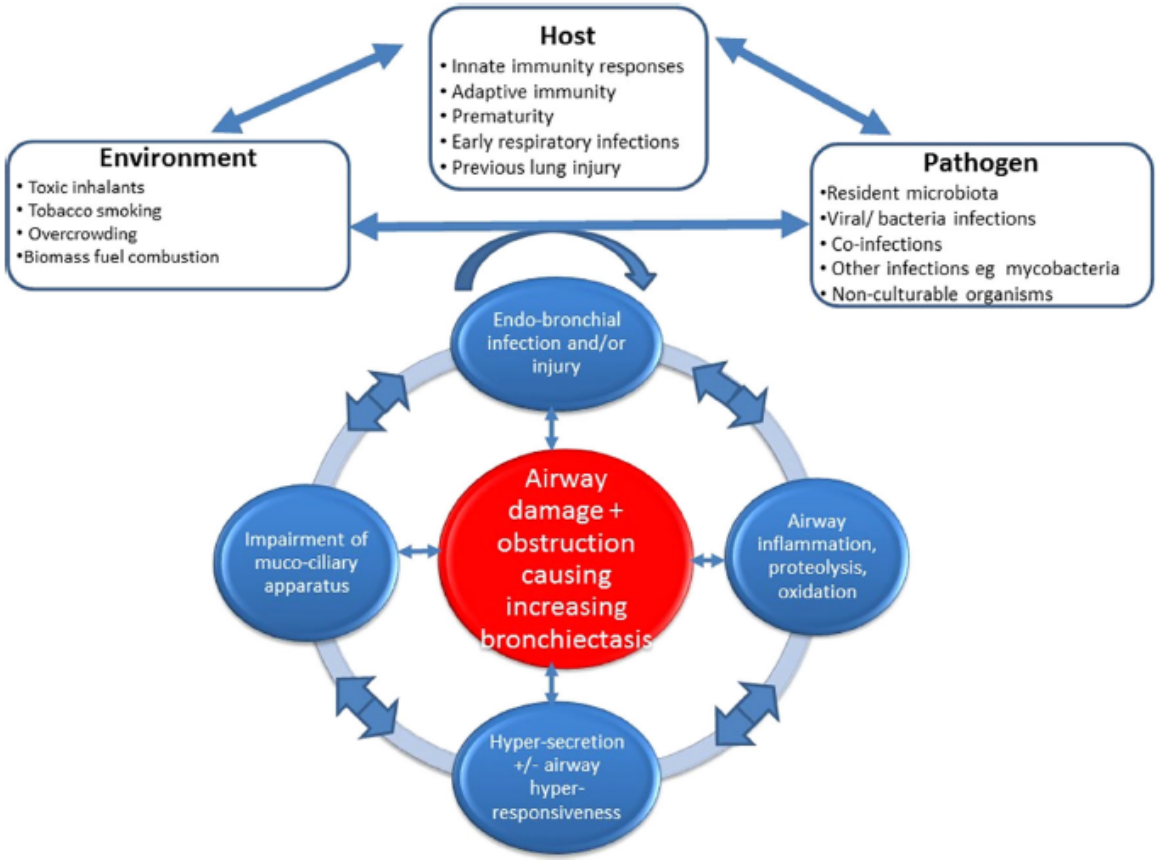


Fig. 1. Pathogenesis of bronchiectasis (Adapted from[186] with permission from Taylor and Francis Ltd, available at www.tandfonline.com).

Pediatric Pulmonology 51:450–469 (2016)

PATOGENIA

Mecanismos Inmunológicos → disregulación ↑ ↓

Infección Haemoph Infl no tipif

Interferón γ-Interleukinas

Mediadores Inflamatorios presentes en BAL:

Manosa ligada a lectina

Fecolina

Mieloperoxidasa de neutrófilos

Moléculas de adhesión intercelular

Factor de necrosis tumoral α-elastasa de neutrófilos-matrixmetalloproteinase (MMP)

Patogenia-Microbiología

- **Bacterias** :Haemoph Infl B no tipif;Strept pneum;Moraxella cath.

  Pseudomona aer.; Aspergillus y Mycobacterias (menos frecuentes)

  Pseudomona = Enfermedad Avanzada

  Infección temprana por organismos comunes +bajo clearence .

- **Virus** : Sarampión - Adenovirus- VSR

  Respuesta inmunológica alterada en relación a receptores Toll,respuestas disminuidas en la función de neutrófilos y macrófagos.

- **Clamydias – Mycoplasmas**.

Adenovirus Species C Is Associated With Chronic Suppurative Lung Diseases in Children

Danielle F. Wurzel,[1,2] Ian M. Mackay,[4] Julie M. Marchant,[1,2] Claire Y. T. Wang,[4] Stephanie T. Yerkovich,[5] John W. Upham,[6] Heidi C. Smith-Vaughan,[7] Helen L. Petsky,[2,3] and Anne B. Chang[2,3,7]

[1]Queensland Children's Medical Research Institute, The University of Queensland, [2]Queensland Children's Respiratory Centre, Royal Children's Hospital, and [3]Queensland Children's Medical Research Institute, Queensland University of Technology, Brisbane; [4]Queensland Paediatric Infectious Diseases Laboratory, Queensland Children's Medical Research Institute, Sir Albert Sakzewski Virus Research Centre, Children's Health Queensland Hospital and Health Service, The University of Queensland, Herston; [5]Queensland Lung Transplant Service, Prince Charles Hospital, and [6]School of Medicine, The University of Queensland, Brisbane; and [7]Child Health Division, Menzies School of Health Research, Charles Darwin University, Darwin, Australia

Results. Species C HAdVs were identified in 23 of 24 (96%) HAdV$^+$ children; 13 (57%) were HAdV-1 and 10 (43%) were HAdV-2. An HAdV$^+$ BAL was significantly associated with bacterial coinfection with *Haemophilus influenzae*, *Moraxella catarrhalis*, or *Streptococcus pneumoniae* (odds ratio [OR], 3.27; 95% confidence interval, 1.38–7.75; $P = .007$) and negatively associated with *Staphylococcus aureus* infection ($P = .03$). Young age was related to increased rates of HAdV$^+$. Blood CD16 and CD56 natural killer cells were significantly more likely to be elevated in those with HAdV (80%) compared with those without (56.1%) ($P = .027$).

Conclusions. HAdV-C is the major HAdV species detected in the lower airways of children with PBB and BE. Younger age appears to be an important risk factor for HAdV$^+$ of the lower airways and influences the likelihood of bacterial coinfection.

Our finding of elevated CD16 and CD56 NK cells in the blood of 80% of HAdV$^+$ children provides indirect evidence of a systemic immune response to HAdV in the airways of these children.

It is indeed plausible that HAdV-C and *H. influenzae* may also play a synergistic role in the initiation and/or exacerbations of chronic suppurative lung diseases in children, and further research is needed.

Table 2. Univariate Logistic Regression Showing Relationships Between Human Adenovirus Status and Bacterial Infection on Bronchoalveolar Lavage

Bacterial Infection	HAdV$^+$ (n = 40)	HAdV$^-$ (n = 205)	OR (95% CI)	*P* Value
Haemophilus influenzae	27 (68%)	96 (47%)	2.36 (1.15–4.83)	.019
Moraxella catarrhalis	14 (35%)	38 (19%)	2.37 (1.13–4.96)	.022
Streptococcus pneumoniae	14 (35%)	46 (22%)	1.86 (.90–3.85)	.094
Staphylococcus aureus	0 (0%)	21 (10.2%)	. . .	.030[a]

Abbreviations: +/–, positive/negative detection; CI, confidence interval; HAdV, human adenovirus; OR, odds ratio.

[a] Calculated using Fisher exact test.

MICROBIOLOGIA

BQT POST IRAB BACTERIOLOGIA (n=296)

ESPUTO/ ASPIRADO BRONQUIAL

* Flora polimicrobiana	43.0 %
* *H. influenzae B*	18.4 %
* *St. pneumoniae*	6.9 %
* *P. aeruginosa*	4.5 %
* *H. influenzae b* (β)	2.0 %
* *Staph. Aureus*	1.5 %
* *Moraxella catarralis*	1.5 %
* *H. influenzae b + St. Pneumoniae*	1.5 %
* *St. pneumoniae + Staph. aureus*	1.5 %
* Otros asociaciones	6.8 %
* Sin identificar	12.4 %

Murtagh P.et al 2002

Bronquitis Prolongada (PBB)

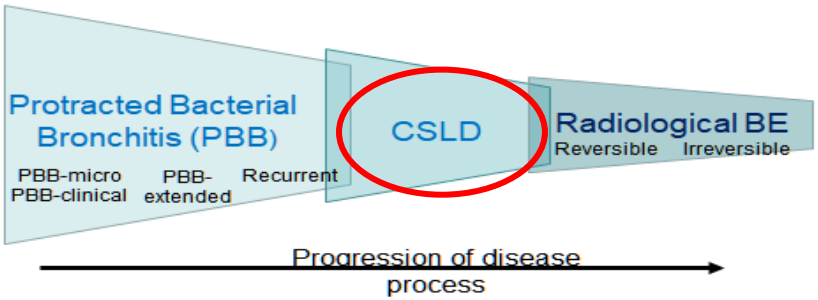
- Tos crónica productiva (igual o mayor a 4 semanas)
- Evidencia de respuesta clínica a atb(amoxic+ác clav,)2 semanas
- Ausencia de otra causa demostrable de tos .

Does failed chronic wet cough response to antibiotics predict bronchiectasis?

Vikas Goyal,[1,2] Keith Grimwood,[1,3] Julie Marchant,[1,2] I Brent Masters,[1,2] Anne B Chang[4,5]

- Children with chronic wet cough that does not resolve after 4 weeks of appropriate oral antibiotics have increased likelihood of bronchiectasis on a CT scan.
- A chest CT scan should be considered in children with persistent wet cough after appropriate antibiotics, especially if the child is Indigenous.

In our retrospective review of 144 children with chronic wet cough, those who did not respond to at least 4 weeks of oral antibiotics were at significantly greater risk of having radiographic changes of bronchiectasis than children whose chronic wet cough responded to this treatment. Being Indigenous was the only other factor independently associated with bronchiectasis, which is consistent with findings from other studies.[21 22]



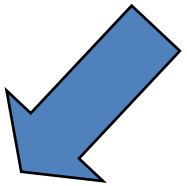
Goyal V, *et al. Arch Dis Child* 2014;**0**:1–4. doi:10.1136/archdischild-2013-304793

DIAGNÒSTICO

- Requiere la correlación de los dos componentes
- CLÍNICA IMÁGENES

TOS CRÓNICA PRODUCTIVA

•TC de TÓRAX (HR)



•dilataciòn del bronquio superando el diàmetro del vaso acompañante.

•Ausencia de la disminuciòn de calibre a medida que se alcanza la periferia del pulmòn

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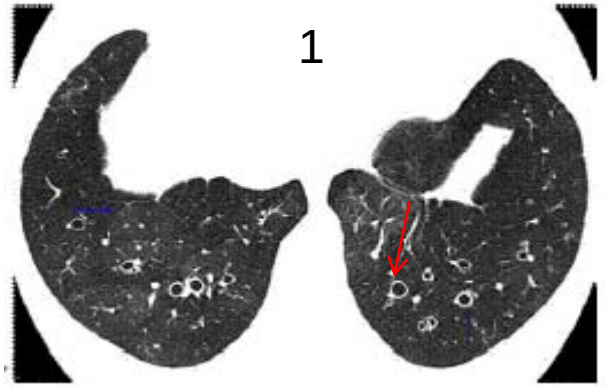
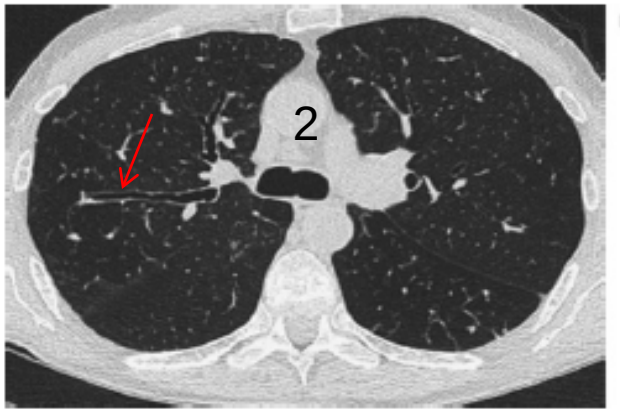
DIAGNÓSTICO

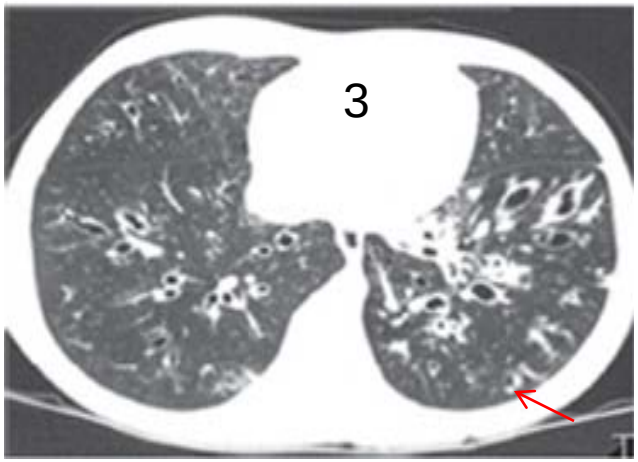
Table 1
Bronchiectasis: HRCT findings

Direct Signs	Indirect Signs
1. Bronchial dilatation Increased bronchoarterial ratio Contour abnormalities	1. Bronchial wall thickening Best assessed visually on images obtained at right angles through vertically oriented airways
2. Lack of airway tapering >2 cm distal to point of bifurcation	2. Mucoid impaction/fluid-filled airways Tubular or Y-shaped structures; branching or rounded opacities in cross section ± air-fluid levels
3. Airway visibility within 1 cm of the costal pleura of fissures	3. Bronchiolitis Clustered ill-defined centrilobular nodules with a tree-in-bud configuration
	4. Mosaic attenuation caused by air trapping Best identified on expiratory HRCT images
	5. Mosaic perfusion of the pulmonary identified on contrast-enhanced dual energy CT of the pulmonary parenchyma
	6. Bronchial artery hyperplasia

Modified from Naidich DP, Webb WR, Grenier PA, et al. Imaging of the airways. Philadelphia: Lippincott Williams & Wilkins; 2005. p. 109.







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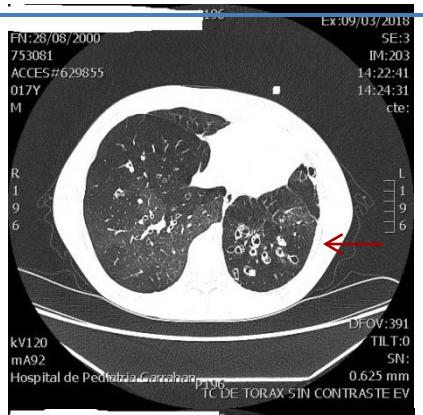
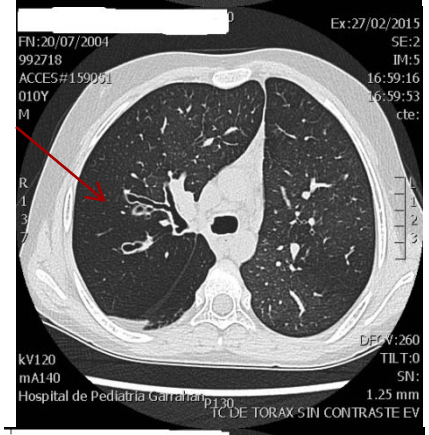
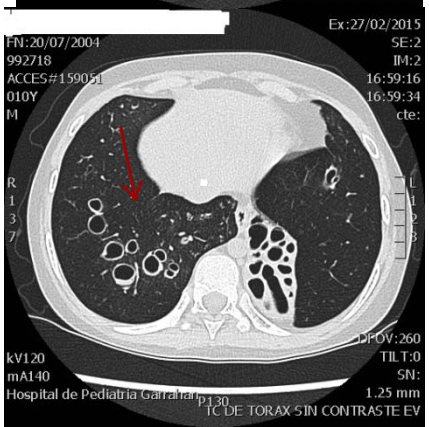
Clin Chest Med 33 (2012) 233–248
doi:10.1016/j.ccm.2012.02.007

BRONQUIECTASIAS/CLASIFICACIÓN
Criterios de Reid

- Cilíndricas : solo imagen de dilatación .
- Varicosas: (por su similaridad con las várices venosas) combina áreas dilatadas con constricciones focales
- Quísticas : progresiva dilatación , finaliza en grandes quistes ,sáculos , en racimos de uva.







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DIAGNÓSTICO

- Los criterios aplicados para adultos pueden no ser absolutamente adecuados en niños.

- Se un propone un cociente B/A de 0,8 en vez del clásico mayor de uno

Bronchoarterial Ratio on High-Resolution CT Scan of the Chest in Children Without Pulmonary Pathology

Need to Redefine Bronchial Dilatation

CHEST

The adult criteria have been predominantly based on a study on six adults with bronchiectasis by Naidich and colleagues[20] nearly 3 decades ago, whereby airways are considered dilated if their internal diameter is larger than the outer diameter of the adjacent pulmonary vessel (ie, the BA ratio > 1).[8]

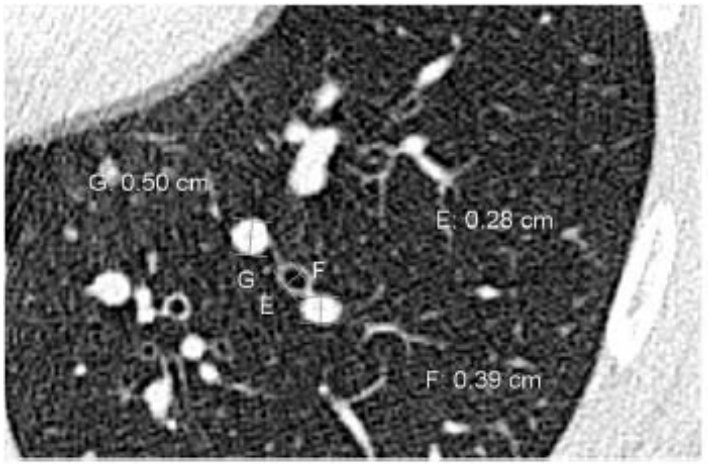

FIGURE 1. CT image showing electronic caliper markings and measurements of bronchus (E) and adjoining vessel (F). Note vessel G does not have an adjoining airway.

The findings from our study indicate that the airway should be considered dilated if the BA ratio is >0.76 (0.626 + [2 × 0.068]).

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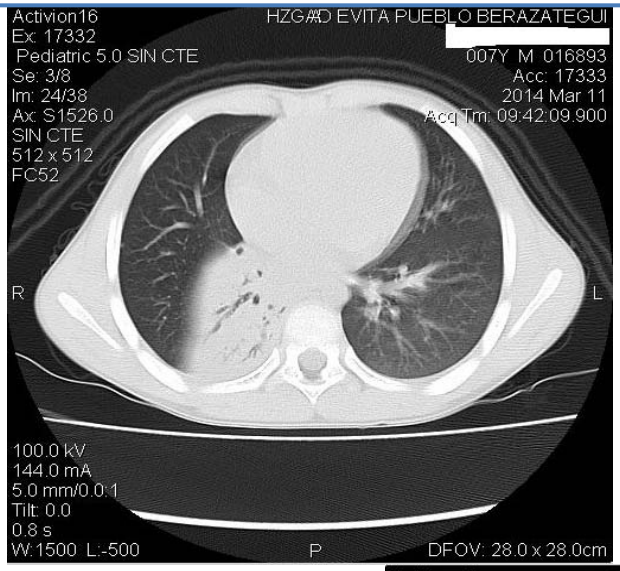
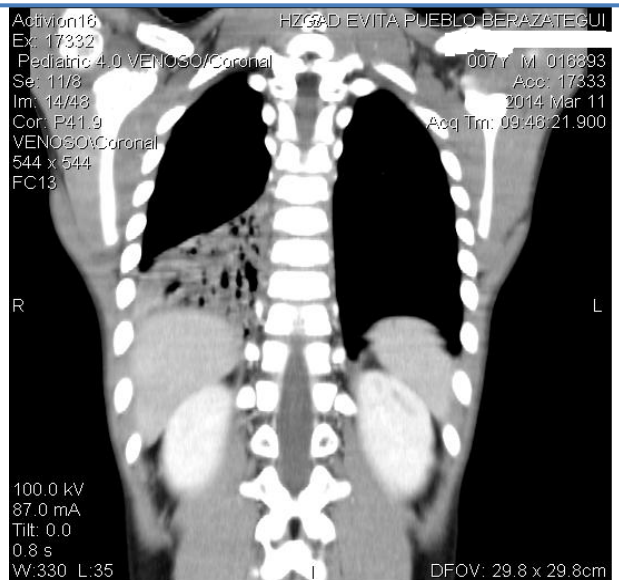
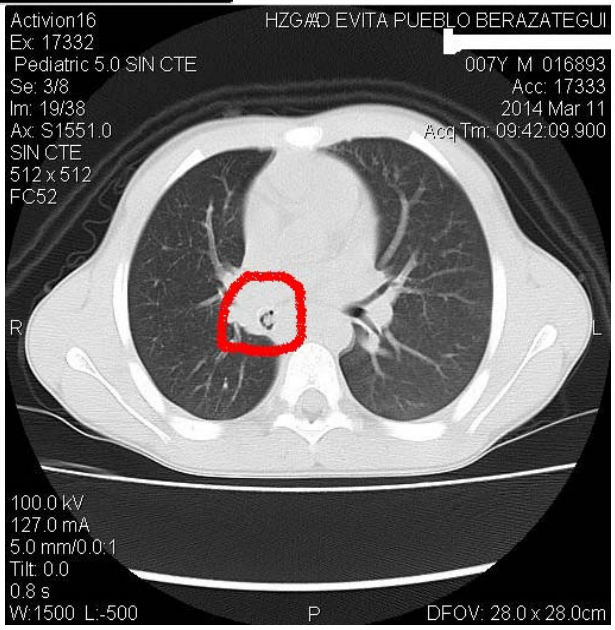
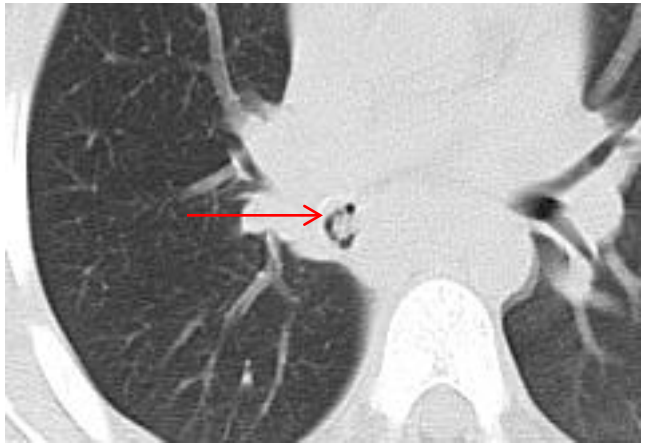
BRONQUIECTASIAS : CUERPO EXTRAÑO









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Bronquiectasias:Cuerpo Extraño

Resolution of Severe Bronchiectasis After Removal of Long-Standing Retained Foreign Body

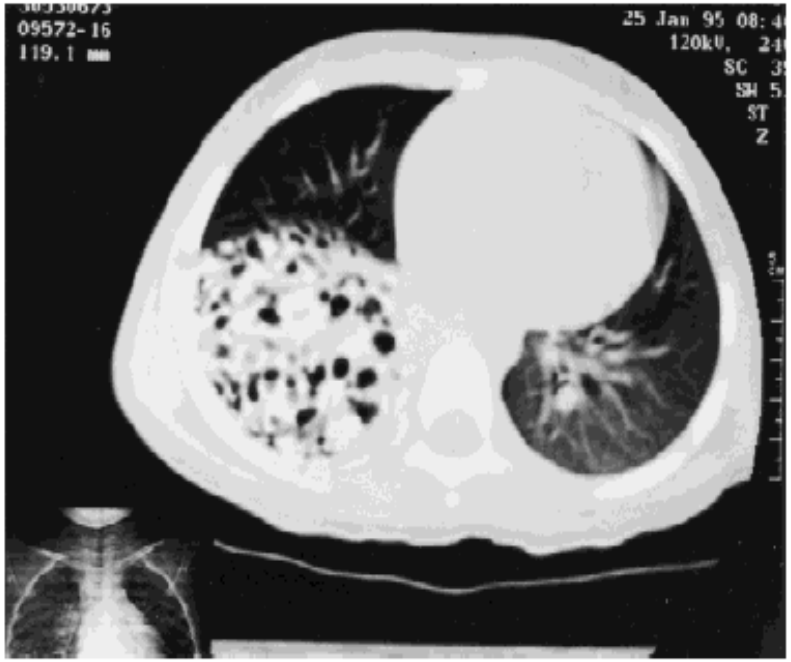

Fig. 1. Computed tomography of chest demonstrating saccular bronchiectasis in right lower lobe.

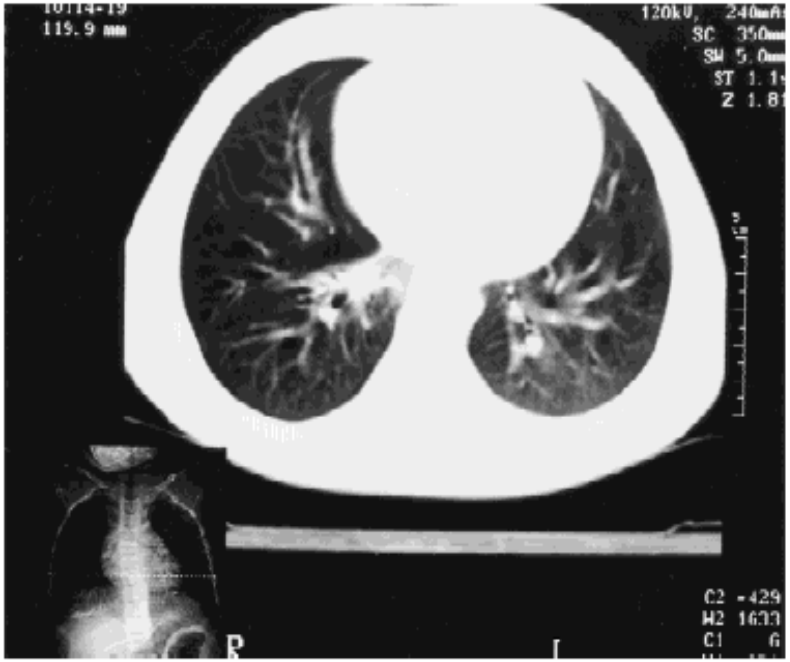

Fig. 3. Resolution of bronchiectasis 6 months after removal of obstruction, with minimal residual bronchiectatic changes.

Pediatric Pulmonology 25:130–132 (1998)

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BRONQUIECTASIAS/SEVERIDAD

EXPERT REVIEWS

Defining severity in non-cystic fibrosis bronchiectasis

Expert Rev. Respir. Med. 8(2), 249–262 (2014)

Table 1. Modifiers of disease severity in bronchiectasis.

Clinical parameters	Features of mild bronchiectasis or good prognosis	Features of severe bronchiectasis or poor prognosis
Bacteriology	No pathogens *Haemophilus influenzae* colonization	***Pseudomonas aeruginosa*** MRSA Enteric Gram-negative pathogens Higher bacterial load
Radiology	<3 lobes involved Tubular bronchiectasis	**>3 lobes involved** **Cystic dilatation** **Bronchial wall thickening** Large airway plugging **Mosaicism** **Emphysema**
Pulmonary function tests	Normal spirometry	**Airflow obstruction** Restriction Increased RV/TLC ratio Reduced K_{CO}
Exercise capacity/dyspnea	No dyspnea	**MRC dyspnea score 4/5**
Symptoms	<5 ml sputum volume Mucoid or mucopurulent sputum Mild cough or cough only with exacerbations	>25 ml/day sputum **Purulent sputum when stable** Severe cough
Etiology	No co-morbidities	**COPD-associated bronchiectasis** Rheumatoid arthritis-associated bronchiectasis
Exacerbations	<3 per year	Three or more exacerbations per year **Severe exacerbations requiring hospital admission**

Factors marked in **bold** are those shown to be most strongly or most consistently associated with severe disease across studies. The data supporting these are discussed in the relevant sections in the text.

OPD: Chronic obstructive pulmonary disease; MRC: Medical Research Council; MRSA: Methicillin-resistant *Staphylococcus aureus*; RV: Residual volume; TLC: Total ng capacity.

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BRONQUIECTASIAS/SEVERIDAD

EXPERT REVIEWS

Defining severity in non-cystic fibrosis bronchiectasis

Expert Rev. Respir. Med. 8(2), 249–262 (2014)

Table 3. Calculation of the bronchiectasis severity index.

Severity criteria	0 points	1 point	2 points	3 points	4 points	5 points	6 points
Age (years)	<50		50–69		70–79		80+
BMI kg/m^2	>18.5		<18.5				
FEV_1% predicted	>80%	50–80%	30–49%	<30%			
Hospital admissions in the past 2 years	No					Yes	
Exacerbation frequency in last 12 months	0–2		3 or more				
MRC dyspnea score	1–3		4	5			
Colonization status	Not colonized	Chronic colonization		*Pseudomonas aeruginosa* colonization			
Radiological severity	<3 lobes involved	3 or more lobes or cystic changes					

FEV_1: Forced expiratory volume in 1 s; MRC: Medical Research Council.

BRONQUIECTASIAS/SEVERIDAD

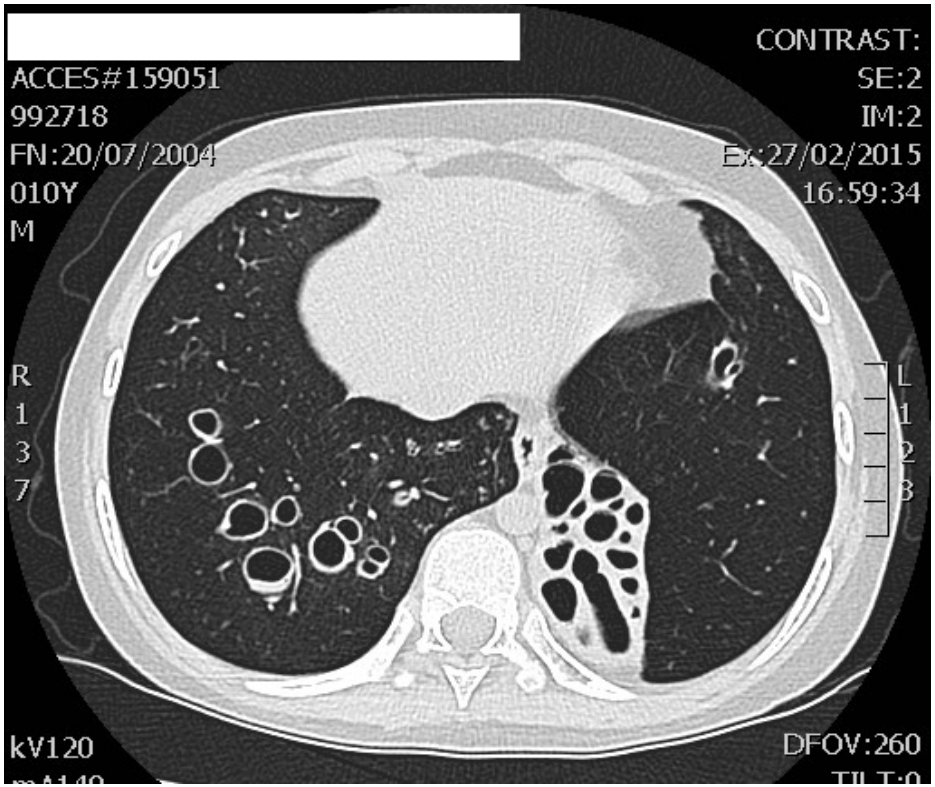
EXPERT REVIEWS

Defining severity in non-cystic fibrosis bronchiectasis

Expert Rev. Respir. Med. 8(2), 249–262 (2014)

Table 2. Features included in various radiological scoring systems for use in non-cystic fibrosis bronchiectasis and cystic fibrosis.

Radiological features	Score			
	Reiff	*Chalia*	*Brody*	*Robinson*
Lobes involved	X	X	X	X
Degree of dilatation	X	X	X	X
Bronchial wall thickening		X	X	X
Mucous plugging		X	X	
Emphysema		X	X	
Mosaicism		X		
Air trapping		X	X	X
Consolidation/collapse		X	X	X
Bullae		X	X	
Nodules		X		
Intralobular septal thickening		X		
Ground glass		X	X	X



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FUNCIÓN PULMONAR

Do New Zealand Children With Non-Cystic Fibrosis Bronchiectasis Show Disease Progression?

TABLE 2—Subgroup Analysis of Bronchiectasis and Lung Function Tests (Polgar Reference)

Group	% Predicted FEV1[1] (CI)	*P*-value	% Predicted FEV1/year[1]	*P*-value
Gender				
Male	61 (54–68)	0.04	−1.2 (−2.7 to +0.4)	ns
Female	72 (64–79)		−1.1 (−2.7 to +0.9)	
Ethnicity				
European	81 (68–94)	0.03	−0.9 (−4.1 to +1.9)	ns
Pacific Island	66 (59–72)		−0.7 (−2.1 to +1.1)	
Maori	60 (50–70)		−2.2 (−4.5 to 0.0)	
Other	41 (10–71)		—	
Etiology				
Post-infectious	64 (54–74)	ns	−2.2 (−4.6 to −0.2)	ns
Primary immunodeficiency	67 (51–83)		−2.4 (−6.0 to +1.1)	
Post-oncology disease	84 (68–100)		−2.4 (−5.2 to +1.9)	
Other	61 (45–77)		−1.6 (−5.8 to +2.5)	
Unknown	64 (56–72)		+0.3 (−1.4 to +2.2)	
Chronic *Haemophilus influenzae*	62 (54–71)	ns	−1.5 (−3.1 to +0.5)	ns
No *Haemophilus influenzae*	68 (62–75)		−0.9 (−2.4 to +0.7)	
Asthma	60 (52–68)	0.02	−1.4 (−3.2 to +0.3)	ns
No asthma	72 (65–79)		−1.0 (−2.4 to +0.9)	
Chest deformity	59 (51–67)	0.01	−2.1 (−3.8 to −0.4)	ns
No chest deformity	72 (65–79)		−0.5 (−2.1 to +1.4)	
Digital clubbing	59 (52–67)	0.02	−2.2 (−3.9 to −0.4)	ns
No digital clubbing	72 (65–79)		−0.2 (−1.9 to +1.6)	
NZDep				
1–3	50 (30–70)	ns	−0.5 (−4.8 to 3.7)	ns
4–7	74 (64–84)		−0.1 (−2.6 to 2.1)	
8–10	65 (58–71)		−1.7 (−3.0 to −0.1)	
Chronic *Pseudomonas* infection	47 (21–73)	ns	−2.8 (−8.3 to 2.6)	ns
No *Pseudomonas*	67 (62–72)		−1.0 (−2.2 to 0.2)	
Routine admissions	58 (44–74)	ns	−1.9 (−4.7 to 1.3)	ns
No routine admissions	67 (62–73)		−1.0 (−2.2 to 0.3)	

Pediatric Pulmonology 46:131–138 (2011)

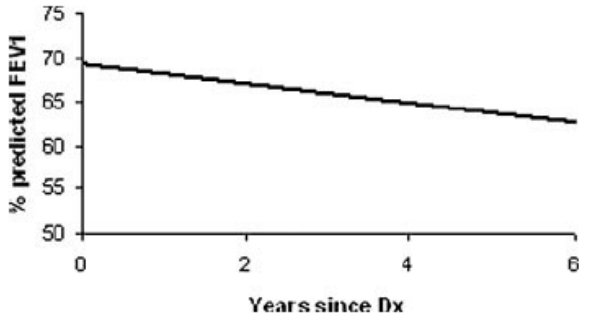

Fig. 3. Pictorial representation illustrating the trend in percent predicted FEV_1 over time for all patients (n = 64). (NB: The graph represents an "average" patient and assumes a linear relationship extrapolated over 6 years).

45% de la cohorte presentó caída de la función pulmonar (media fvc -0,7 %/año; media vef1 -1,6%/año)

no hubo asociación entre etiología y caída de la función pulmonar

sexo masculino , aborígen , hipocratismo digital , deformidad torácica, comorbilidad con asma ;tiempo de evolución ;se asoció con peores resultados al inicio del seguimiento.

hipocratismo digital -signo de mal pronóstico-

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Función pulmonar

Non-cystic fibrosis bronchiectasis in childhood: longitudinal growth and lung function

Figure 2 Evolution of height and BMI-for-age z-scores with time (n = 59, 2 years). BMI, body mass index.

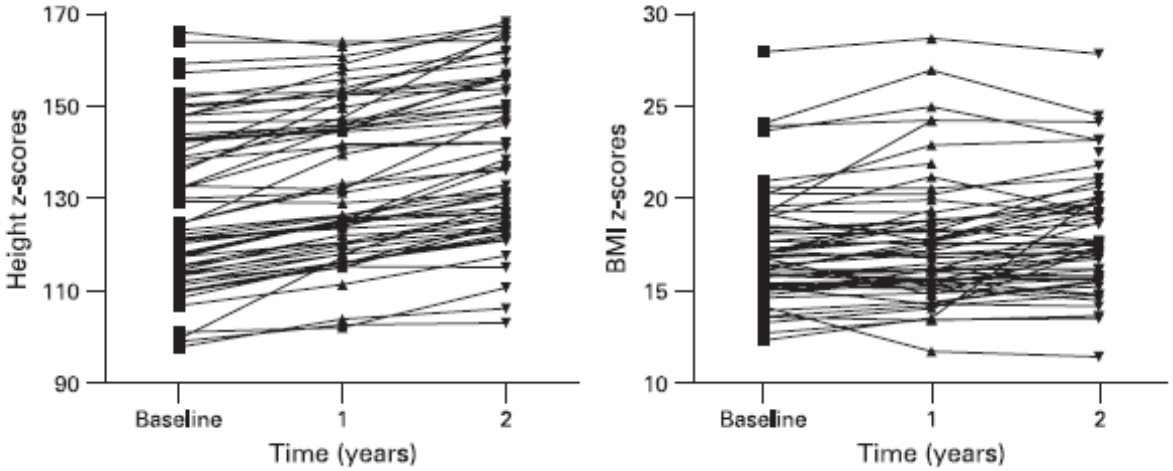
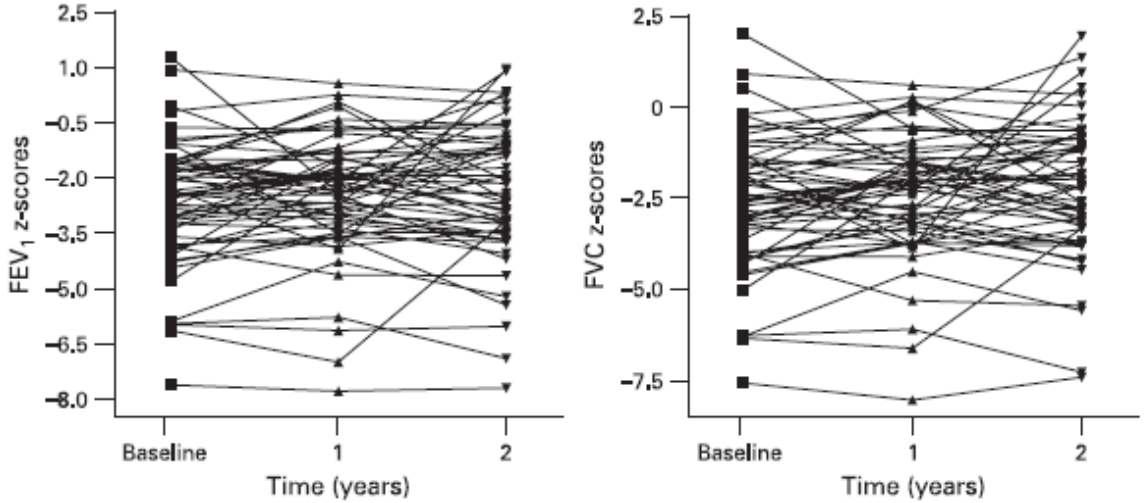


Figure 1 Evolution of FEV_1 and FVC z-scores with time (n = 59, 2 years). FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity.



51 pacientes .(61% con etiología confirmada)entre 2 y 5 años de seguimiento
Estabilidad en peso-talla-IMC
Estabilidad en función pulmonar
Los niños ingresados con mayor edad tenìan mayor compromiso inicial

Thorax 2009;**64**:246–251. doi:10.1136/thx.2008.100958

Longitudinal Growth and Lung Function in Pediatric Non-Cystic Fibrosis Bronchiectasis

What Influences Lung Function Stability?

Nitin Kapur, MD; Ian Brent Masters, PhD; and Anne B. Chang, PhD

- Cohorte de 52 niños BQT no FQ (Brisbane-Australia)Fx pulmonar/Bmi/sexo ,edad,etiología. Seguimiento a 3-5 años
- Función pulmonar estable ,BMI estable a los 3 y 5 años. Menor función pulmonar al inicio , menor BMI
- Sexo , etiología de las bqt , compromiso TAC no predice cambios en la fx pulmonar.
- Diagnosticados después del 2000 más jóvenes que los diagnosticados antes
- Baja función pulmonar al comienzo mayor frecuencia de exacerbaciones
- Niños con vef1 menor a 80 %del pred. mejoraron más que aquellos con fx pulmonar normal.
- Cada exacerbación (con hospit.) caía 1,6 % vef1.

CHEST 2010; 138(1):158–164

CONCLUSIONES

Table 5. Speculation on new developments that may change our understanding and our clinical management of bronchiectasis in the next 5 years.

Emerging treatment approach	Expected/desired impact	Future direction
New inhaled and oral antibiotics	Improved patients outcome and quality of life at the expense of increased antibiotic resistance	Optimal patient group to benefit and optimal treatment regimes are to be identified
Neutrophil-specific therapies (neutrophil elastase inhibitors, CXCR2 antagonists, others)	Unclear. Awaiting results of ongoing randomized trials	Directing therapies using specific neutrophil biomarkers to patients most likely to benefit
Molecular microbiology techniques	A deeper understanding of the role of bacteria in fundamental pathophysiology- including the onset of exacerbations and response to treatment	Linking identified microbiota, diversity and bacterial load data to important clinical end points
Genetics	It is likely that significant numbers of patients with bronchiectasis have unidentified immune defects Pharmacogenetics Genetic modifiers of prognosis	Large registries linked to DNA biobanks will enable genome-wide association studies and genotype/phenotype linkage
Biomarker-guided therapy	Directing anti-inflammatory treatments toward patients likely to benefit	Understanding disease heterogeneity in terms of 'inflammatory phenotypes'
Risk stratification tools	Directing therapies and resources toward patients most likely to benefit	Incorporating tools into clinical practice and guidelines
Multicenter registries	Comprehensive understanding of the natural history of bronchiectasis, including less common etiologies and patients groups that cannot be studied in single centers	Linking registries to DNA and other 'biobanks' for translational research. Facilitating recruitment into multicenter trials

CONCLUSIONES

- Deben investigarse exhaustivamente las causas de las BQ
- La etiología en nuestro medio es principalmente post infecciosa
- La función pulmonar , el crecimiento y desarrollo y las exacerbaciones deben tener un estricto seguimiento
- Nuevas estrategias terapéuticas aparecerán en los próximos años ligadas al reconocimiento de los orígenes de la enfermedad
- Necesidad de obtener registros multicéntricos para conocer la prevalencia real e incorporarlos a programas multidisciplinarios como en FQ.


MUCHAS GRACIAS !!!!!

II CURSO ANUAL

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Mayo - Noviembre 2018

> **Inicio:** Lunes 7 de Mayo

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+ Actividad web complementaria
Workshops en cada encuentro

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- Estudios diagnósticos y equipamiento del laboratorio de sueño
- Síndrome de apnea obstructiva del sueño
- Hipoventilación Alveolar Periférica
- Control central de la ventilación
- Trastornos no respiratorios del sueño
- Ventilación
- Monitoreo de la ventilación

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