SIAIP
Società Italiana di Allergologia e Immunologia Pediatrica

Le diagnosi differenziali dell'asma

L'asma che non è asma

F. Cardinale

UOC di Pediatria (Medicina e Pneumologia)

Azienda Ospedaliero - Universitaria
"Policlinico – Giovanni XXIII" - Bari

Christian, anni 11

APR: D.A
W
azione stagionale (mag-giu)

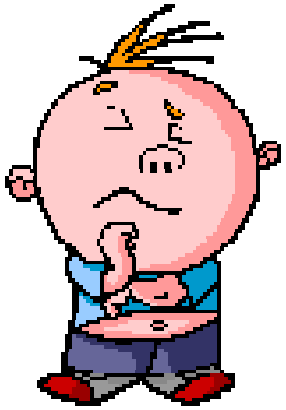
Ipotesi?

enza degli episodi di asma,
frequentemente il ricorso ai CS orali.
ato due volte per asma.
SPT acari (10x9 mm e 8x6 mm),
parietaria (6x8 miceti (Alternaria 5x3 mm)

APP: Il paziente, nonostante impieghi tre die,
Salm 50 mcg x 2/die, MK 5 mg/ trollo
dell'asma. In particolare, la mac rtopnea,
sudorazione profusa, tachicardia esi
Tra un episodio e l'altro, riferita catarrale
Tolleranza allo sforzo ridotta
ACT score: 11 (v.n. >19)

Che fare?

SPIROMETRIA (in corso di terapia con CSI + MK): FEV1 97%, FVC 96%,
MEF25-75 102%; reversibilità (400 mcg salb): negativa



"Not all wheezing and only rarely persistent cough is asthma ..."

Biopsia
BAL
Espettorato indotto
ECP, Eosinofili
FeNO, CO …
sIL2R, sIL5, TNF…

Skin test
IgE specifiche

anamnesi

2. Ostruzione bronchiale reversibile

3. Iperreattività vie aeree

Esame clinico
Spirometria
Test di broncodilatazione

Variabilità del PEF
TPBA (metacolina, aria fredda istamina, EIA…)

PATOLOGIE CONGENITE O ACQUISITE CON WHEEZING

Comuni	Poco comuni	Rare
"Asthma syndrome" prescolare	Displasia broncopolmonare	Scompenso cardiaco congestizio
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S. da aspirazione ricorrente	Fibrosi cistica DCP	Masse mediastiniche
S. disfunzionali		Bronchiolite obliterante interstiziopatie
SIRT		Immunodeficienze

Importance of Acute *Mycoplasma Pneumoniae* and *Chlamydia Pneumoniae* Infections in Children with Wheezing

Esposito S, Eur Respir J 2000;16:1142

71 bb 2-14 aa (età M 4.5 aa) con wheezing infettivo e 80 controlli, sottoposti a studio per MP e CP

Infezione da MP e CP più frequente nei pz con wheezing (età > 5 aa)

Anamnesi di ricorrenza più frequente nei pz con inf. da MP e CP

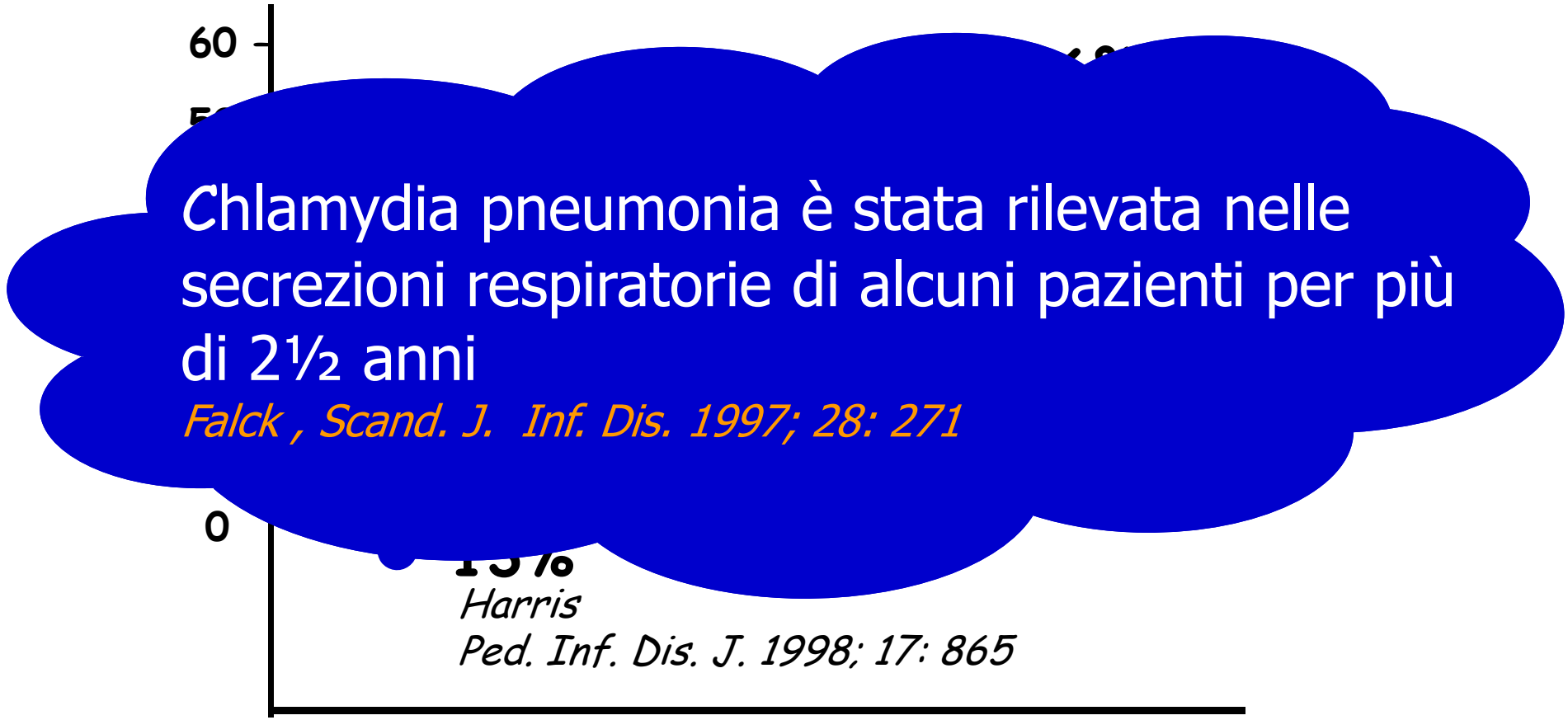
Maggior frequenza di recidiva nei pz con inf. da MP e CP non trattati con antibiotico

	Children with wheezing	Controls	p-value
M. pneumoniae			
2–4 yrs	4/40 (10.0)	2/34 (5.9)	0.68*
≥5 yrs	12/31 (38.7)	4/46 (8.7)	0.0003+
C. pneumoniae			
2–4 yrs	4/40 (10.0)	2/34 (5.9)	0.68*
≥5 yrs	7/31 (22.6)	0/46 (0)	0.001+

Table 3. – Incidence of recurrent episodes in children with wheezing in different age groups

Age group yrs	Infected#	Not infected#	p-value
2–4 yrs	8/8 (100.0)	9/32 (28.1)	0.003*
≥5 yrs	12/16 (75.0)	2/15 (13.3)	0.002+

PERSISTENZA DI C. PNEUMONIAE NELLE COLTURE DOPO INFEZIONE ACUTA

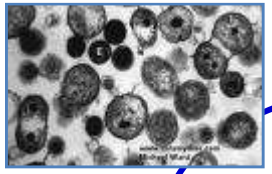


Pz. Con colture persistentemente positive per C. pneumoniae

Gentile concessione di A. Boner

CICLO VITALE DELLA CHLAMYDIA

Hahn Ann All Asthma Immunol 1999; 83: 271



Corpo Elementare (CE) (1)

forma elettrondensa
extracellulare
metabolicamente inerte
ma **coltivabile**

legame (2)

cellula bersaglio

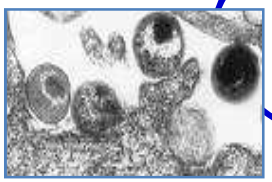
penetrazione cellulare
via endocitosi **(3)**

sopravvivenza
grazie all'inibizione
della fusione lisosomiale
(4)

trasformazione
(5)

Corpo Reticolato (CR)

forma **intracellulare**
metabolicamente
attiva ma **non coltivabile**



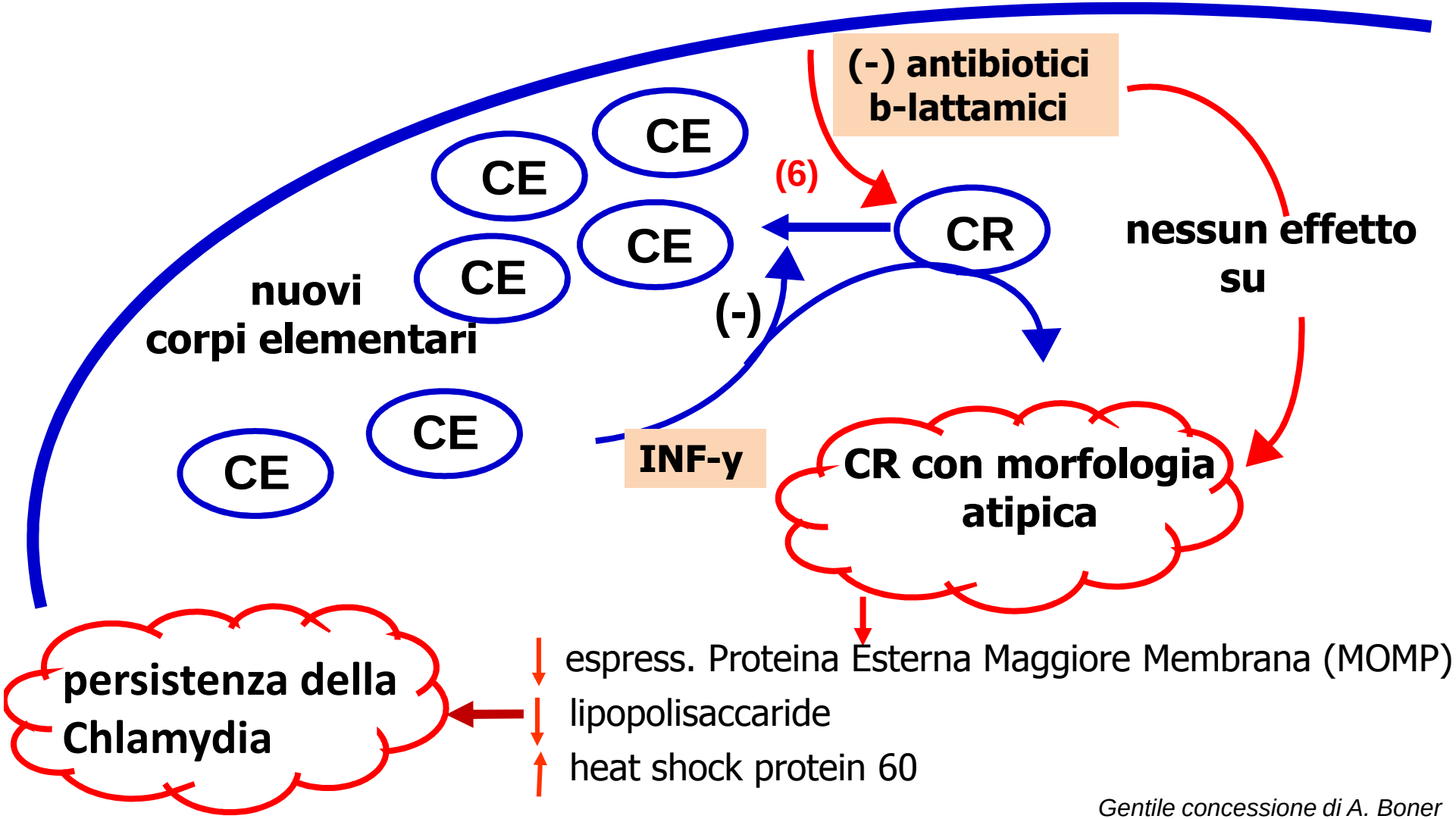
formazione
di nuovi CE
(6)

rilascio tramite
esocitosi o
lisi cellulare
(7)

Gentile concessione di A. Boner

CICLO VITALE DELLA CHLAMYDIA E RISPOSTA DELL'OSPITE

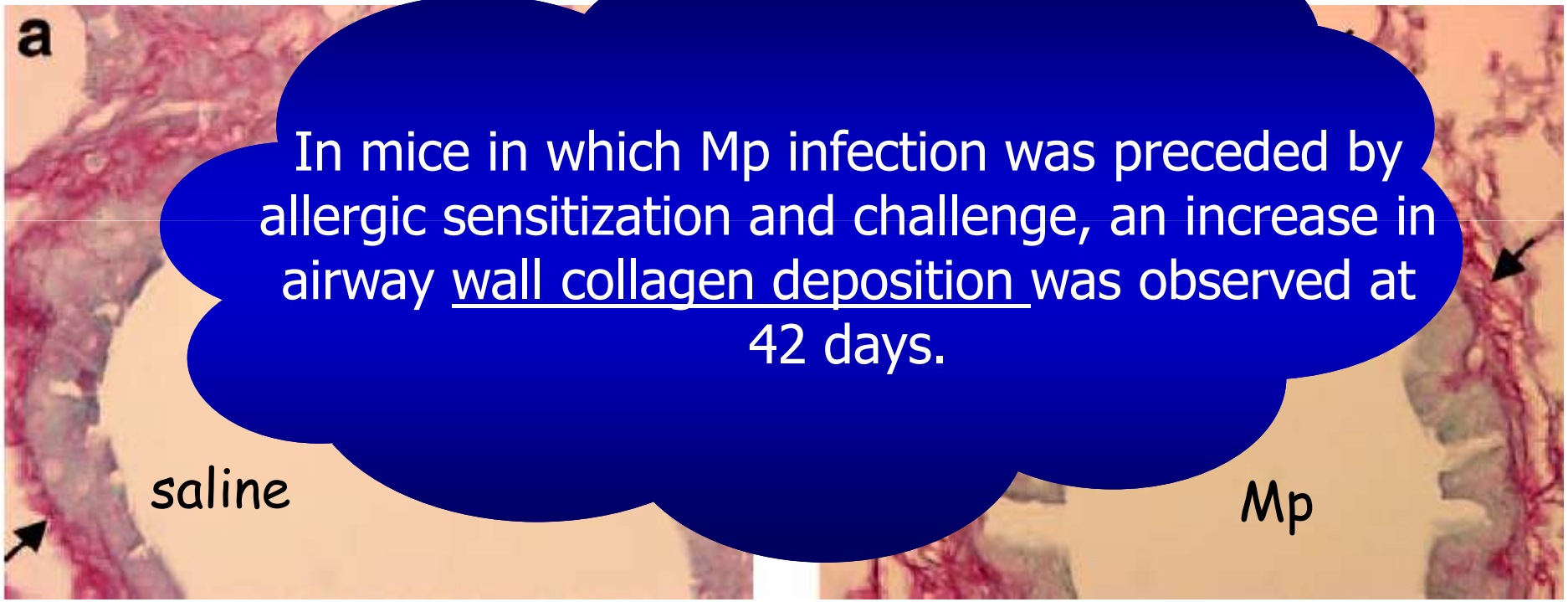
Hahn Ann All Asthma Immunol 1999; 83: 271



Gentile concessione di A. Boner

Cross-sectional view (x200) of **airway collagen deposition** (arrowheads) in allergen-sensitized and challenged animals **42 days** after intratracheal inoculation with saline solution (left, a) or *M. pneumoniae* (right, b).

Chu AJPLCMP 2005; 289: L125



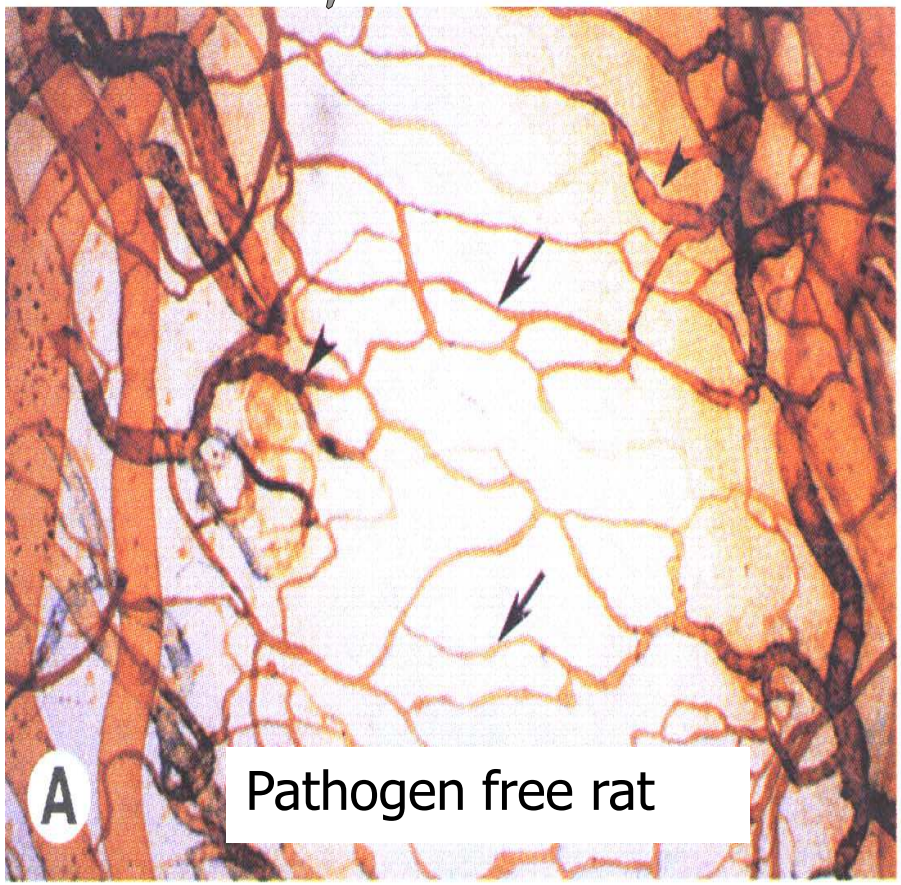
In mice in which Mp infection was preceded by allergic sensitization and challenge, an increase in airway wall collagen deposition was observed at 42 days.

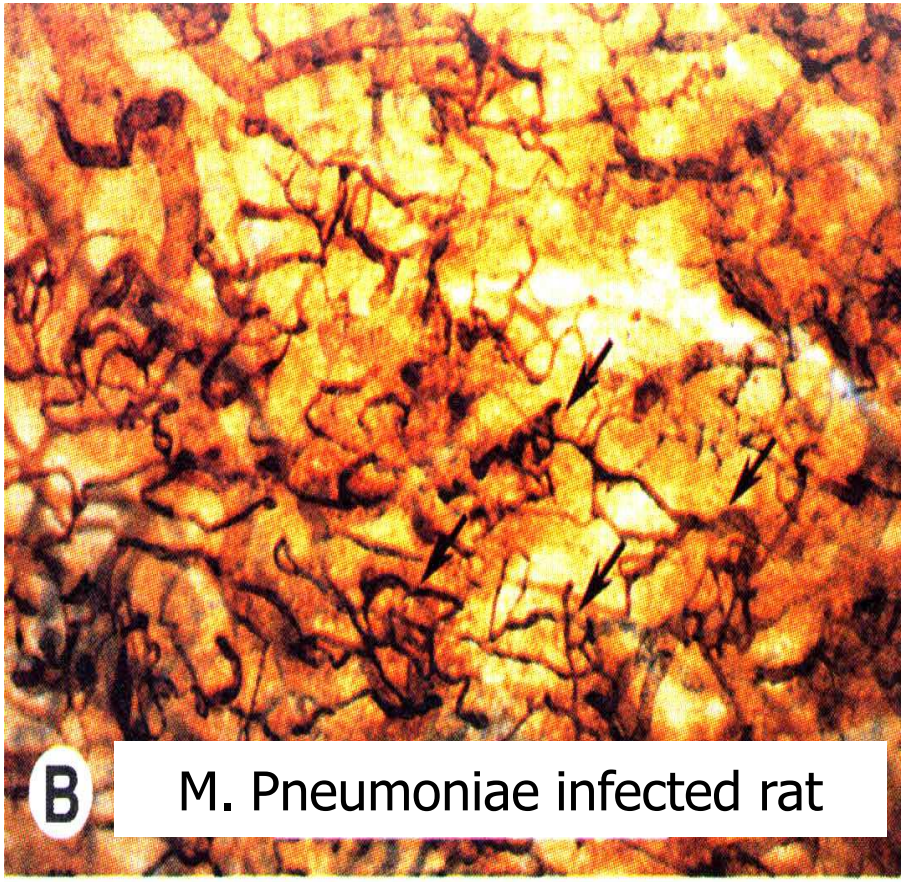
Ovoalbumin sensitized and challenged mice.

Gentile concessione di A. Boner

MYCOPLASMA INFECTION MODEL OF CHRONIC AIRWAY INFLAMMATION

Mc Donald AJRCCM 2001; 164: S39





Microvasculature in the tracheal mucosa

Gentile concessione di A. Boner

Emergence of macrolide-resistant strains during an outbreak of Mycoplasma infections in children

Cardinale & Chironna, J Antimicr Chemother 2011;66:734

43 bb (età 0-16 aa) ospedalizzati per LRTI da **Mycoplasma Pn.** durante una epidemia (aprile-settembre 2010)

Caratterizzazione ceppo di Mycoplasma Pn. + resistenza ai macrolidi (mutazione A2063G e A2064G) in PCR

In 11/43 **(23%)** isolati resistenza ai macrolidi

Nessuna associazione tra mutazione e sottotipo 1/2 del Mycoplasma

In **3 bb** mutazione acquisita dopo terapia

Patient	Gender	Age	Date of sample collection	Macrolide susceptibility (mutation)[a]	Subtype	MPN528d[b]
1011	M	7 years	02/01/2010	S	1	A
1066	M	6 years	01/02/2010	S	1	A
1256	M	7 years	13/04/2010	S	1	A
1328	M	13 years	19/05/2010	**R (A2064G)**	1	A
1331	M	4 years	20/05/2010	S	1	A
1339	F	8 years	22/05/2010	S	1	A
1348	F	13 years	25/05/2010	S	2	C
1360	F	15 years	31/05/2010	S	1	A
1387	F	10 years	14/06/2010	S	2	C
1473	F	8 years	19/06/2010	**R (A2063G)**	1	A
1406	M	14 years	21/06/2010	S	1	A
1403	M	5 years	21/06/2010	S	1	A
1421	F	7 years	28/06/2010	S[c]	2	C
1421/II			05/07/2010	S[c]	—	—
1421/III			09/07/2010	**R (A2063G)**[c]	—	—
1425	F	6 years	28/06/2010	S	1	A
1435	F	5 years	01/07/2010	S	1	A
1444	F	5 years	03/07/2010	S	ND	ND
1445	F	4 years	03/07/2010	S	1	A
1454	F	16 years	06/07/2010	S	1	A
1458	M	18 months	07/07/2010	S	1	A
1462	M	7 years	09/07/2010	**R (A2064G)**	1	A
1464	M	7 years	10/07/2010	S	1	A
1466	M	8 years	12/07/2010	**R (A2064G)**	1	A
1480	F	4 years	14/07/2010	S	2	C
1481	M	2 years	15/07/2010	**R (A2063G)**	ND	ND
1489	M	10 years	16/07/2010	S	1	A
1487	F	7 years	16/07/2010	S	2	C
1488	F	16 years	16/07/2010	S[c]	1	A
1488/II			28/07/2010	S[c]	—	—
1488/III			06/09/2010	**R (A2063G)**[c]	—	—
1513	F	7 years	27/07/2010	S	1	A
1515	M	4 years	27/07/2010	S	1	A
1516	F	10 years	28/07/2010	S	1	A
1522	M	8 years	29/07/2010	S	1	A
1524	M	3 years	29/07/2010	**R (A2063G)**	1	A
1529	F	13 years	30/07/2010	S	1	A
1536	F	4 years	02/08/2010	S	2	C
1537	M	7 years	07/08/2010	**R (A2063G)**	1	A
1547	M	11 years	07/08/2010	S	1	A
1558	F	12 years	12/08/2010	S[c]	1	A
1558/II			14/09/2010	**R (A2063G)**[c]	—	—
1561	M	15 months	13/08/2010	**R (A2064G)**	ND	ND
1574	M	3 years	20/08/2010	S	1	A
1603	M	6 years	02/09/2010	S	1	A
1606	F	2 years	03/09/2010	S	2	C
1607	M	3 years	03/09/2010	S	1	A
1631	F	13 years	10/09/2010	S	1	A

PATOLOGIE CONGENITE O ACQUISITE CON WHEEZING

Comuni	Poco comuni	Rare
"Asthma syndrome" prescolare	Displasia broncopolmonare	Scompenso cardiaco congestizio
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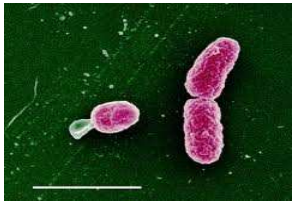
S. da aspirazione ricorrente	Fibrosi cistica DCP	Masse mediastiniche
S. disfunzionali		Bronchiolite obliterante interstiziopatie
SIRT		Immunodeficienze



Bronchite batterica persistente (PBB)

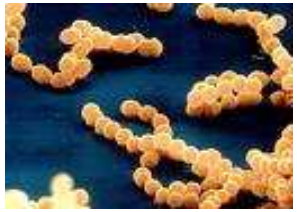
Tosse cronica (>4 sett.)
produttiva

[…] we however speculate that untreated PBB leads to intensification of airway neutropilia with subsequent airway distruction, progressing to CSLD and subsequently bronchiectasis

Risoluzione con terapia antibiotica

Assenza "specific pointers"

Chang, Ped Pulmonol 2008;43:519



Bronchite batterica persistente (PBB)

- Età: qualunque (soprattutto prescolare)
- Frequenza: 20-40% dei casi di tosse cronica nel bambino
- Eziologia: *Streptococcus Pn., Haemophilus Infl., Moraxella*
- Tosse cronica (> 4 settimane) produttiva (talvolta associata a wheezing)
- Neutrofilia nel BAL
- Rx torace nella norma
- Sintomi sistemici aspecifici e di lieve entità
- Esacerbazione della sintomatologia in concomitanza di infezioni virali intercorrenti
- Assenza di "specific pointers" per altre eziologie
- Risoluzione della sintomatologia dopo trattamento antibiotico protratto (almeno 10-14 gg)

Chang, Ped Pulmonol 2008;43:519

CHRONIC COUGH

Outcomes in children treated for persistent bacterial bronchitis

Donnelly, Thorax 2007;62:80–84

Studio retrospettivo su 81 bb con diagnosi di BBP basata su:

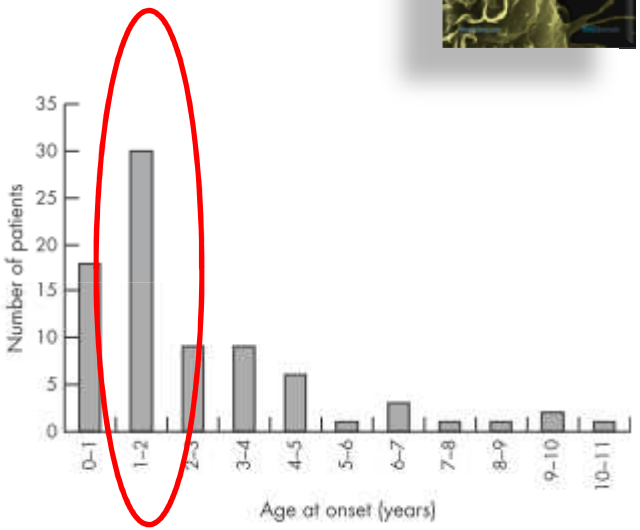
- Tosse produttiva da >1 mese
- Risposta a terapia antibiotica

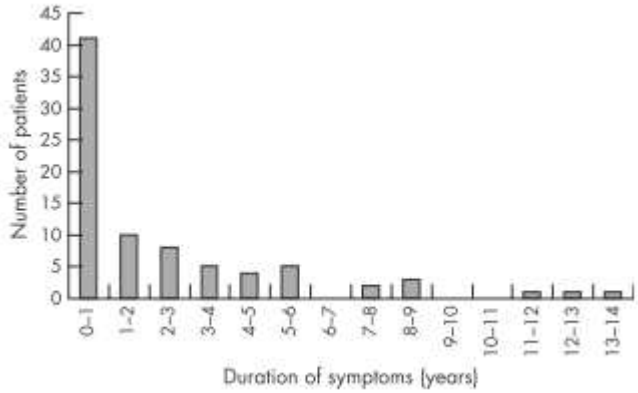
Motivo frequente di consultazione "asma persistente"
48/81 (59%) erano trattati con farmaci anti-asmatici

Età maggiore incidenza **<2 aa**
Nel **59%** sintomi presenti da più di 12 mesi

Colture espettorato nel 63% (pos. *H. Influenziae* 81% e *S. Pneumoniae* 37%)

Risoluzione sintomi nel 51% dopo 2 cicli antibiotici (nel 13% necessari 6 cicli)





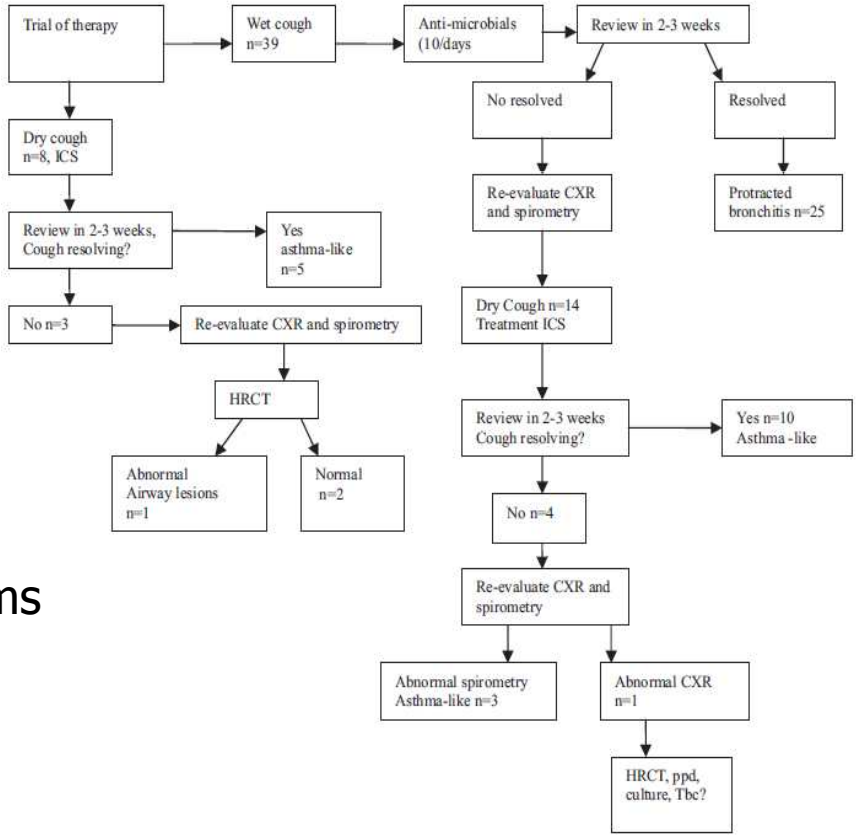
AMERICAN COLLEGE OF CHEST PHYSICIANS®

Evaluation of Chronic Cough in Children*

Asilsoy, Chest 2008; 134:1122–1128

Studio prospettico su 108 bb (6-14 aa) con tosse cronica >4 sett.

Applicazione algoritmo diagnostico secondo LG ACCP 2006



Nel 25% → Asma e asthma-like symptoms
Nel **23.4%** → BBP
Nel 20.3% → UADS
Nel 4.6% → RGE

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

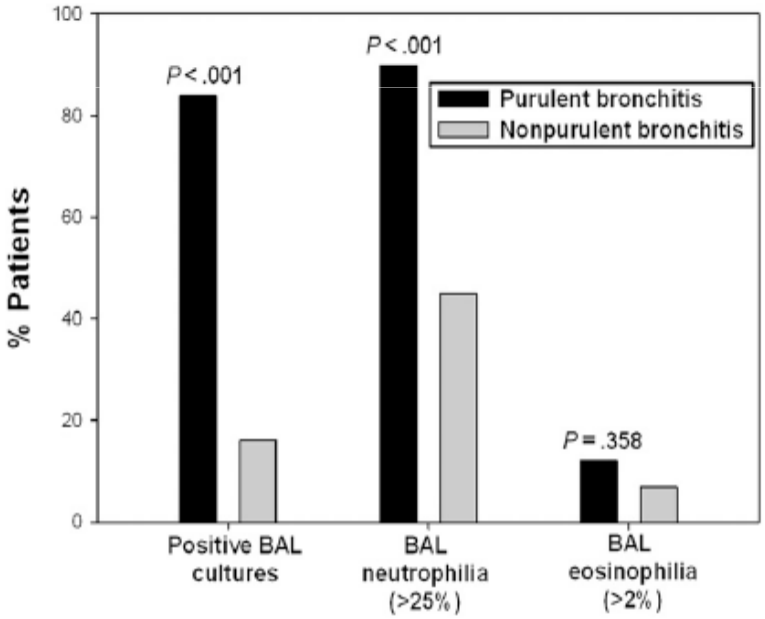
Bronchoscopic Findings in Children With Chronic Wet Cough

Zgherea, Pediatrics 2012; January 9 (e-pub)

Studio retrospettivo sui records di 197 bb sottoposti a FBS per **tosse cronica produttiva**, non responsiva alle comuni terapie

Presenza di **bronchite purulenta nel 56%** dei casi e bronchite non purulenta nel 44%

Positività colturale del BAL nel **46%** dei casi: Haemophilus influenzae (49%), Streptococcus pneumoniae (20%), Moraxella catarrhalis (17%), Staphylococcus aureus (12%), e Klebsiella Pneumoniae (1 pz)



Bronchite purulenta alla FBS associata a positività del BAL *(P<.001)*

PATOLOGIE CONGENITE O ACQUISITE CON WHEEZING

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S. da aspirazione ricorrente	Fibrosi cistica DCP	Masse mediastiniche
S. disfunzionali		Bronchiolite obliterante interstiziopatie
SIRT		Immunodeficienze

[…] there is an ongoing debate with inconclusive evidence regarding this chicken-and-egg question…

Weinberger, Pediatrics 2007;120:855

Gastroesophageal Reflux in Infants with Wheezing

Sheikh S et al., Ped Pulmonol 1999;28:181

84 bb (M 8.7 m) con wheezing "difficile"quotidiano studiati con pH-metria

54 (64%) positivi per GER, di cui 24 (44%) in assenza di sintomi gastro-intestinali

Familiarità per asma meno frequente in bb con GER

Dopo t. antireflusso, maggior necessità di CSI nei paz. non affetti da GER

TABLE 1—Demographic Parameters[1]

Parameter	Infants with GER	Infants without GER	*P* value
Total number	54	30	
Gender, i.e., male:female	39:15	18:12	
Age of onset of respiratory symptoms (months)	2.20 ± 1.36	3.03 ± 2.05	N.S.
Duration of symptoms (months)	6.62 ± 4.48	5.30 ± 3.71	N.S.
Age at pH probe studies (months)	8.74 ± 4.6	8.43 ± 4.30	N.S.
Time between initial visit and pH probe study (months)	1.43 ± 0.65	2.03 ± 1.05	N.S.
Exposure to smoking	11/54 (20%)	8/30 (26.6%)	N.S.
Family history of asthma	16/54 (29%)	24/30 (80%)	<0.005

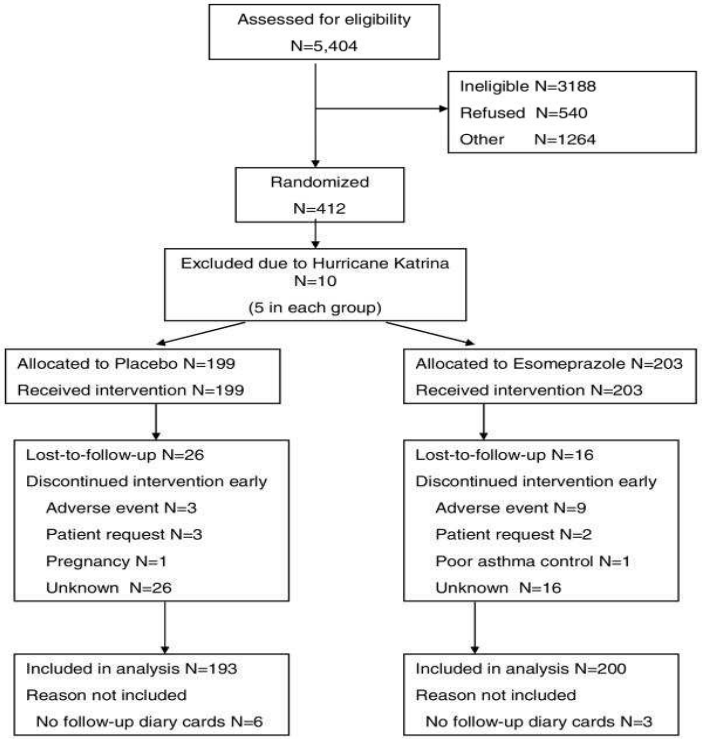
The NEW ENGLAND JOURNAL of MEDICINE

Efficacy of Esomeprazole for Treatment of Poorly Controlled Asthma

Mastronarde, NEJM 2009;360:1487

412 adulti con asma non controllato con CSI
senza sintomi o con sintomi minimi di RGE
(40% circa con pH-metria pos.) randomizzati per:

- Esomeprazolo 24 sett
- Placebo



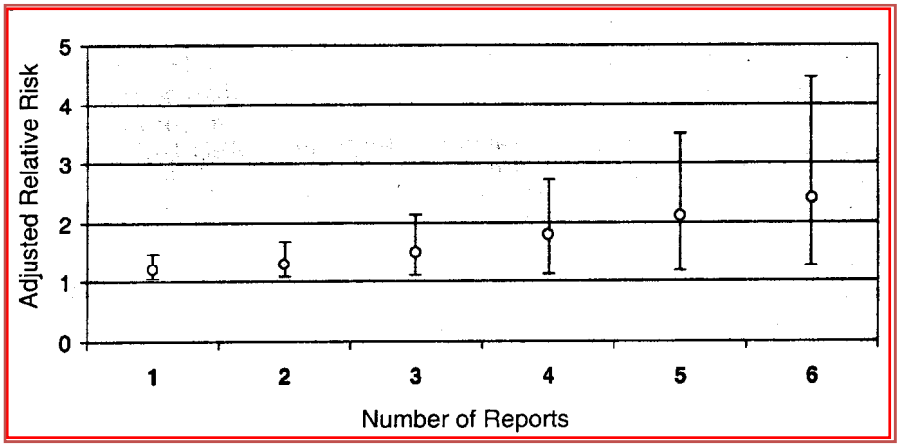
Nessuna differenza per nessuno degli outcomes
(episodi di loss of control, funzionalità respiratoria, QoL, symptom score, reattività bronchiale)

Nessuna differenza intra-gruppi (responders *vs* non responders) in rapporto alla pH-metria

Bottle Feeding in the Bed or Crib Before Sleep Time and Wheezing in Early Childhood

Celedon JC, Pediatrics 2002;110:e77

448 bb studiati prospetticamente dalla nascita per wheezing



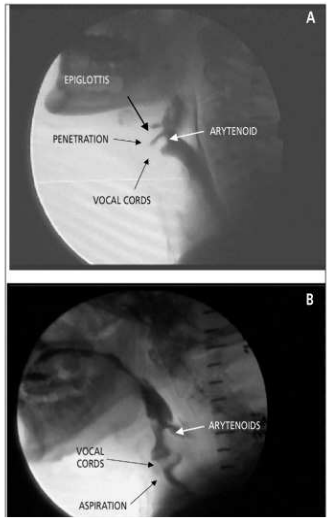
Rischio di **wheezing ricorrente** e asma a **5 anni** correlato con <u>allattamento al biberon in culla o nel letto nel **1°** anno di vita</u>

TABLE 2. Relation Between Bottle Feeding in the Bed or Crib Before Sleep Time in the First Year of Life and Recurrent Wheezing and Asthma at Age 5 Years Among 448 Study Participants

Number of Reports of Bottle Feeding in the Bed or Crib Before Sleep Time	OR (95% CI)			
	Recurrent Wheezing (n = 38)*		Asthma (n = 38)†	
	Unadjusted	Adjusted‡	Unadjusted	Adjusted‡
0	1.0	1.0	1.0	1.0
1	1.3 (1.08–1.66)	1.3 (1.05–1.66)	1.4 (1.12–1.72)	1.3 (1.07–1.69)
2	1.8 (1.16–2.77)	1.8 (1.11–2.77)	1.9 (1.25–2.95)	1.8 (1.13–2.86)
3	2.4 (1.25–4.62)	2.3 (1.17–4.61)	2.7 (1.40–5.06)	2.4 (1.21–4.84)
4	3.2 (1.35–7.70)	3.1 (1.23–7.67)	3.7 (1.57–8.68)	3.3 (1.29–8.18)
5	4.3 (1.46–12.82)	4.1 (1.30–12.76)	5.1 (1.76–14.89)	4.4 (1.37–13.83)
6	5.8 (1.57–21.35)	5.4 (1.36–21.23)	7.1 (1.97–25.55)	5.9 (1.46–23.39)

Chronic Aspiration Without Gastroesophageal Reflux As a Cause of Chonic Respiratory Symptoms in Neurologically Normal Infants

Sheikh S, Chest 2001;120:1190



112 bb con sintomi respiratori cronici <u>neurologicamente sani</u> studiati con Ph-metria e videofluoroscopia (VFS) durante la deglutizione

In 13 **(11.6%)** (età M 5.9 m) **VFS patologica** con pH-metria normale

Sintomi non-respiratori più frequentemente riportati erano sputo degli alimenti e/o crisi di soffocamento durante il pasto

Table 2—*Presenting Symptoms*

Presenting Symptoms	Patients, No.
Respiratory symptoms	
Wheezing alone	4
Chronic cough and wheezing	2
Stridor and wheezing	5
Recurrent pneumonia	2
Apnea and pneumonia	1
Feeding problems	
Spitting alone	4
Spitting and gagging	5
Spitting/gagging and choking episodes	1
No feeding problems	3

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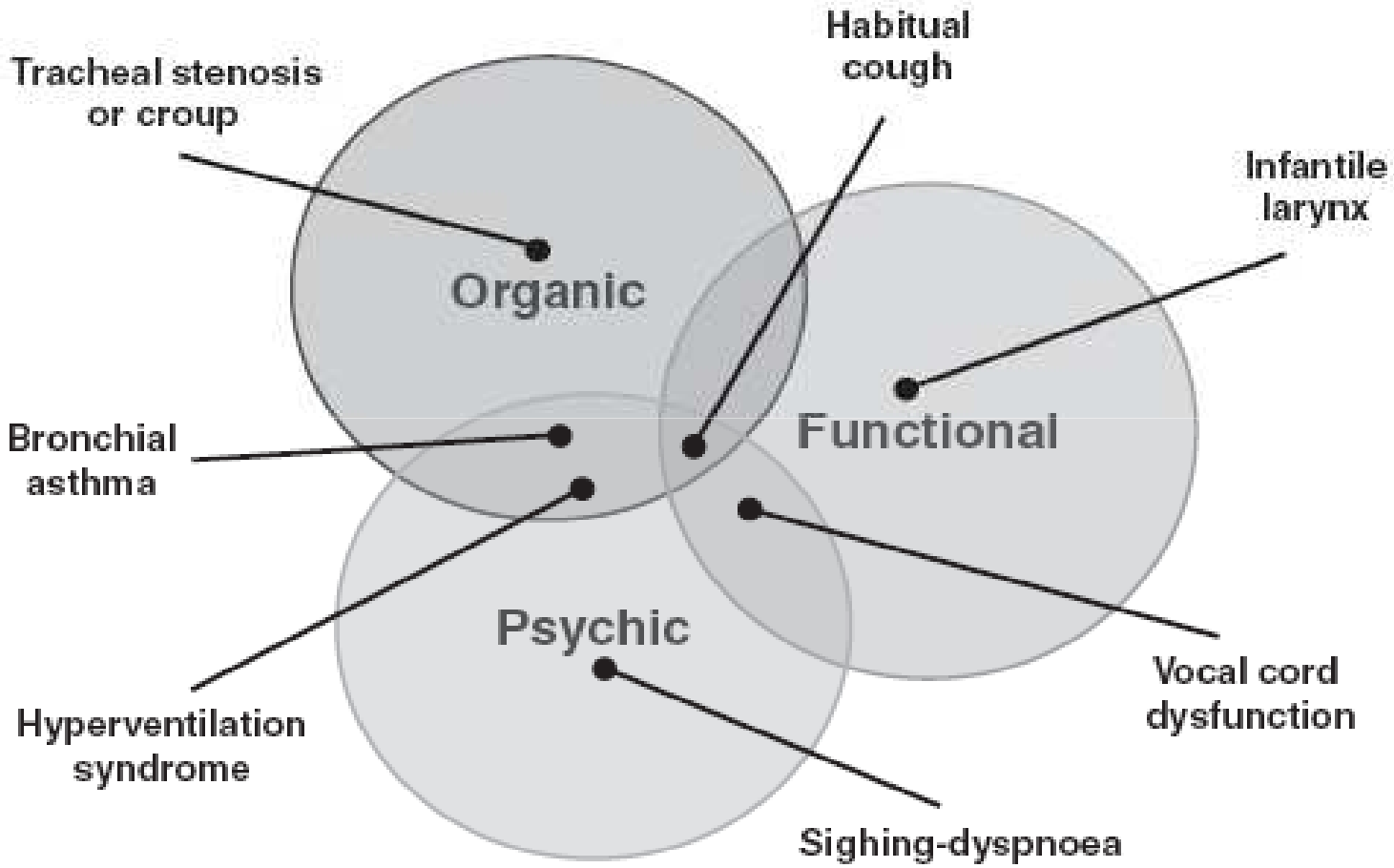
"Asthma syndrome" prescolare	Displasia broncopolmonare	Scompenso cardiaco congestizio
Infezioni - Chlam./Mycopl. - Pertosse - Tbc - BBP	Corpi estranei (trachea, bronchi esofago)	Archi vascolari anomali Tracheo-broncomal.
S. da aspirazione ricorrente	Fibrosi cistica DCP	Masse mediastiniche
S. disfunzionali		Bronchiolite obliterante interstiziopatie
SIRT		Immunodeficienze

Patologie respiratorie disfunzionali nel bambino

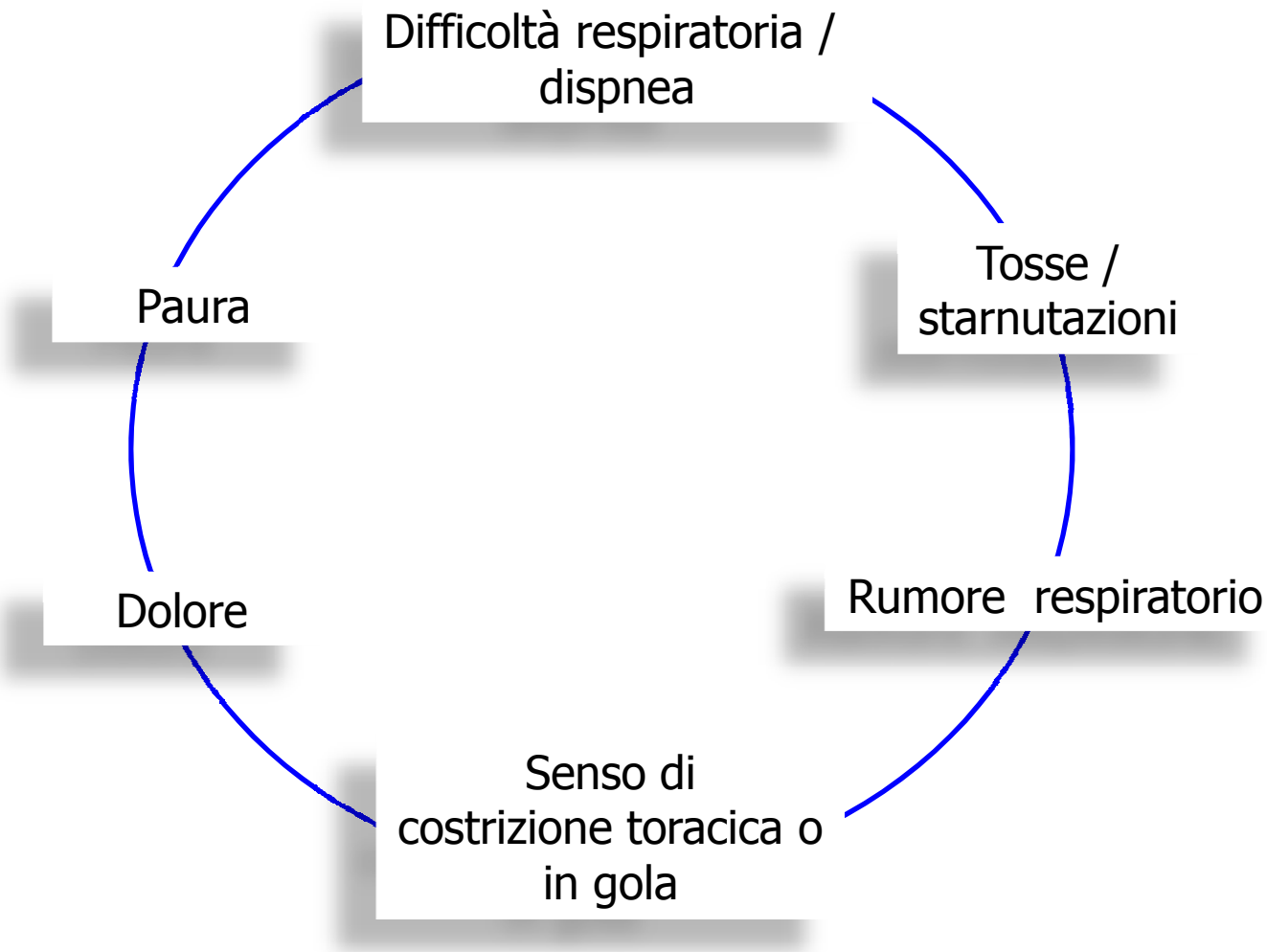
- VCD (*Vocal Cord Dysfunction*)
- Sindrome da iperventilazione
- Tosse psicogena ("habit-cough syndrome")
- Dispnea psicogena ("sighing dyspnea")
- Miscellanea: "throat clearing tic", vocalizzazioni, starnutazioni parossistiche, dolore toracico

Niggemann, Pediatr Allergy Immunol 2002;13:312



Niggemann, Pediatr Allergy Immunol 2010;21:895

PSYCOGENIC AND FUNCTIONAL BREATHING DISORDERS



Niggemann, Pediatr Allergy Immunol 2002;13:312

Niggemann, Pediatr Allergy Immunol 2010;21:895

...When the suspicion of functional breathing disorders?

Table 1. Criteria for differentiation of functional respiratory symptoms in children and adolescents

Usually no nocturnal symptoms
Occur suddenly (even at rest)
No typical triggering factors
Variable duration
May be quickly regressive
Tachypnea (no objective dyspnea)
Do not respond to adequate conventional pharmacotherapy
Normal diagnostic test results (during episodes of symptoms)

Niggemann, Pediatr Allergy Immunol 2010;21:895

CHEST Special Features

Diagnostic Criteria for the Classification of Vocal Cord Dysfunction

Morris, Chest 2010;138:1213

Table 2—*Differential Diagnosis of Laryngeal Movement Disorders*

Airway Disorder	Associated Conditions
VCD	
Psychogenic VCD	Somatoform disorder
	Conversion disorder
	Psychiatric illness
	Abuse
	Other components (anxiety disorder, stress, depression)
Exercise VCD	Exercise
Irritant VCD	Extrinsic
	Chemical irritants
	Olfactory stimuli
	Intrinsic
	GERD
	Rhinitis/postnasal drip
	Sinusitis
Supraglottic disorders	Laryngomalacia
	Exercise-induced supraglottic closure
Laryngospasm	Intubation
	Airway manipulation
	IgE mediated
	Nocturnal aspiration
Vocal cord paresis	Prolonged intubation
Vocal cord paralysis	Head and neck malignancy
	Chest surgery
	Thyroid surgery
	Idiopathic
Neurogenic	Brainstem compression
	Upper motor neuron injury
	Lower motor neuron injury
	Movement disorders
	Adductor laryngeal breathing dystonia

"POLO"
(Periodic Occurrence of Laryngeal Obstruction")

Paralisi/paresi delle CV (es. malformazione di Chiari tipo 1)

VCD (*Vocal Cord Dysfunction*)

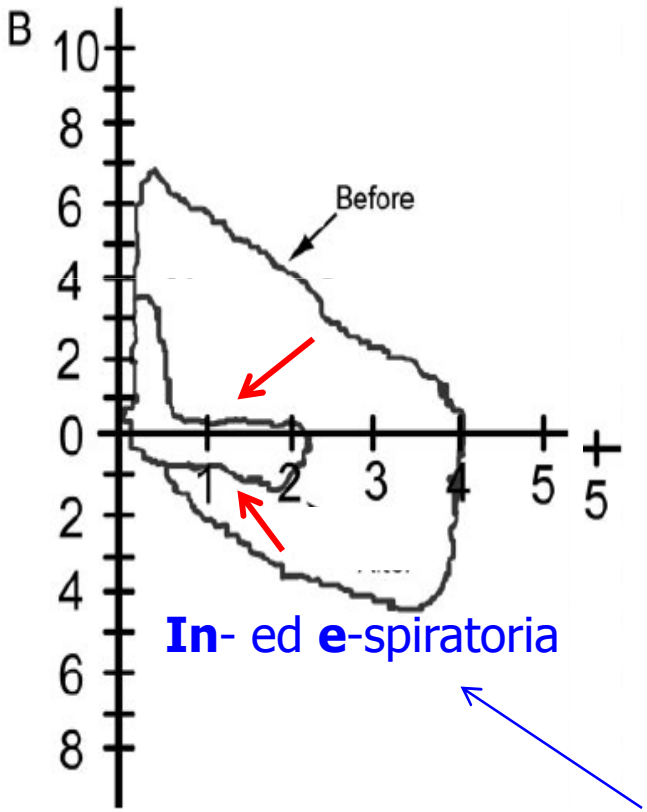
- Adduzione paradossa delle CV durante la inspirazione (normalmente la glottide si apre durante l'inspirazione e si adduce durante la espirazione)
- Più freq. nell' adolescente (segnalati casi neonatali) e nelle F (rapp. F/M 3:1)
- Coesistenza asma in ≅ 1/3 dei casi (coesistenza VCD in ≅ 15% casi di asma)
- Favorita da stress psicologici, esercizio fisico, iperventilazione, irritanti
- Clinica: Esordio improvviso → Dispnea inspiratoria (talora in- ed espiratoria), tirage, senso di soffocamento, "distress" respiratorio, tachipnea, tachicardia, talora tosse
- EO: tipico stridore; possibili sibili (spesso muto); assenza desaturazioni (raram. ipossia)
- Diagnosi: clinica, laringoscopia, spirometria (eseguire in fase acuta)
- Durata minuti, ore o giorni; risoluzione spesso spontanea
- Terapia: logopedia, ipnosi, psicoterapia, inspirazione contro resistenza, CPAP, Heliox, panting, anticolinergici, ansiolitici, postura, biofeedback, botox…

Mikita, Allergy Asthma Proc 2006;27:411
Morris, Chest 2010;138:1213
Butani, AAAI 1997;79:91
Niggemann, PAI 2002:13:312

VCD

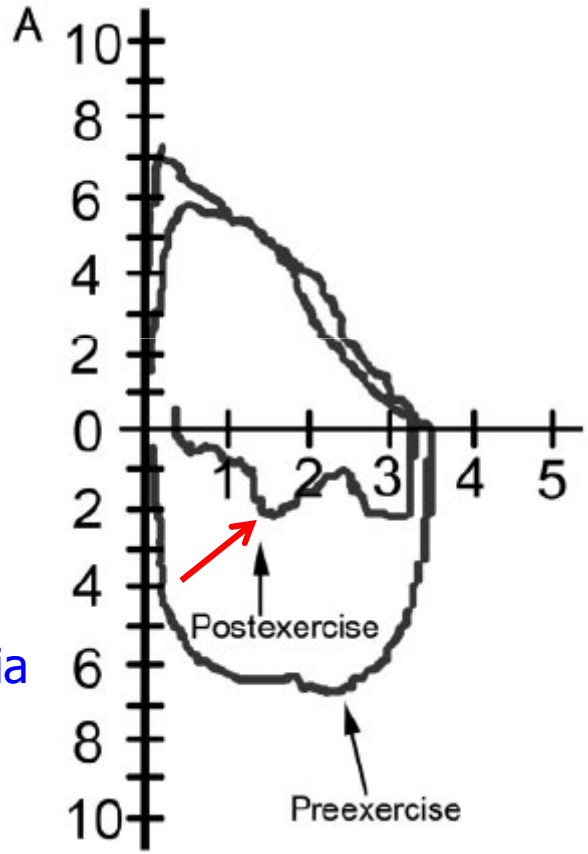
Due fenotipi

Spontanea



In- ed **e**-spiratoria

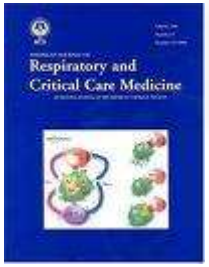
Dopo sforzo



In-spiratoria

Due sottotipi

Weinberger, Pediatrics 2007;120:855



Clinical Features of Vocal Cord Dysfunction

Newman, AJRCCM 1995;152:1382

Studio retrospettivo su 95 adulti con VCD diagnosticati con FLS

In 53/95 di VCD comorbidità con asma

Nei casi di VCD isolata prevalenza sesso F e media 4.8 anni di sintomi

In 34/42 casi di VCD isolata uso di PDN quotidiano (media: 29 mg/die)

Media accessi al **PS 10/anno** e ospedalizzazioni **6/anno** richiedenti nel **28% intubazione**

Nell'**11%** dei casi ostruzione solo **e**-spiratoria

TABLE 3

MEDICAL UTILIZATION AS DEMONSTRATED BY HOSPITAL ADMISSIONS AND EMERGENCY ROOM VISITS IN THE YEAR PRECEDING ADMISSION*

	VCD	VCD + Asthma	Asthma
Duration of symptoms, yr	4.8 ± 5.2†	14.1 ± 13.9	15.7 ± 13.8
Prednisone dose, mg	29.2 ± 28.7	21.31 ± 23.6	25.5 ± 25.3
Duration of prednisone, yr	4.3 ± 10.9	4.0 ± 4.1	3.3 ± 5.4
ER visits, year prior to admission	9.7 ± 7.9‡	5.5 ± 6.2	4.5 ± 4.8
Admissions, year prior to admission	5.9 ± 6.1‡	6.7 ± 11.9‡	3.1 ± 4.7
Patients intubated, n	12	12	12

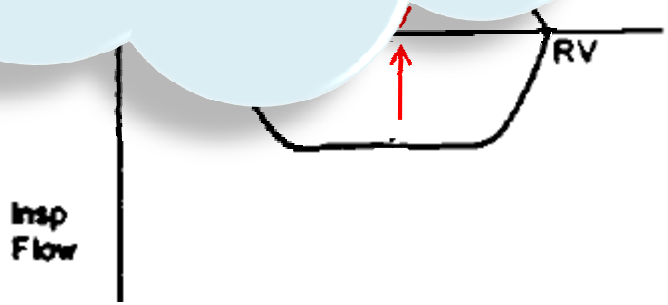
* Also shown is prednisone dose and usage. Values are means ± SD.
† $p < 0.001$ compared with control asthmatics.
‡ $p < 0.05$ compared with control asthmatics.

LARYNGOSCOPIC FINDINGS IN ASYMPTOMATIC PATIENTS WITH VCD

	VCD		VCD + Asthma	
Laryngoscopic Finding	(n)	(%)	(n)	(%)
Normal	14	39	12	25
Inspiratory closure only	7	19	12	25
Expiratory closure only	4	11	8	17
Both inspiratory and expiratory closure	11	31	16	33

Quando una curva F/V è tronca?

Flow-volume loops
[…] In symptomatic patients, this is extremely helpful in suggesting the diagnosis of VCD, but does not exclude the diagnosis in asymptomatic individuals…



$$\frac{FEF_{50}}{FIF_{50}} > 2.2$$

Morris, Chest 2010;138:1213

CRITERI DIAGNOSTICI PER VCD

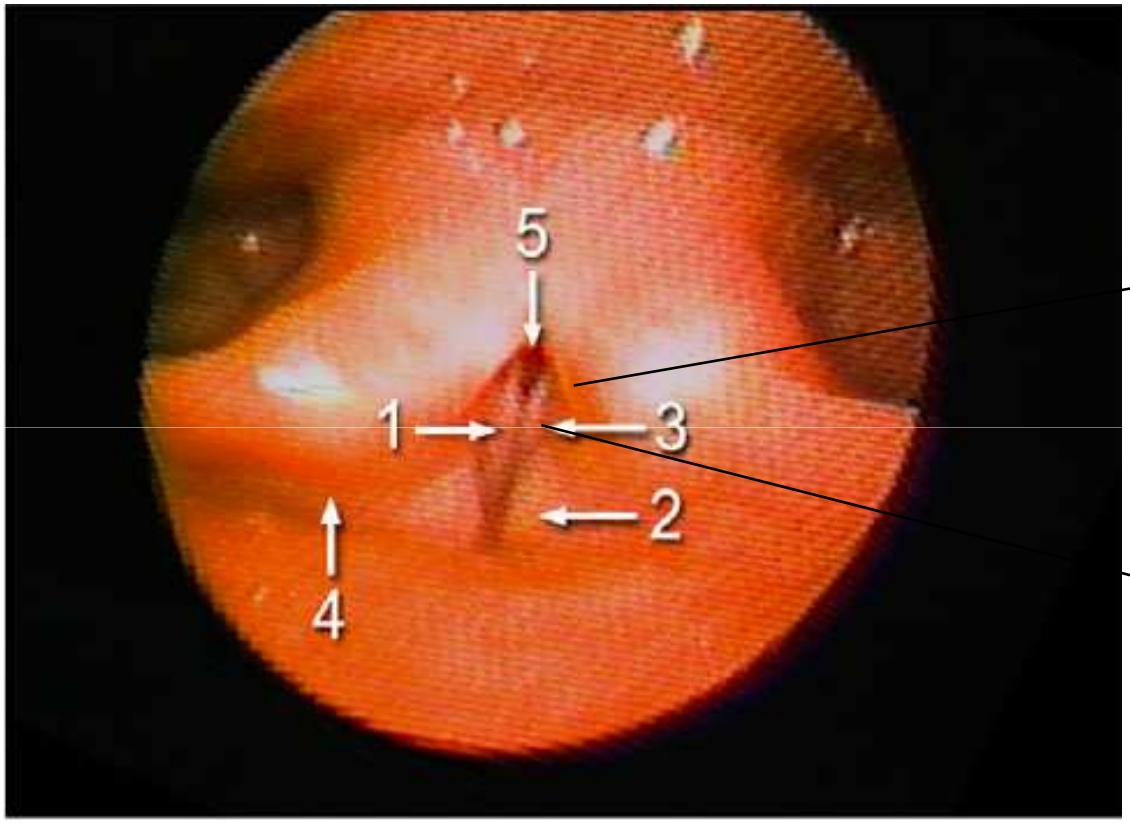
Table 3—*Diagnostic Criteri*

Clinical symptoms	Prolonged symptoms
	Recurrent, intermitte
	Shortness of breath
	Upper airway stridor
	Reproducible causati
Laryngoscopy	Adduction of vocal co
	or both inspirati
	>50% Closure of co
	Intermittent findings
	May be normal wh
	May normalize wit
	"Posterior chinking"—variable finding
PFT (criteria for suspected VCD)	Normal spirometry (no response to bronchodilator)
	Negative bronchoprovocation testing
	Abnormal (truncated or flattened) inspiratory FVL

[...] The **reference standard** for diagnosing VCD is laryngoscopic visualization of paradoxical motion of vocal cords

Butani, AAAI 1997;79:91

Morris, Chest 2010;138:1213



"[…] Greater than 50% inspiratory closure of vocal cords is sufficient for diagnosis…

Posterior "*Diamond-shaped chink*"

Morris, Chest 2010;138:1213

Table 4—*Clinical Findings From VCD Literature*

Demographics	Patients (N = 1,587)
Age, mean ± SD, y	29.6 ± 15.7
Adults (≥ 18 y)/pediatrics (< 18 y)	792 (70)/339 (30)
Male/female	377 (30)/880 (70)
PFT	847 (54)
FVL truncation	390 (46)
Normal/obstruction	368 (43)/145 (17)
Bronchoprovocation testing/reactive	171/46
Endoscopy findings	978 (62)
Inspiratory adduction	315 (32)
Expiratory adduction	88 (9)
Posterior chink	29 (3)
Associated etiology	
Asthma	445 (28)
Exercise	269 (17)
Psychiatric/emotional	270 (17)
Gastroesophageal reflux	267 (17)
Chemical irritants	103 (6)
URI	98 (6)

Morris, Chest 2010;138:1213

Patologie respiratorie disfunzionali nel bambino

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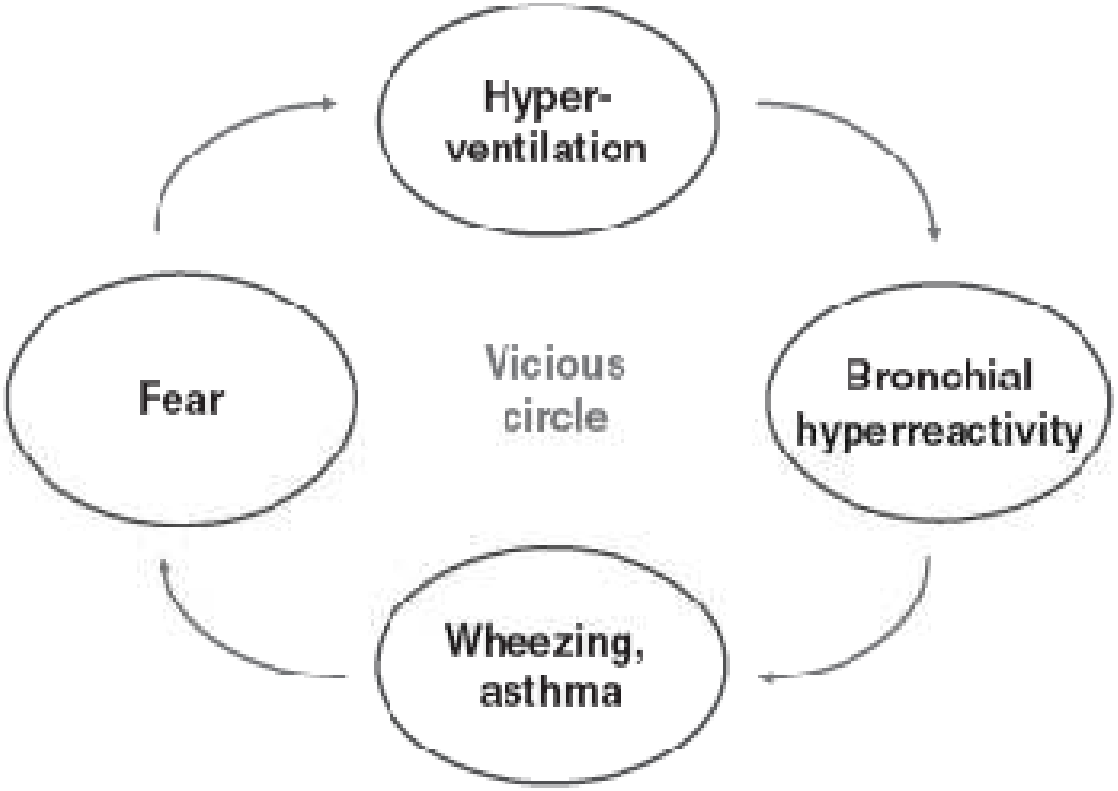
Niggemann, Pediatr Allergy Immunol 2002;13:312

SINDROME DA IPERVENTILAZIONE (HVS)

- Massima incidenza 13-14 aa; rapporto F/M 2:1
- Fattore scatenante: ansia, preoccupazione sullo stato di salute e sessualità
- Frequente concomitanza con asma (con cui può entrare in *feedback positivo*: iperventilazione → BHR → asma → ansia → iperventilaz.
- Clinica: respiro frequente o corto, fame d'aria, vertigini, cardiopalmo, stordimento, astenia, parestesie, sudorazioni, cefalea, dolore toracico
- Possibile causa di ipocapnia e alcalosi repiratoria (raramente tetania)
- Diagnosi: test di Nijmegen (vn <23), test di iperventilazione
- Prognosi: possibile persistenza fino 40% dei casi in età adulta
- Terapia: respirazione dentro sacchetto di carta, ansiolitici, Butheiko, psicoterapia

Niggemann, Pediatr Allergy Immunol 2002;13:312
Gardner, Chest 1996;109:516



Niggemann, Pediatr Allergy Immunol 2010;21:895

HYPOCAPNIA

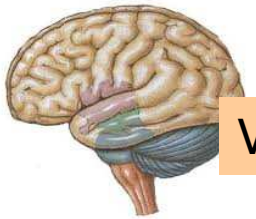
JOHN G. LAFFEY, M.D., AND BRIAN P. KAVANAGH, M.B.

Laffej, NEJM 2002;347:43

TABLE 2. ADVERSE NEUROLOGIC AND MYOCARDIAL EFFECTS OF HYPOCAPNIA.

- Brain injury in neonates
  - Multicystic encephalomalacia
  - Cystic periventricular leukomalacia
  - Pontosubicular necrosis
  - Cerebral infarction
  - Reactive hyperemia and hemorrhage
- Impairment of cerebral function in adults
  - Increased time to regain consciousness, increased reaction times
  - Poorer psychomotor performance, diminished higher intellectual functions
  - Personality changes
- Myocardial effects
  - Decreased myocardial oxygen supply
    - Reduced coronary flow and collateral flow
    - Increased coronary vascular resistance, increased risk of coronary-artery spasm
    - Increased coronary microvascular leakage
    - Increases in platelet count and aggregation
  - Increased myocardial oxygen demand
    - Increased oxygen extraction
    - Increased (and later decreased) contractility
    - Increased intracellular calcium concentration
    - Increased systemic vascular resistance
  - Myocardial ischemia
  - Reperfusion injury

Sintomatologia HVS



Vasocostrizione cerebrale

Tremori

Tinnito

Disturbi visivi

Capogiri

Cefalea

Allucinazioni

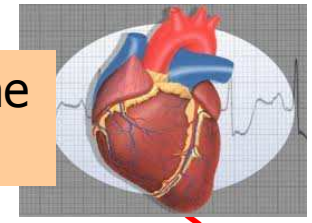
Atassia

Perdita di coscienza

Parestesie

Tetania

Vasocostrizione cardiaca

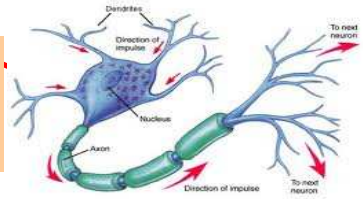


Tachicardia

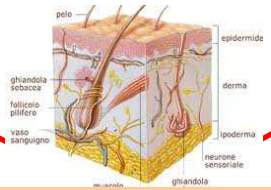
Dolore toracico

Sottoslivellamento ST (ECG)

Ipereccitabilità neuronale



Senso di freddo alle estremità



Vasocostrizione cutanea

Patogenesi incerta

Fame d'aria

Vomito

Sudorazioni

Epigastralgie

Gardner, Chest 1996;109:516 (modif.)

Hyperventilation Syndrome in Children and Adolescents: Long-Term Follow-up

Herman, Pediatrics 1981;67:183

Records di **34 bb** (<18 aa) con HVS osservati in 25 anni (1950-1975) c/o la Mayo Clinic, Rochester, USA

Questionari di recall

Identificati 5 sottotipi di HVS

Tetania presente nel 18% e **convulsioni** nel 3% dei casi

Al follow-up 40% continuavano ad avere HVS in età adulta

TABLE 2. Symptoms of Hyperventilation

Symptom	Patients	
	No.	%
Tachypnea	30	88
Anxiety	27	79
Breathlessness	26	76
Light-headedness	18	53
Paresthesias	18	53
Choking feeling	11	32
Chest pain	6	18
Blurred vision	4	12
Feeling of impending doom	3	9
Confusion	3	9
Dry mouth	1	3
Hallucinations	1	3
Other	13	38

TABLE 3. Signs of Hyperventilation

Sign	Patients	
	No.	%
Tachycardia	6	18
Tetany	6	18
Unconsciousness	4	12
Diaphoresis	2	6
Chvostek sign positive	1	3
Seizure	1	3
Other	1	3

Prevalence of dysfunctional breathing in patients treated for asthma in primary care: cross sectional survey

Mike Thomas, R K McKinley, Elaine Freeman, Chris Foy

Thomas, BMJ 2001;322:1098–100

307 adulti (17-65 aa) con asma reclutati da una General Practice

Questionario di Nijmegen (postale)

In 227 questionario valutabile
63/219 **(28%)** score di Nijmegen >23

Pazienti con score+ più frequentemente femmine e di età inferiore

Nessuna correlazione con la severità dell'asma

Table 2 Numbers (percentages) of respondents with positive scores for dysfunctional breathing by age and sex

	Age <40 years	Age ≥40 years	Total
Men	7/25 (28)	10/62 (16)	17/87 (20)
Women	14/38 (37)	32/94 (34)	46/132 (35)
Total	21/63 (33)	42/156 (27)	63/219 (29)

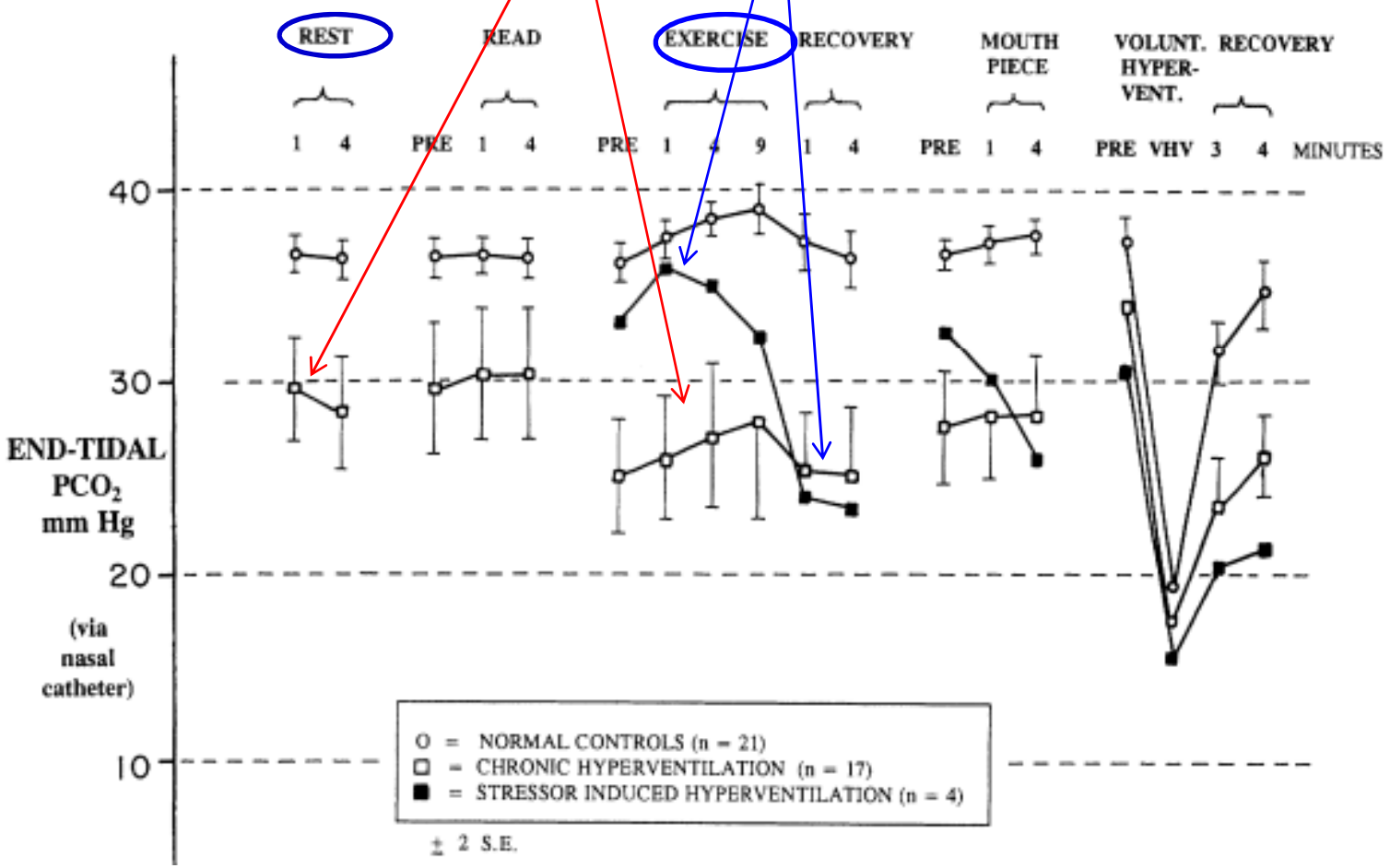
British Thoracic Society treatment step	Positive score* n=63	Negative score (n=156)
1	14 (22)	35 (22)
2	21 (33)	51 (33)
3	14 (22)	45 (29)
4	14 (22)	23 (14)
5	0	2 (1)

*≥23 on Nijmegen questionnaire.

2 forme di HVS

Forma acuta

Forma cronica



Gardner, Chest 1996;109:516

Diagnosi di HVS

Score di Nijmegen

16 items per sintomi associati a "respiro difficile"

Score ≥23 suggestivo per HVS

Table 1 Nijmegen questionnaire. Respondents are asked to ring the score that best describes the frequency with which they experienced the symptoms listed

Symptom	Never	Seldom	Sometimes	Often	Very often
Chest pain	0	1	2	3	4
Feeling tense	0	1	2	3	4
Blurred vision	0	1	2	3	4
Dizziness	0	1	2	3	4
Confusion or loss of touch with reality	0	1	2	3	4
Fast or deep breathing	0	1	2	3	4
Shortness of breath	0	1	2	3	4
Tightness across chest	0	1	2	3	4
Bloated sensation in stomach	0	1	2	3	4
Tingling in fingers and hands	0	1	2	3	4
Difficulty in breathing or taking a deep breath	0	1	2	3	4
Stiffness or cramps in fingers and hands	0	1	2	3	4
Tightness around the mouth	0	1	2	3	4
Cold hands or feet	0	1	2	3	4
Palpitations in the chest	0	1	2	3	4
Anxiety	0	1	2	3	4

Van Dixhoorn, J Psycosom Res 1985;29:199
Thomas, BMJ 2001;322:1098

Diagnosi di HVS

HYPERVENTILATION PROVOCATION TEST

Iperventilazione con almeno 20 atti respiratori profondi

Howell, Thorax 1997;52:S30
Morgan, Thorax 2002;57(suppl. II):31

Test positivo
se il pz riconosce
i sintomi nel loro
complesso
come gli stessi
accusati nella
vita di ogni giorno

Hornsveld, Lancet 1996;348:154

Iperventilazione per 3′, in modo da produrre una caduta prolungata della P_{CO_2} alveolare (end-tidal) o arteriosa di $\leq$50% (o <2.4 kPa), seguito da 3-10′ di respiro normale

Hornsveld , Lancet 1996;348:154
Ringsberg, JACI 1999;103:601

Test positivo
se il pz riconosce
con uno score $\geq$3
almeno 2 items
maggiori del
Nijmegen

Ringsberg, JACI 1999;103:601

Vansteeinkinste, ERJ;1991:4:393

Sforzo fisico appropriato per 10′, seguito da 3′ di iperventilazione spontanea

Gardner, Chest 1996;109:516

Test positivo
se $EtCO_2$ in
qualunque momento
<30 mm/Hg

Gardner, Chest 1996;109:516

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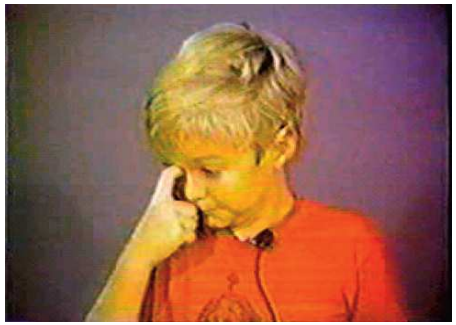
Niggemann, Pediatr Allergy Immunol 2002;13:312

Tosse psicogena ("habit-cough syndrome")

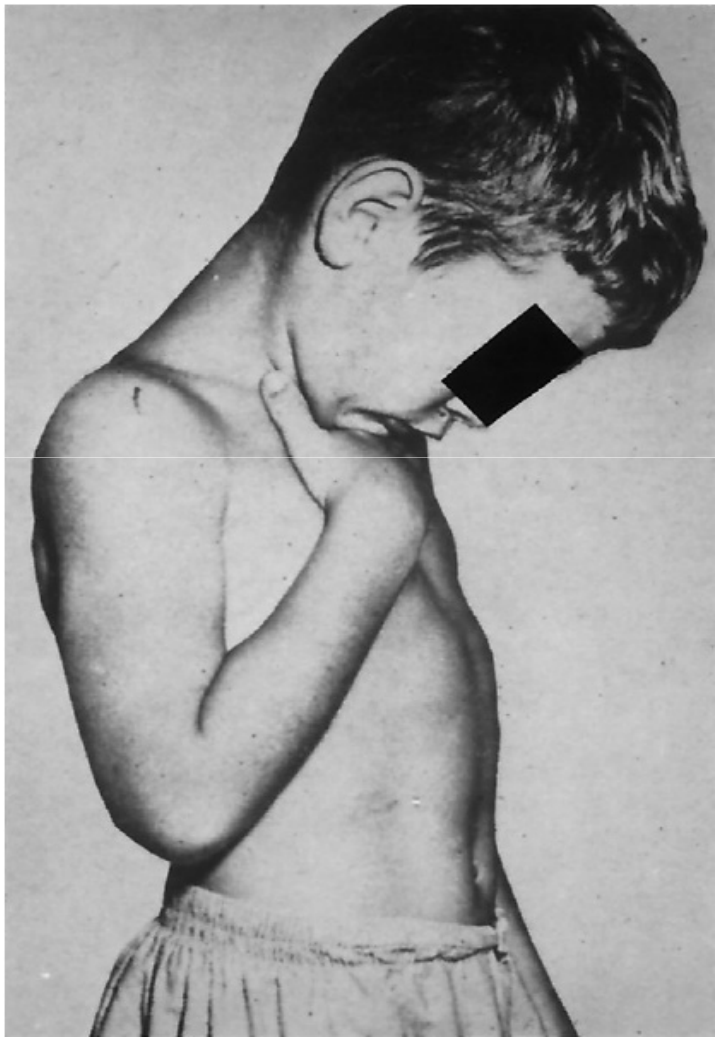


- Età terza infanzia-adolescenza
- Esordio spesso dopo una URTI
- Esclusivamente diurna e in veglia
- Talvolta associata a movimenti di flessione del mento sul collo
- Frequente associazione con DAR e intestino irritabile
- Timbro caratteristico, abbaiante, gutturale, sonora, inconfondibile
- Più disturbante per i conviventi che per il paziente
- Peggiora in presenza del medico e di altre persone
- Così intensa da rappresentare motivo di "crisi" familiari e ritiro da scuola
- Segnalata causa di fratture costali
- Habitus psichico tipo disturbi di conversione, fobie, ansia, ricerca di attenzione
- Terapia: psicoterapia, biofeedback, lenzuolo toracico, lidocaina spray

Niggemann, Pediatr Allergy Immunol 2010;21:895 (modif)
Butani, Ann Allergy Asthma Immunol 1997;79:91

"Habit cough"

the "chin-on-chest" posture



Butani, Ann Allergy Asthma Immunol 1997;79:91

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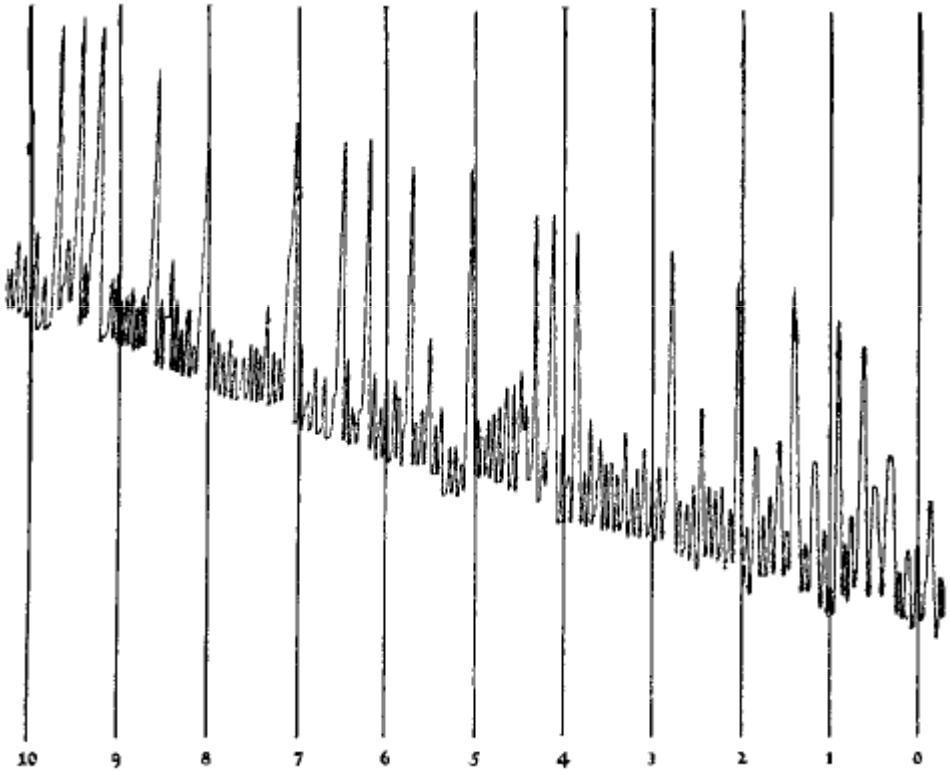
Niggemann, Pediatr Allergy Immunol 2002;13:312

Dispnea psicogena ("sighing dyspnea")

- Età terza infanzia – adolescenza
- Descritta come impossibilità a "prendere l'aria" o "fare un respiro sufficiente" o "pieno"
- Pattern respiratorio caratterizzato da attacchi di respiratori profondi intervallati da periodi di respiri di normale profondità, senza variazioni della FR
- Attacchi solitamente a riposo (d.d. con malattie organiche)
- Non dispnea visibile
- Associazione con altri sintomi, tipo aerofagia, senso di peso, costrizione al torace, eruttazioni
- Obiettività negativa
- Necessario escludere patologie organiche, spt di tipo cardiologico e tiroideo
- Storia naturale poco nota

Niggemann, Pediatr Allergy Immunol 2010;21:895 (modif)
Butani, Ann Allergy Asthma Immunol 1997;79:91

Pattern ventilatorio nella “sighing dyspnea”



Butani, Ann Allergy Asthma Immunol 1997;79:91

PATOLOGIE CONGENITE O ACQUISITE CON WHEEZING

Comuni	Poco comuni	Rare
"Asthma syndrome" prescolare	Displasia broncopolmonare	Scompenso cardiaco congestizio
Infezioni - Chlam./Mycopl. - Pertosse - Tbc - BBP	Corpi estranei (trachea, bronchi esofago)	Archi vascolari anomali Tracheo-broncomal.
S. da aspirazione ricorrente	Fibrosi cistica DCP	Masse mediastiniche
S. disfunzionali		Bronchiolite obliterante interstiziopatie
SIRT		Immunodeficienze

Cosa si sa della SIRT (Airway Sensory Hyperreattivity)

Prevalenza poco conosciuta (adolescenti 13-19 aa: 0.9%)

Andersson, Int J Hyg Environ Health 2008; 211:690

Correlazione con ↑ espressione "*Transient receptor potential vanilloid-1*" (TRPV-1), fibre CGRP+, polimorfismi gene NK-2R, ↑ livelli di sostanza P nel nasal washing

Gronenberg, Am J Respir Crit Care Med 2004;170:1276
Park, Thorax 2006;61:1070
O'Connel 1995;152:2068
Cho, JACI 2003;112:695

Aumentata reattività alla capsaicina (non alla metacolina)

Millqvist, Allergy 2000;55:540

Aumentata sensibilità "multiorgano" (naso = "*Chemical Sensitivity S.*")

Johansson, Chest 2006; 129:1623

Storia naturale poco nota (non evoluzione in asma)

Chang, Ped Pulmonol 1999;28:59

Inefficacia antibiotici, CS e beta-2

Chang, Arch Dis Child 1999; 80:211

Increased Expression of Transient Receptor Potential Vanilloid-1 in Airway Nerves of Chronic Cough

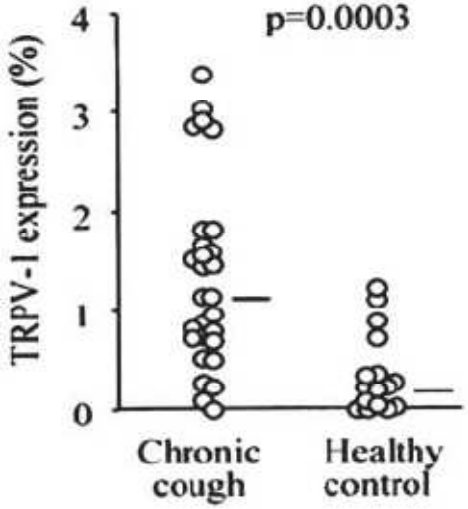
Gronenberg, AJRCCM 2004;170:1276

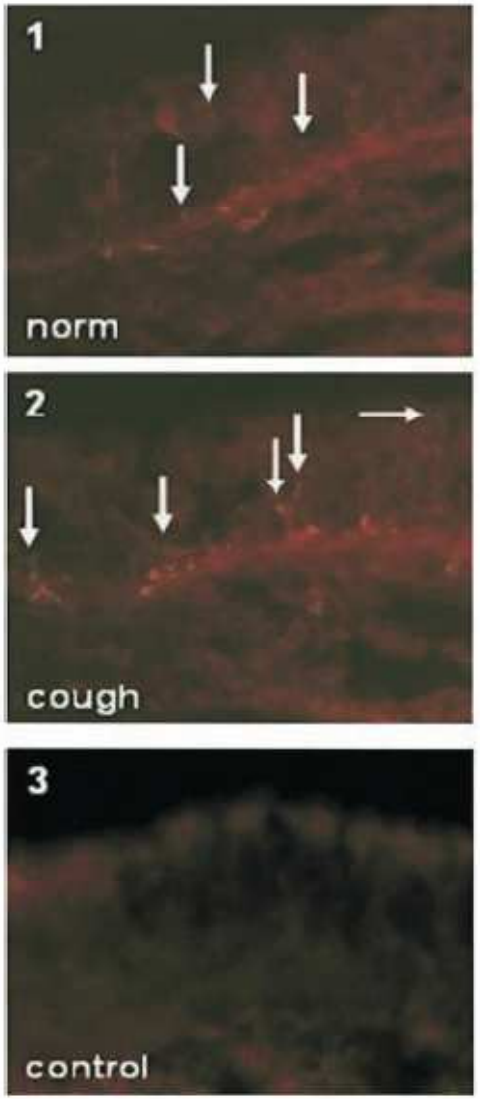
Studio della espressione del *Transient Receptor Potential Vanilloid-1* nelle vie aeree di pz con **tosse cronica** da cause diverse e iperreattività alla capsaicina

FBS e biopsia bronchiale

Aumentata espressione (5x) del **TRPV-1**

Correlazione tra risposta alla capsaicina ed espressione TRPV-1





CHEST Original Research
COUGH

Relationship Between Self-Reported Odor Intolerance and Sensitivity to Inhaled Capsaicin*

Proposed Definition of Airway Sensory Hyperreactivity and Estimation of Its Prevalence

Johansson, Chest 2006; 129(6):1623

Studio di correlazione tra ipersensibilita agli odori (valutata mediante questionario) e positività al test di inalazione della capsaicina

Table 3—*Distribution of Gender, Mean Age, and Results of Capsaicin Inhalation Test in Four Groups (Total n = 103) With Different Odor Intolerance (by CSS-SHR Score)**

Groups	Men/Women, No.	Mean Age, yr	Coughs After Inhalation Test: Saline Solution	Coughs After Inhalation Test: 0.4 µmol/L Capsaicin	Coughs After Inhalation Test: 2.0 µmol/L Capsaicin	Positive Capsaicin Test Results
A (n = 40)	12/28	53	0.4 (0–1.0)	5.9 (3.4–8.4)	24.8 (17.6–32.0)	13 (33) [4/9]
B (n = 21)	7/14	46	0.1 (0–0.4)	2.0 (0–4.3)	10.9 (4.3–17.4)	2 (10) [0/2]
C (n = 21)	11/10	48	0.5 (0–1.3)	1.4 (0.5–2.3)	8.7 (3.2–14.1)	1 (5) [0/1]
D (n = 21)	14/7	41	0	1.2 (0.3–2.2)	6.6 (2.7–10.5)	0 (0)

*Values are given as the mean (95% CI) or No. (%) [men/women], unless otherwise indicated.

Pz con cut off > 43 (ipersensibiltà oggettiva agli odori)

13/16 (81%) positivi al test alla capsaicina avevano un test positivo di ipersensibilità agli odori

PATOLOGIE CONGENITE O ACQUISITE CON WHEEZING

Comuni	Poco comuni	Rare
"Asthma syndrome" prescolare	Displasia broncopolmonare	Scompenso cardiaco congestizio
Infezioni - Chlam./Mycopl. - Pertosse - Tbc - BBP	Corpi estranei (trachea, bronchi esofago)	Archi vascolari anomali Tracheo-broncomal.
S. da aspirazione ricorrente	Fibrosi cistica DCP	Masse mediastiniche
S. disfunzionali		Bronchiolite obliterante interstiziopatie
SIRT		Immunodeficienze

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Wheezing in Infants with Cystic Fibrosis: Clinical Course, Pulmonary Function, and Survival Analysis

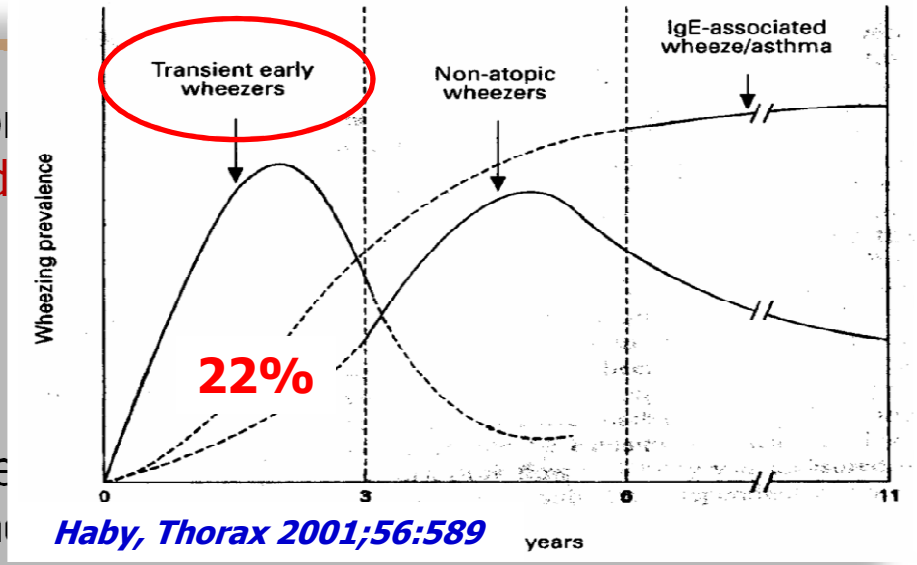
Kerem, Pediatrics 1992;90:703

229 bb con FC diagnosticata tra il 1965 e il 1979
<u>prima dei 2 anni</u>

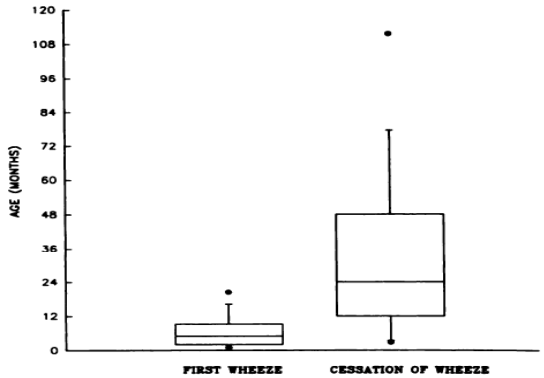
Wheezing p
primi 2 aa d

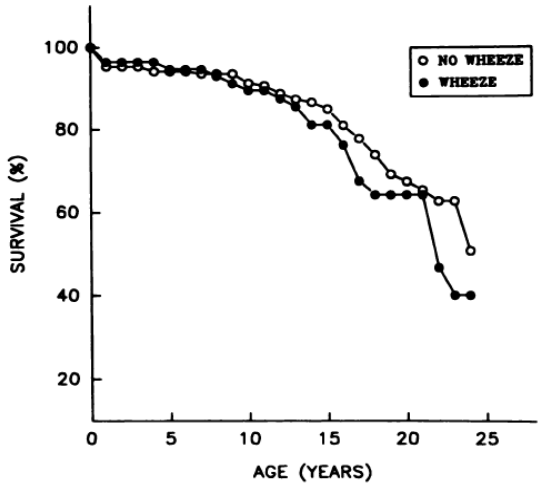
Risoluzione
i 4 aa

Correlazione
rinite (ma n



Haby, Thorax 2001;56:589





A 13 aa FEV_1 significativamente ↓ nel gruppo FC+wheezing *vs* FC non-wheezing

[…] While a chronic wet cough **does not exclude asthma**, in the majority of children the presence of chronic wet cough **does not equate to asthma…**

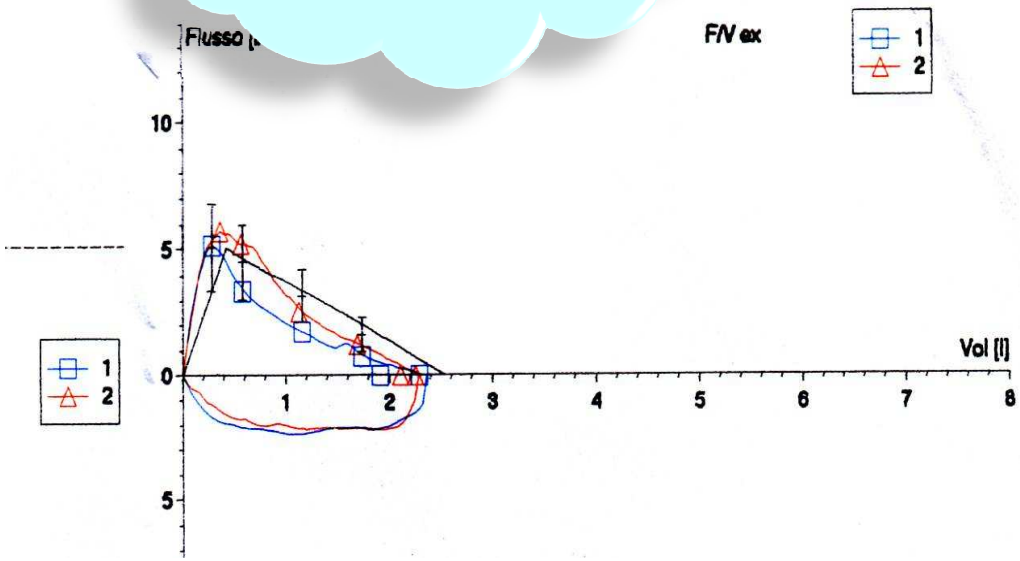
Chang, Ped Pulmonol 2008;43:519

Antonio, anni 9

Wheezing, dispnea da sforzo, tosse produttiva nei periodi intercritici

	Teor	Pre	%Pre/P	Post	%Post/P	%2/1
VC IN .....[l]	2.61	2.34	89.8	2.25	86.2	95.9
IC.....[l]	1.76					
ERV.....[l]	0.85					
FVC.....[l]	2.53	2.29	90.4	2.25	88.7	98.2
PEF.....[l/s]	5.06	5.18	102.4	5.75	113.6	110.9
FEV 1.....[l]	2.17	1.91	88.1	2.10	97.[illegible]	110.3
FEV 1 % FVC.....[%]	84.[illegible]	83.[illegible]	98.6	93.64	110.8	112.3
FEV 1 % VC MAX.[illegible]	[illegible]	[illegible]	96.4	93.59	110.7	114.9
FEF 25.....			75.5	5.26	117.1	155.1
FEF 50.....			55.8	2.56	80.6	144.6
FEF 75.....			17.8	1.24	75.8	158.8
MMEF 75/25			56.5	2.39	85.4	151.1
FIV1.....				2.07		93.8
PIF.....				2.20		93.1
FVC IN....			9.8	2.25	86.2	95.9
Sostanza						

Test del sudore
Cl= 72 meq/L



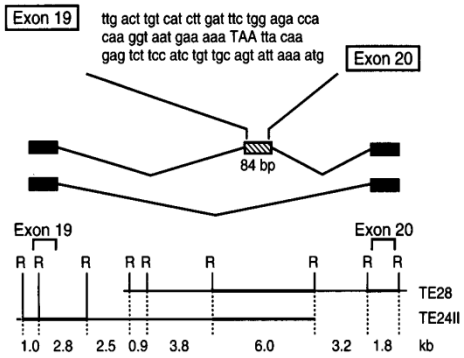
The NEW ENGLAND JOURNAL of MEDICINE

A NOVEL MUTATION IN THE CYSTIC FIBROSIS GENE IN PATIENTS WITH PULMONARY DISEASE BUT NORMAL SWEAT CHLORIDE CONCENTRATIONS

Highsmith, NEJM 1994;331:974

23 pazienti con malattia polmonare suggestiva per FC e **normale test del sudore**

Studio di mutazione (DNA sequencing)



In **13/23** presenza di mutazione puntiforme *(3849+10 kb C-to-T)* nell'**introne 19** del CFTR causa della creazione di un sito alternativo di splicing

Trascritto "normal-spliced": 8% del normale

Nei soggetti affetti presenza di significativa alterazione dei potenziali nasali

Table 1. Clinical Features and Genotype of Patients with Pulmonary Disease and Normal Sweat Chloride Levels.

Patient No.*	Sex/Age (yr)	Sweat Chloride† (mmol/liter)	FEV_1‡ (% of predicted)	Chest Radiograph	Sputum Microbiology	Pancreatic Exocrine Function§	Haplotype¶	Genotype‖	Ethnic Origin**	Comments††
1	F/20	16	73	Bronchiectatic upper zones	*S. aureus*	Sufficient	BB	Int19/Int19	Pakistani	Parents, paternal grandparents consanguineous
2	F/30	43	69	Bronchiectatic, diffuse	*S. aureus, P. aeruginosa* (mucoid)	Sufficient	CC	Int19/Int19	Ashkenazi Jewish	Parents probably consanguineous; sister died‡‡
3A	F/23	30	92	Diffuse markings	*S. aureus*	Sufficient	DB	Int/19/ΔF	N. European white	Never hospitalized
3B	M/16	44	65	Diffuse markings	*S. aureus, P. aeruginosa* (mucoid)	Sufficient	DB	Int19/ΔF	N. European white	—
4	F/39	42	45	Bronchiectatic, diffuse	*P. aeruginosa* (mucoid)	Sufficient	Uncertain§§	Int19/ΔF	Ashkenazi Jewish	Sister died¶¶
5	M/12	39	75	Diffuse markings	*S. aureus*	Sufficient	DB	Int19/ΔF	N. European white	Never hospitalized
6A	M/32	58	78	Markings, upper lung zone	*S. aureus*	Sufficient	BB	Int19/ΔF	N. European white	Azoospermic, never hospitalized
6B	F/26	19	85	Markings, upper lung zone	*S. aureus*	Sufficient	BB	Int19/ΔF	N. European white	Never hospitalized
7A	M/29	51	47	Bronchiectatic, diffuse	*S. aureus, P. aeruginosa* (mucoid)	Insufficient	Uncertain§§	Int19/ΔF	Ashkenazi Jewish	—
7B	M/27	34	63	Bronchiectatic, diffuse	*P. aeruginosa* (mucoid)	Insufficient	Uncertain§§	Int19/ΔF	Ashkenazi Jewish	Never hospitalized
7C	M/24	50	56	Bronchiectatic, diffuse	*P. aeruginosa* (mucoid)	Insufficient	Uncertain§§	Int19/ΔF	Ashkenazi Jewish	Never hospitalized
8A	F/13	29	22	Bronchiectatic, diffuse	*P. aeruginosa* (mucoid)	Sufficient	CB	Int19/W1282X	Ashkenazi Jewish	—
8B	F/4	45	Not done	Diffuse markings	Not done	Sufficient	CB	Int19/W1282X	Ashkenazi Jewish	—

CRITERI DIAGNOSTICI PER FIBROSI CISTICA

Table 3. Criteria for Diagnosing Cystic Fibrosis (CF) in Children and Infants[18–20]

1 of:	PLUS 1 of:
≥1 Typical phenotypic feature of CF	Elevated sweat chloride level >60 mEq/L (>30 mEq/L of Cl^- in children <2 years) on 2 occasions
Sibling with CF	2 Identified *CFTR* mutations
Positive newborn screening test result	Abnormal nasal potential difference

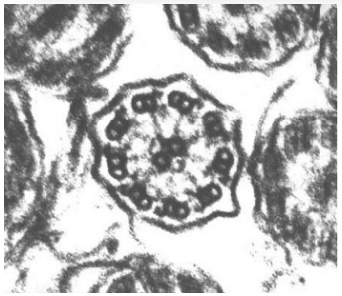
CF, cystic fibrosis; CFTR, cystic fibrosis transmembrane conductor regulator; Cl, chloride.

Chipps, Ann Allergy Asthma Immunol 2010;104:279

REVIEW

Primary ciliary dyskinesia: current state of the art

Andrew Bush, Rahul Chodhari, Nicola Collins, Fiona Copeland, Pippa Hall, Jonny Harcourt, Mohamed Hariri, Claire Hogg, Jane Lucas, Hannah M Mitchison, Christopher O'Callaghan, Gill Phillips



Bush, Arch Dis Child 2007;92:1136

Table 1 Features leading to the diagnosis of PCD

Presenting feature	Number (%) of cases (n = 55)
Significant neonatal respiratory distress	37 (67)
Abnormal situs	38 (69)
Cough most days	46 (84)
Sputum production	24 (44)
Rhinorrhoea from the newborn period	42 (76)
Wheeze	16 (29)
Sinusitis	6 (11)
Serous otitis media	28 (51)
Hearing loss	14 (25)
Diagnosis made in a sibling	6 (11)

Modified from Coren *et al.*[2] Most children had multiple symptoms, typically a combination of upper and lower airway disease.

PATOLOGIE CONGENITE O ACQUISITE CON WHEEZING

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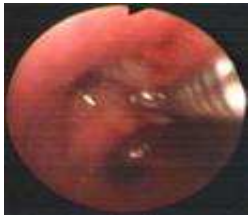
S. disfunzionali		Bronchiolite obliterante interstiziopatie
SIRT		Immunodeficienze

Investigation of young children with severe recurrent wheeze: any clinical benefit?

S. Saglani*, A.G. Nicholson#, M. Scallan¶, I. Balfour-Lynn*, M. Rosenthal*, D.N. Payne* and A. Bush*

Saglani, Eur Respir J 2006;27:29



47 bb con "difficult wheezing"

(5-58 mesi)

- TC torace
- Brushing
- T. Sudore
- Profilo immunologico
- Ph-metria GE
- FBS

In 37/47 anomalie FBS

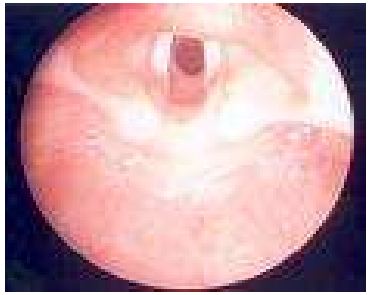
13/37 **(35%)** anomalie strutturali delle vie aeree

TABLE 5 Results of the investigations in young children with severe wheeze (divided according to age group)

	Group			p-value
	<18 months	18–36 months	>36 months	
Subjects n	19	13	15	
On inhaled steroids	7/19 (37)	10/13 (77)	11/15 (73)	<0.05 group 1 *versus* 2 and 3
On oral steroids	4/19 (21)	4/13 (31)	3/15 (20)	NS
Total IgE IU	14 (1–64)	19 (3–635)	154 (16–2605)	<0.01 group 3 *versus* 1 and 2
IgE RAST ⩾1 positive	5/18 (28)	4/13 (31)	9/15 (60)	NS
CT scan abnormality	6/11 (55)	2/9 (22)	7/11 (63)	NS
Abnormal pH study	7/14 (50)	8/10 (80)	10/11 (91)	<0.05 group 1 *versus* 2 and 3
Structural abnormality on FOB	10/19 (53)	1/13 (8)	2/15 (13)	<0.01 group 1 *versus* 2 and 3
Positive bacterial growth on BAL	9/16 (56)	5/13 (38)	5/15 (33)	NS
Good quality EB	15/18 (83)	10/13 (77)	11/15 (73)	NS
EB RBM thickened score >1	0/14 (0)	1/10 (10)	9/11 (82)	<0.01 group 3 *versus* 1 and 2
EB eosinophilia score >0	5/15 (33)	4/10 (40)	7/11 (64)	NS
Abnormal IgG, IgA, IgM	2/14 (14)	0/12 (0)	3/15 (20)	NS

Data are presented as n/n (%). Ig: immunoglobulin; RAST: radioallergosorbent test; CT: computed tomography; FOB: fibreoptic bronchoscopy; BAL: bronchoalveolar lavage; EB: endobronchial biopsy; NS: nonsignificant.

7 regole + 1 per sospettare una malformazione delle vie aeree nel wheezing



1. Esordio solitamente entro i 6 mesi di vita
2. Sintomi scatenati da vir
3. Wheezing spesso no "the happy wheezer")
4. Wheezing generalm aO2
5. Wheezing in assenza di retrazioni s tali
6. Wheezing refrattario alla terapia antiasmatica (β-agonisti, steroidi)
7. Rumore udibile anche nei periodi intercritici (senza il fonendoscopio)
8. Wheezing attenuato da alcune posizioni (opistotono)

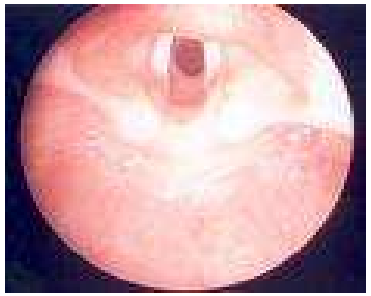
RGE spesso associato

Finder, Curr Prob Pediatr 1999;29:65 (modif)

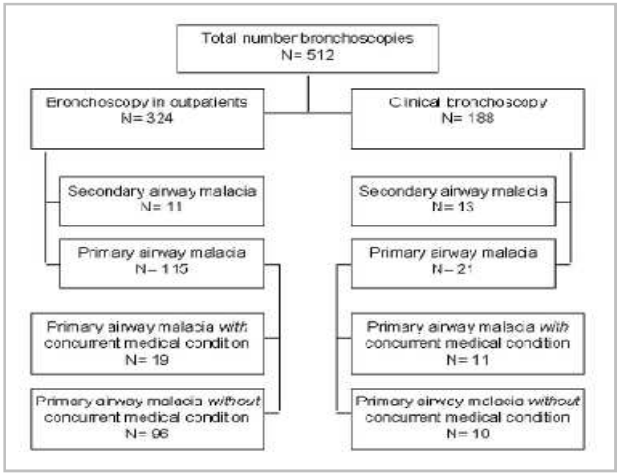
Tracheomalacia and Bronchomalacia in Children*

Incidence and Patient Characteristics

Boogard, Chest 2005;128:3391



Studio retrospettivo
512 FBS effettuate tra il 1997 e il 2004

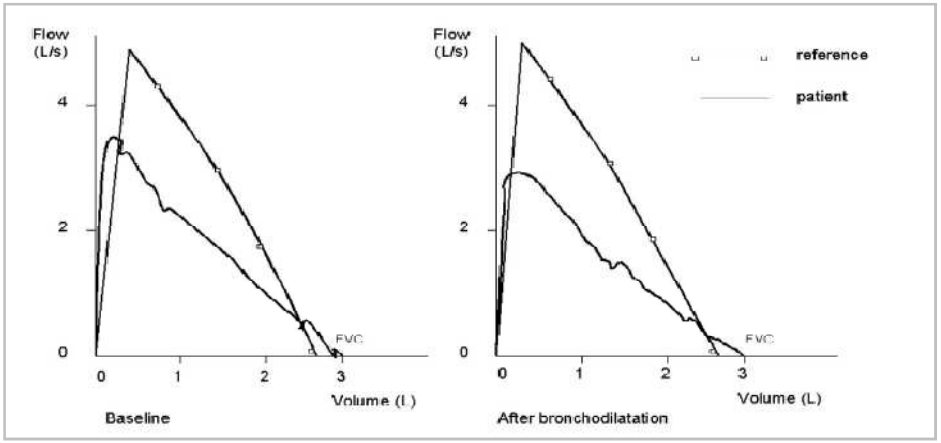


Malacia delle vie aeree presente in 160 **(≈35%)**
(età media 4 aa)

Nell'82% dei casi Primaria

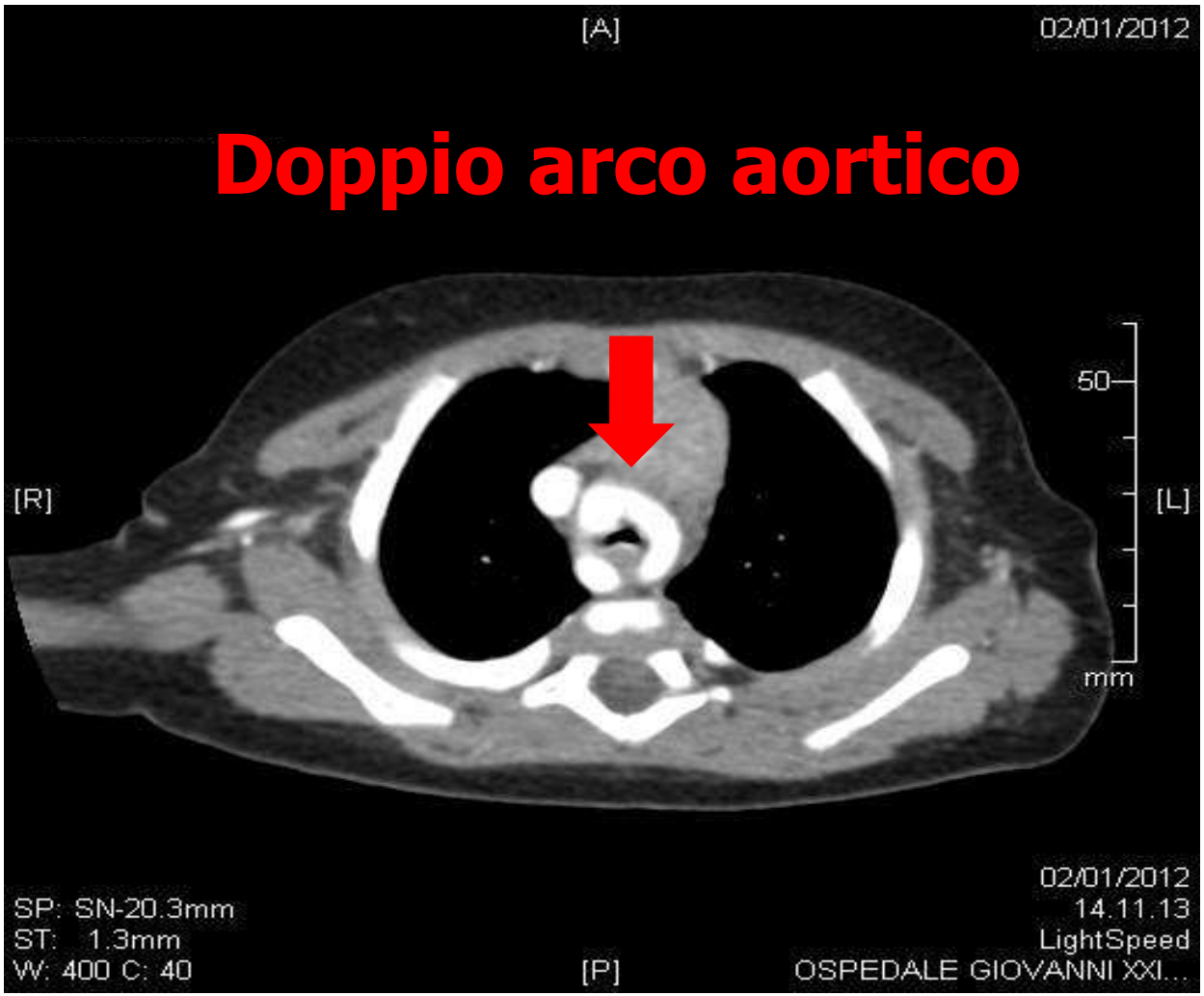
Nel 52% dei casi la dg non era sospettata

Spirometria compatibile con un'asma (ma PEF <<< FEV1)



Nicole, 2 mesi

Storia di stridore respiratorio congenito
Giunge al PS per insufficienza respiratoria severa con acidosi (pH 7.05)



Maria Rosaria, anni 8 e 7 mesi

Bambina affetta da trisomia 21

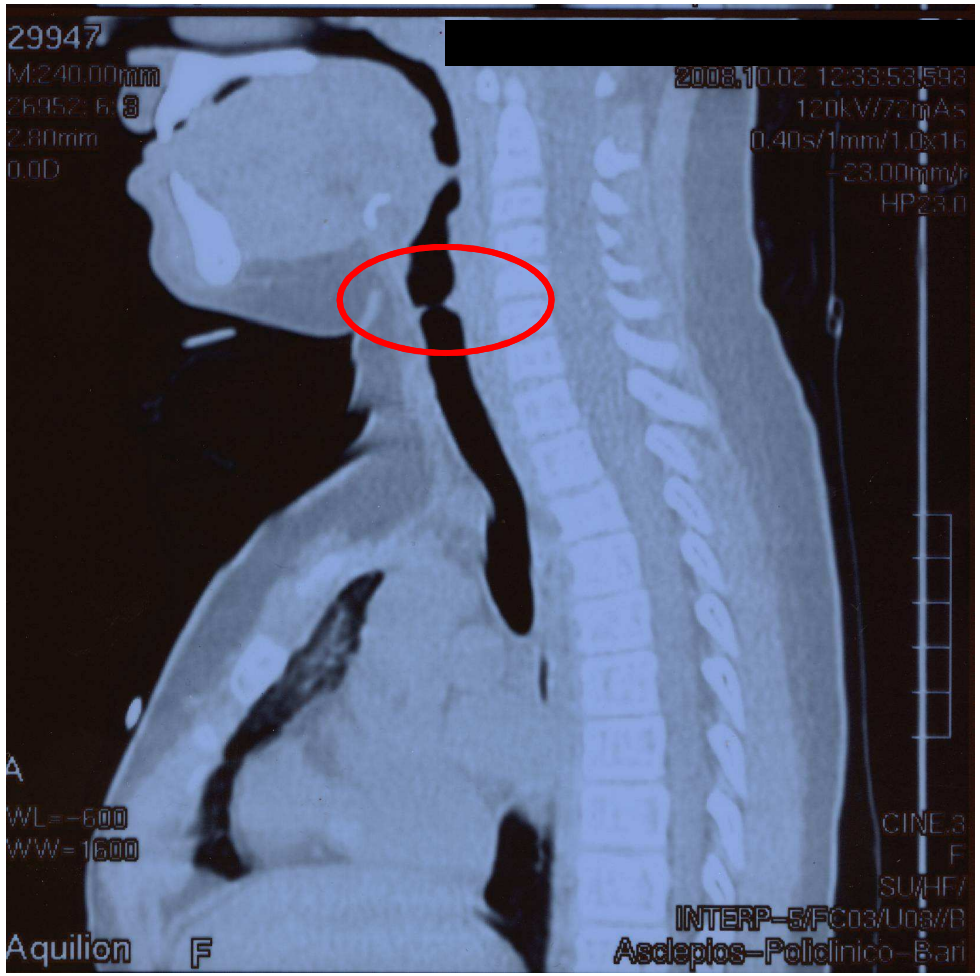
Nell'APR episodi sporadici (3-4/anno) di dispnea e "rumore respiratorio", mai tali da richiedere ricovero o accesso al PS

Da 3 giorni tosse e dispnea ingravescente in- ed espiratoria

Viene condotta al PS

Sat.O2 = 96% in aria ambiente

E.O.: dispnea mista (in- ed esp.)
OT: riduzione diffusa del MV



Airway Anomalies in Children with Down Syndrome: Endocopic Findings

Bertrand P, Ped Pulmonol 2003; 36: 137

Studio retrospettivo
su 24 bb con **S. di Down**
e 324 bb non Down
con sintomi respiratori
ricorrenti

Anomalie anatomiche
(spesso multiple)
malformative significativam.
più frequenti nei paz. con
s. Di Down **(≈ 10 x)**

<u>Solo il 25% dei bb con Down
non presentavano anomalie</u>

TABLE 2—Comparison of Endoscopic Findings in DS and Non-DS Patients[1]

Endoscopic finding[2]	DS, no. of patients (%)	Non-DS, no. of patients (%)	*P*
Laryngomalacia	12 (50)	63 (19)	0.0004
Subglottic stenosis	1 (4)	12 (3.7)	n.s.[3]
Tracheomalacia	8 (33)	24 (7.4)	0.0001
Tracheal bronchus	5 (21)	7 (2.1)	0.002
Tracheal web	1 (4)	2 (0.6)	n.s.
Tracheal stenosis	1 (4)	4 (1.2)	n.s.
Bronchomalacia	5 (21)	27 (8.3)	0.09
Supernumerary segmental bronchi	1 (4)	9 (2.7)	n.s.
Abnormal segmental bronchial branching	7 (29)	11 (3.3)	0.0001
No structural abnormalities found	6 (25)	209 (65)	0.0002
Number of patients	24	324	

[1]Some patients presented with more than one endoscopic finding.
[2]Statistical analysis was performed with chi-square and Fisher's exact test.
[3]n.s., nonsignificant.

PATOLOGIE CONGENITE O ACQUISITE CON WHEEZING

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S. da aspirazione ricorrente	Fibrosi cistica DCP	Masse mediastiniche
S. disfunzionali		Bronchiolite obliterante interstiziopatie
SIRT		Immunodeficienze

Classificazione delle interstiziopatie nel bambino

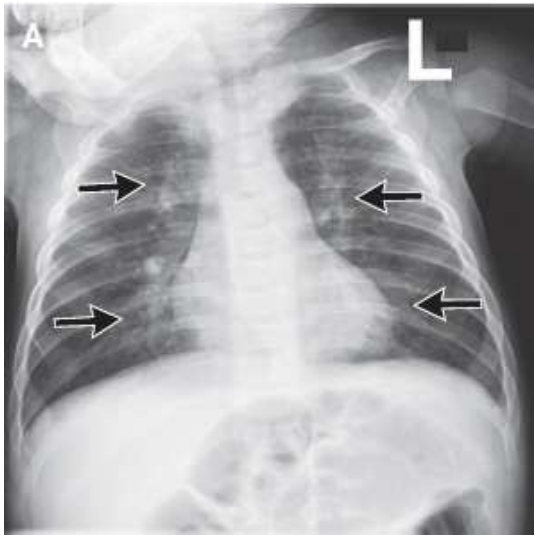
Table 1. Classification of Pulmonary Diseases in Children According to Anatomical Location in the Lung.

Airway
Persistent tachypnea of infancy, or neuroendocrine-cell hyperplasia of infancy
Follicular bronchitis
Bronchocentric granulomatosis
Bronchiolitis obliterans
Interstitium
Nonspecific interstitial pneumonitis (increased numbers of fibroblasts and lymphocytes)
Cellular interstitial pneumonitis, or pulmonary interstitial glycogenosis (increased numbers of mesenchymal cells)
Lymphocytic interstitial pneumonitis (increased numbers of lymphocytes)
Alveolus
Pulmonary alveolar proteinosis
Mutations in the surfactant pathway
Chronic pneumonitis of infancy

Kinane, NEJM 2011;365;2221

Iperplasia delle Cellule Neuroendocrine dell'Infanzia (NEHI)

- Anche denominata "Tachipnea Persistente dell'Infanzia" ("Bronchite follicolare" probabilmente forma *mild* della stessa malattia)
- Eziopatogenesi sconosciuta; esordio intorno ai primi 4-6 mesi di vita
- Sintomatologia: tosse, tachipnea, wheezing, ipossia, distress resp., reperti rantolari / riduzione MV alla auscultazione
- Rx: aspetti di iperinflazione, ispessimenti peribronchiali
- TC torace: infiltrazioni "ground-glass" peri-ilari, air trapping
- Diagnosi: biopsia (OLB o TBB) → CE bombesina+
- Prognosi buona: risoluz. solitamente entro i 4 aa
- Terapia: CS, IVIG ?, azitrom?, idrossiclorochina?



Fan, Ped Pulmonol 2004;38:369 - Kinane, NEJM 2011;365;2221

…e il nostro Christian?

Christian, anni 11

Rx torace: negativo

Test alla Mech: negativo (in corso di terapia di fondo)

pH-metria GE: negativa

Visita ORL + RFS: negativa

Test sudore (genetica in corso): negativo

TAC torace: negativa

Fareste una **FBS?** …stavamo per farla

Una mia collaboratrice (Dott.ssa Binetti) mi dice: "però…quel bambino respira male!…"

Questionario di Nijmegen: positivo (score 33, vn <23)

DIAGNOSI: Sindrome da iperventilazione in asma persistente

AGORÀ 2012

CONGRESSO NAZIONALE DI ALLERGOLOGIA *e* PEDIATRIA

Presidente: F. Cardinale
Presidenti Onorari: L. Cavallo, A. Vacca
Coordinatore: E. Nettis

BARI, 7-9 GIUGNO 2012
Hotel Sheraton Nicolaus