

Asma: Conceptos Actuales de Diagnostico y Tratamiento

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Definición de Asma

El asma es una enfermedad variable (heterogénea) y que se caracteriza normalmente por una inflamación crónica de las vías respiratorias.

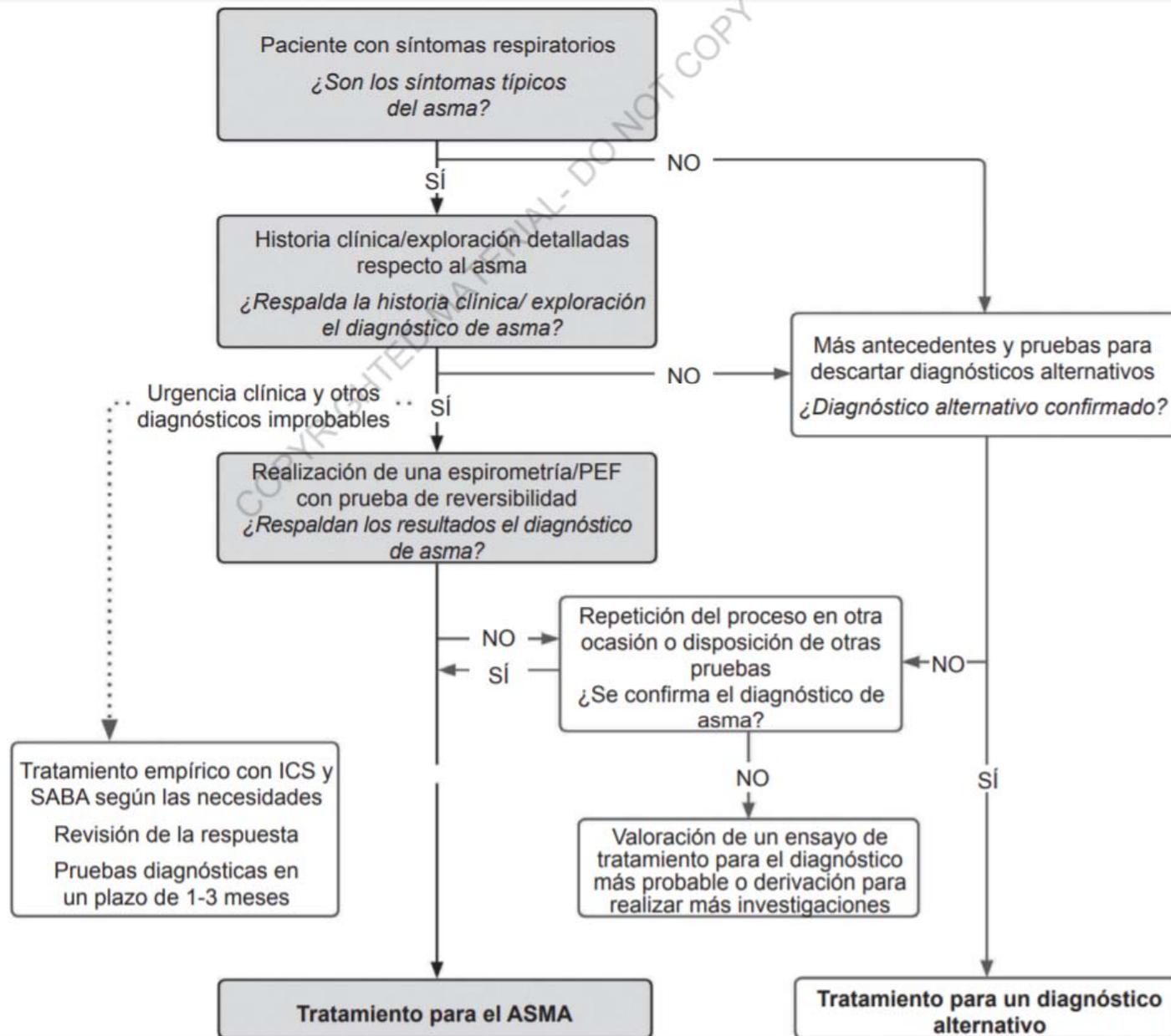
Tiene dos características principales que la definen:

- Antecedentes de síntomas respiratorios, como sibilancias, dificultad respiratoria, opresión torácica y tos, que varían con el tiempo y en intensidad, Y
- Limitación variable del flujo de aire espiratorio.

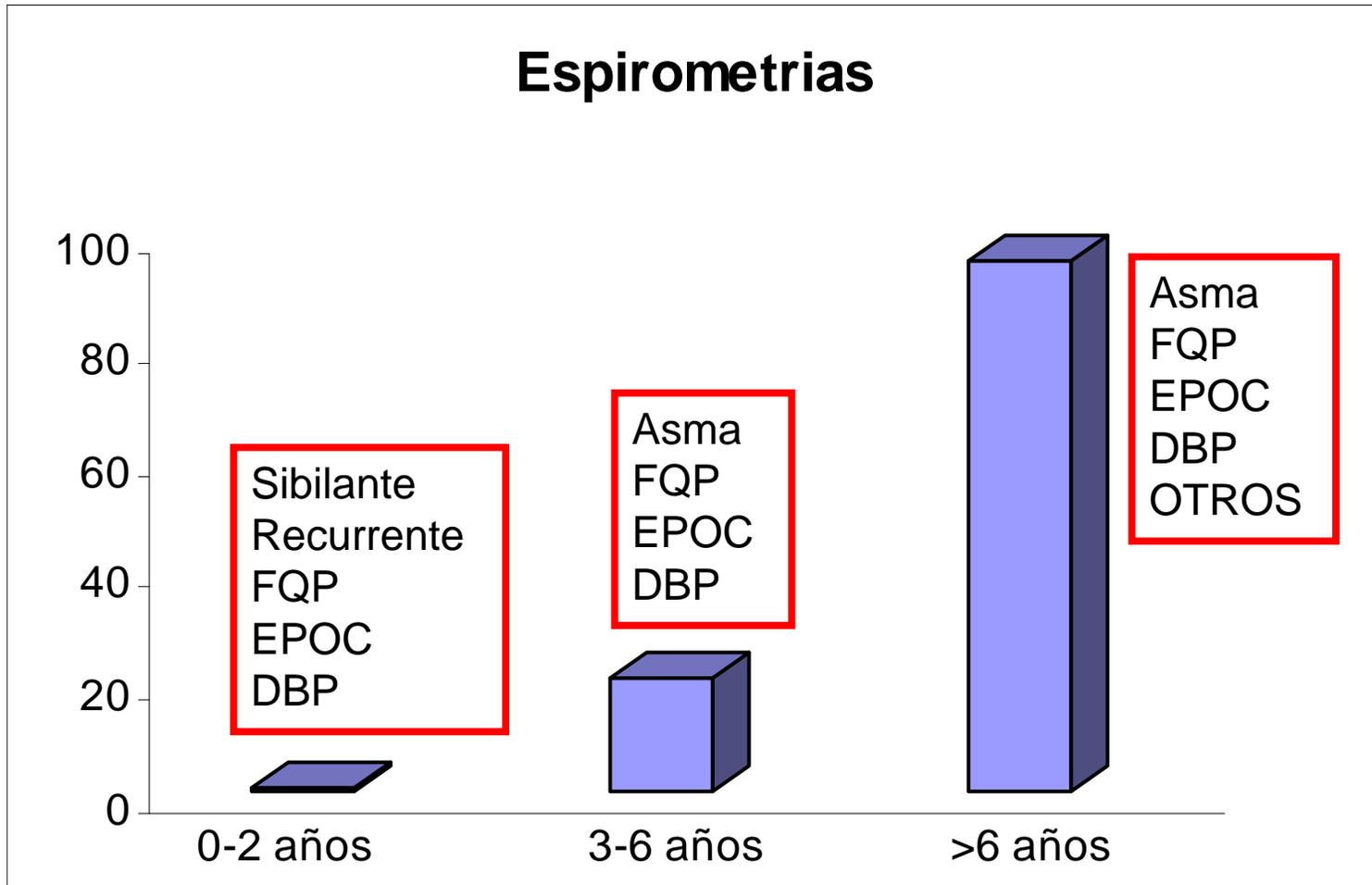
Antecedentes de síntomas respiratorios variables

- Los síntomas típicos son sibilancias, dificultad respiratoria opresión torácica y tos
- En general, las personas asmáticas manifiestan más de uno de estos síntomas
- Los síntomas aparecen de forma variable a lo largo del tiempo y varían en intensidad
- Los síntomas aparecen o empeoran con frecuencia por la noche o al despertarse
- Los síntomas suelen ser desencadenados por el ejercicio, la risa, los alérgenos o el aire frío
- Los síntomas aparecen o se agravan con frecuencia con las infecciones víricas

Diagnóstico de asma en la práctica clínica

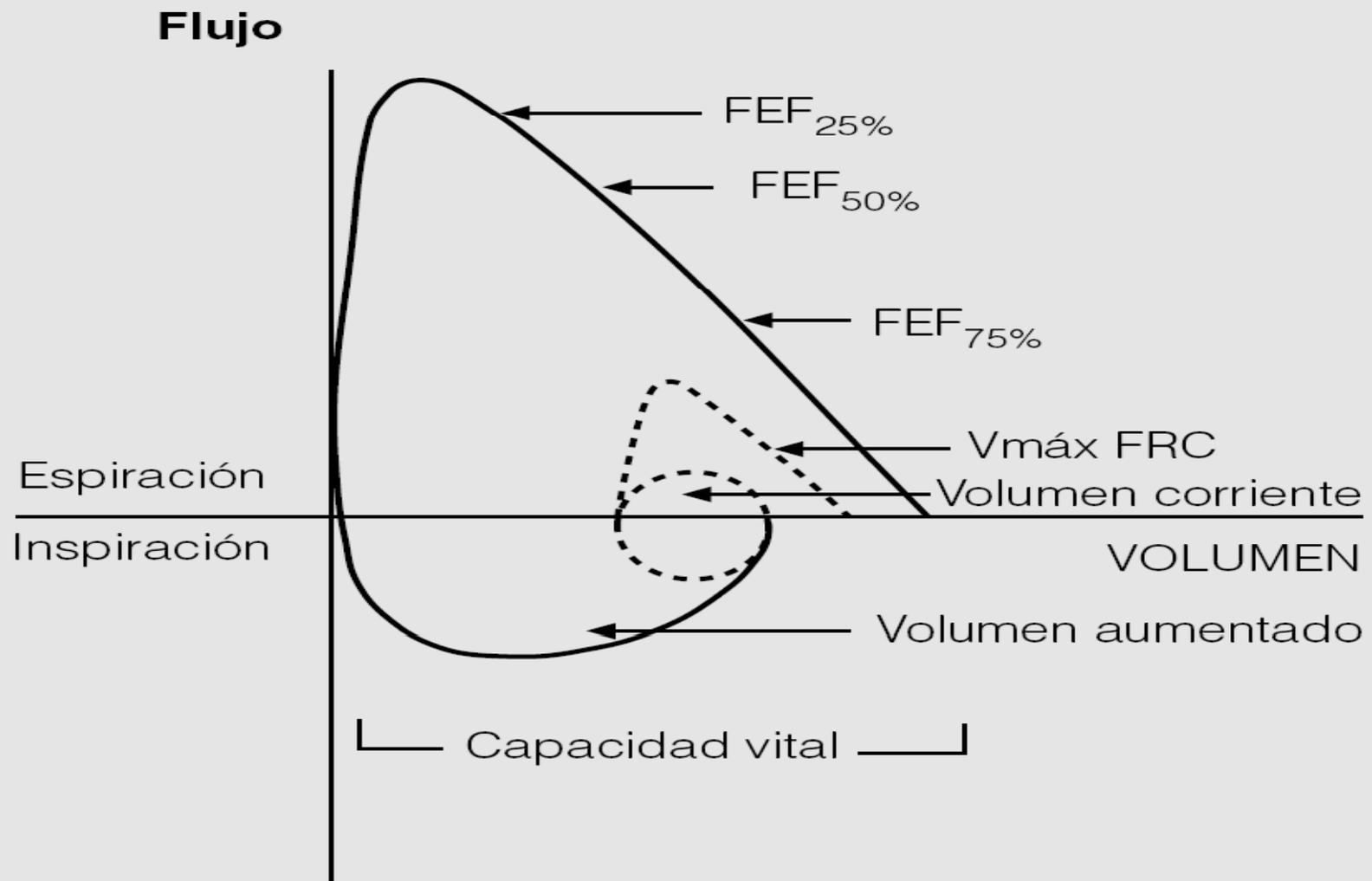


ESPIROMETRÍAS



Que Evaluamos???

- Capacidad Vital Forzada (CVF)
- Flujos Espiratorios Forzados en 0.5 o 1 Segundo ($FEV_{0.5}$, FEV_1)
- FEV_1/CVF
- FEF_{25}
- FEF_{50}
- FEF_{75}
- FEF_{25-75}



- Espiración forzada desde volumen corriente
- Espiración forzada desde volumen aumentado

Spirometric Pulmonary Function in Healthy Preschool Children

HOWARD EIGEN, HARVEY BIELER, DEBRA GRANT, KATHY CHRISTOPH, DELANA TERRILL, DOUGLAS K. HEILMAN, WALTER T. AMBROSIUS, and ROBERT S. TEPPER

Department of Pediatrics, James Whitcomb Riley Hospital for Children, and Department of Medicine, Division of Biostatistics, Indiana University Medical Center, Indianapolis, Indiana

Pediatric Pulmonology 41:735–743 (2006)

Spirometry in 3–5-Year-Old Children With Asthma

Véronique Nève, MD,^{1*} Jean-Louis Edmé, PhD,¹ Patrick Devos,² Antoine Deschildre, MD,³
Caroline Thumerelle, MD,³ Clarisse Santos, MD,³ Catherine-Marie Methlin,¹
Murielle Matran,¹ and Régis Matran, MD, PhD¹

Spirometry in 3- to 6-Year-Old Children with Cystic Fibrosis

Paulo J. C. Marostica, Andrea D. Weist, Howard Eigen, Connie Angelicchio, Kathy Christoph, Julie Savage, Debra Grant, and Robert S. Tepper

Department of Pediatric Pulmonology and Critical Care, James Whitcomb Riley Hospital for Children, Indianapolis, Indiana

Respiratory Research



Research

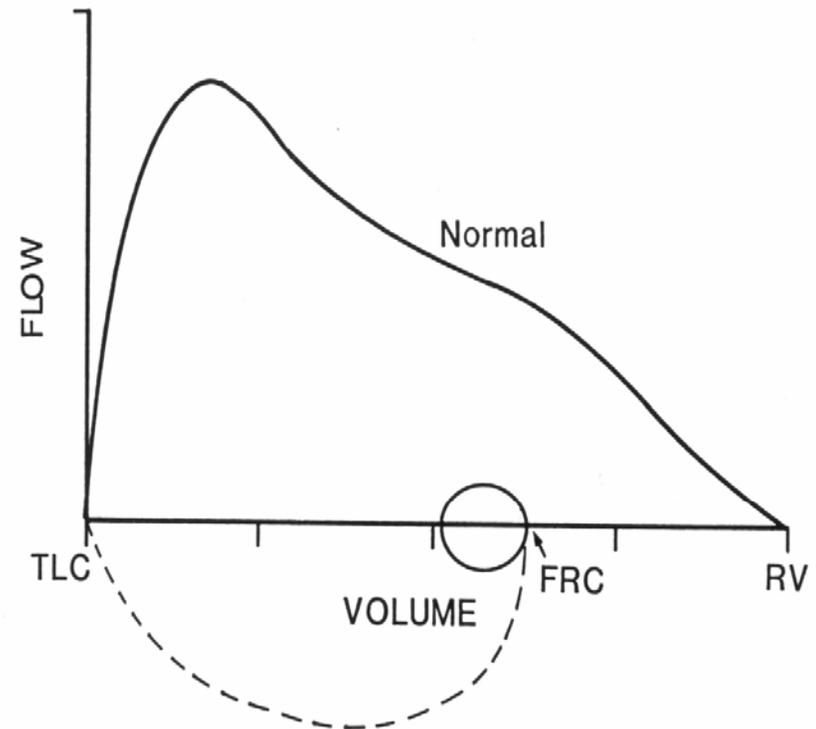
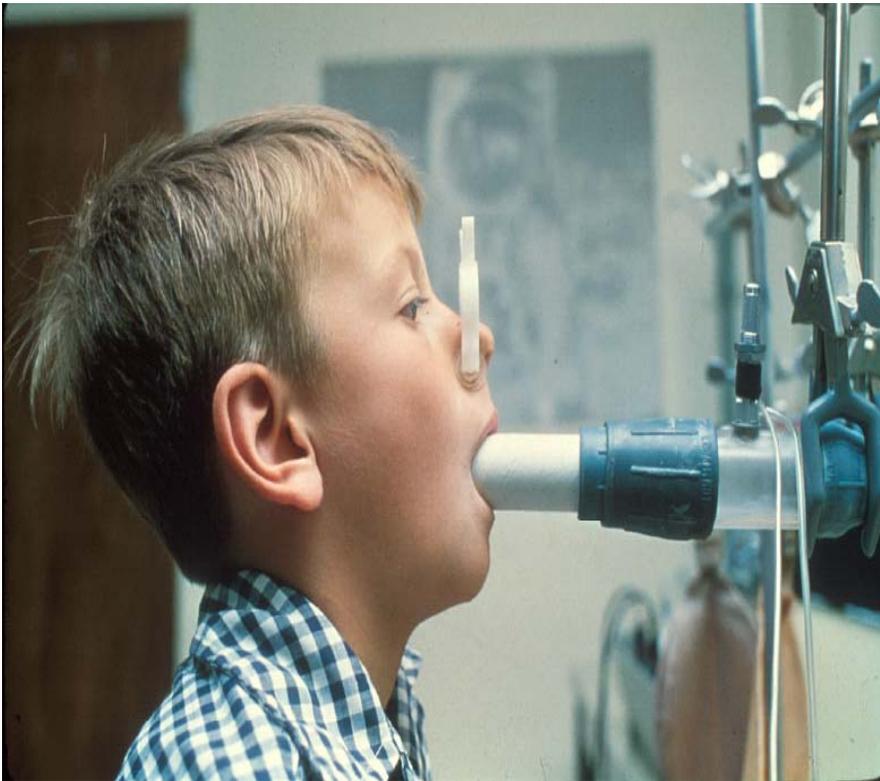
Open Access

Reference values of Forced Expiratory Volumes and pulmonary flows in 3–6 year children: a cross-sectional study

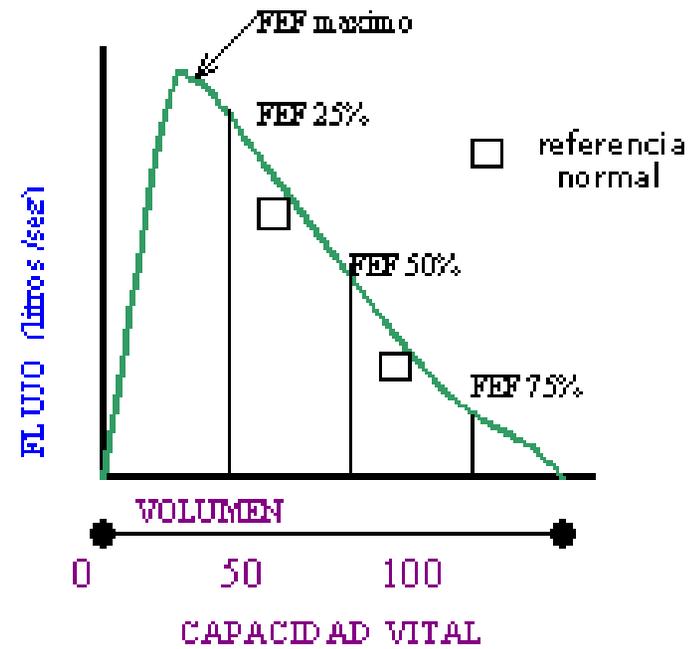
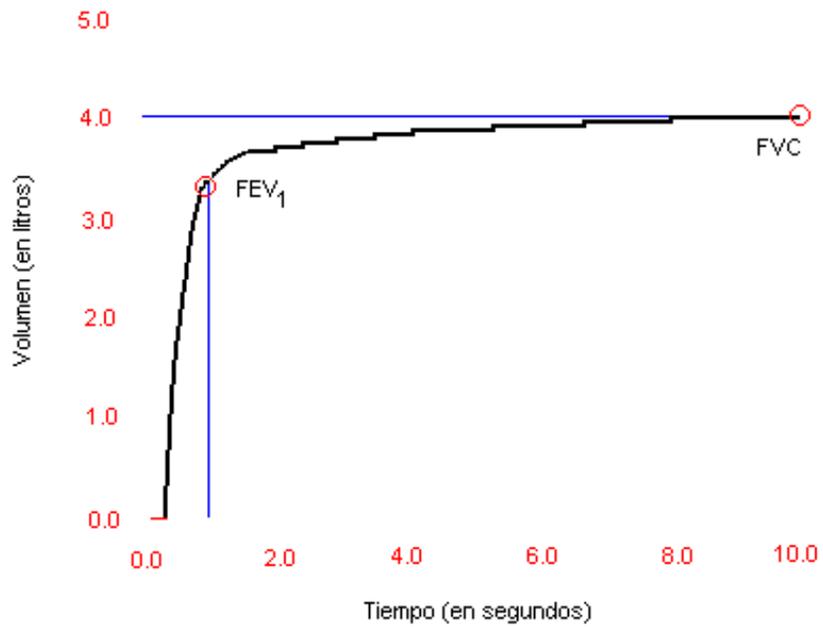
Pavilio Piccioni¹, Alberto Borraccino^{*2}, Maria Pia Forneris¹, Enrica Migliore¹, Carlo Carena³, Elisabetta Bignamini⁴, Stefania Fassio⁴, Giorgio Cordola⁴, Walter Arossa¹ and Massimiliano Bugiani¹

Evaluación de Función Pulmonar

Flujos Espiratorios Forzados en niños mayores de 3 años



CURVAS



Curvas Aceptables y Reproducibles

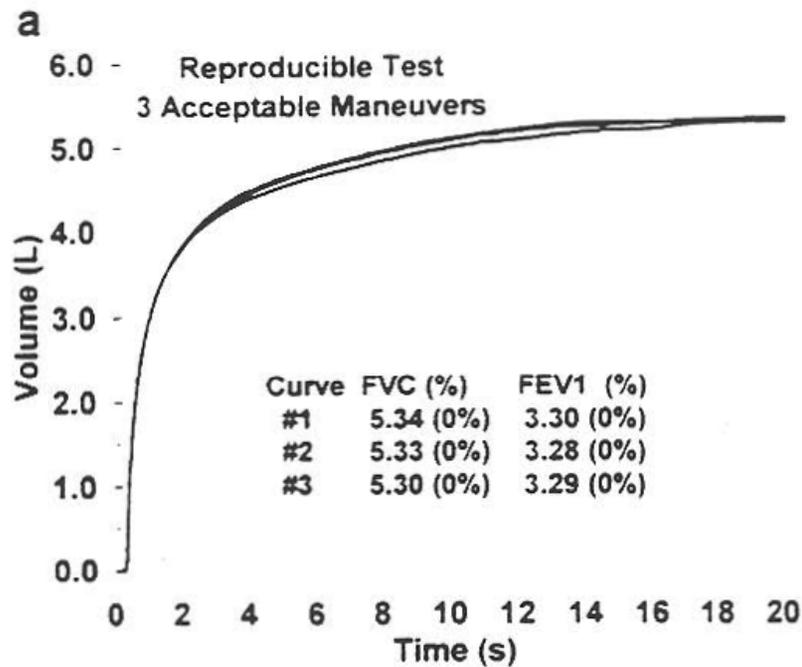


Figure A8a. Reproducible test with three acceptable volume-time curves. Percents are difference from largest value.

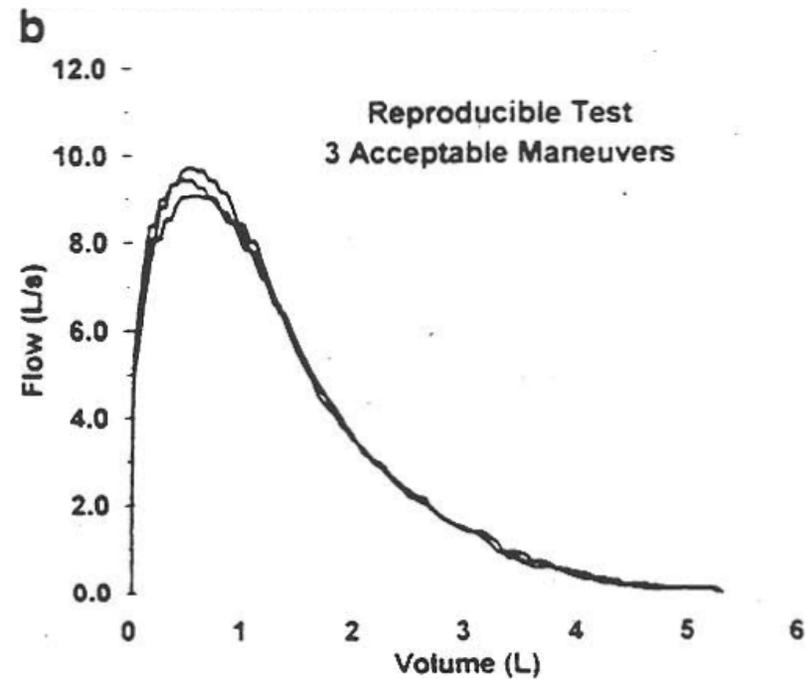
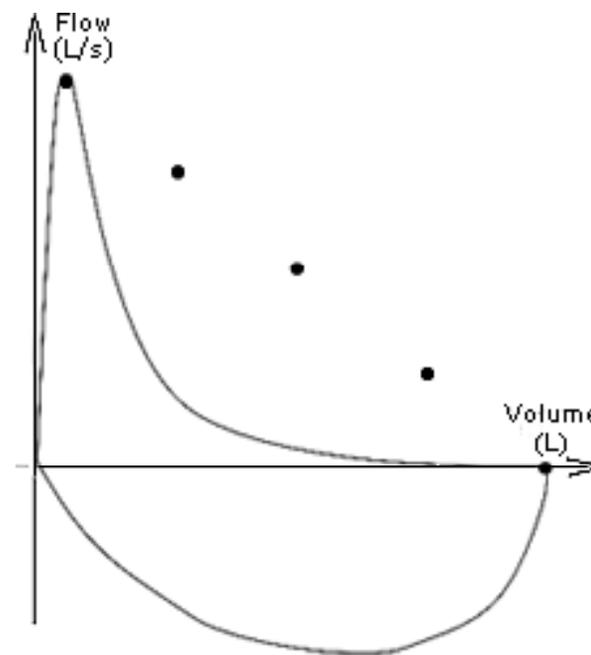
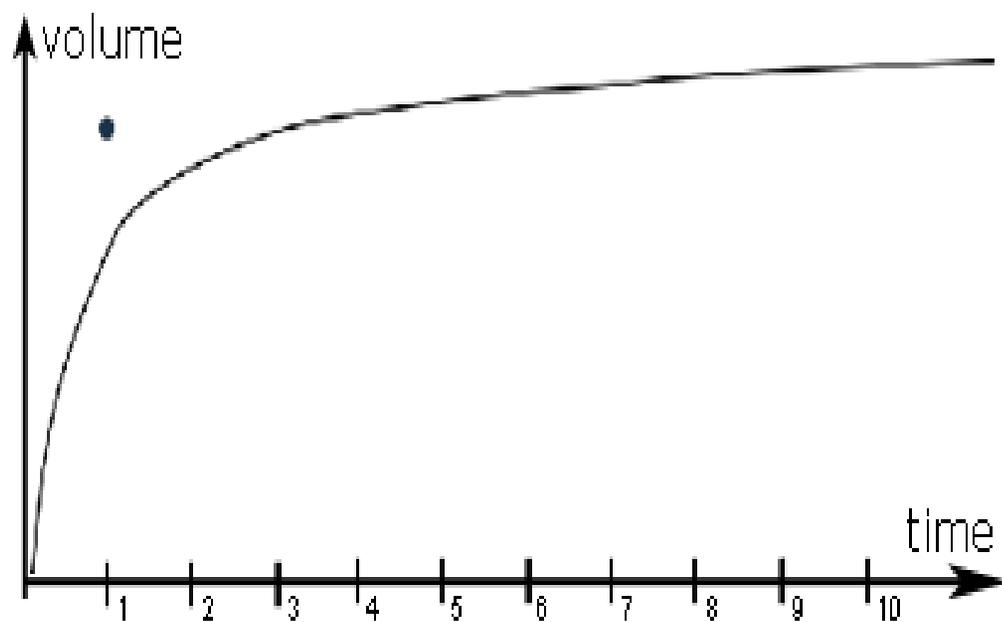
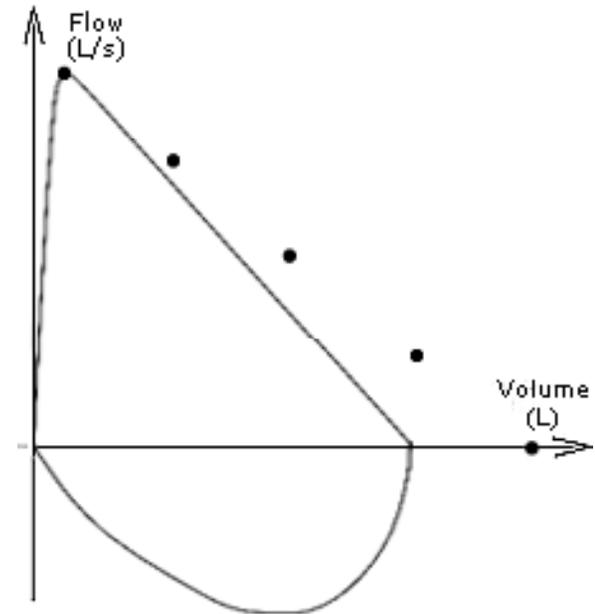
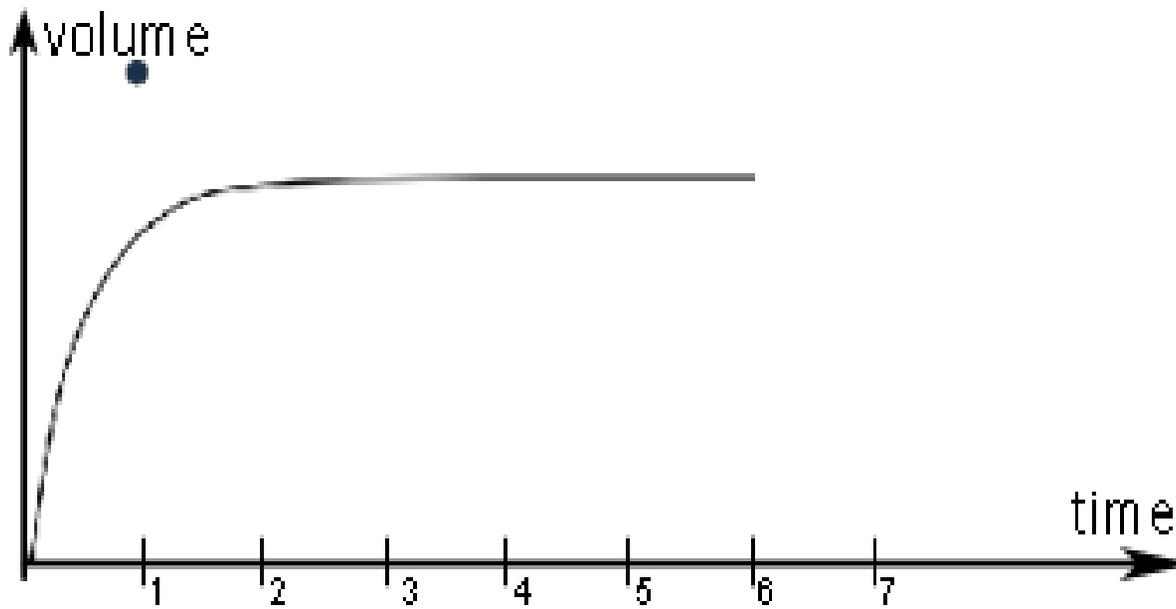


Figure A8b. Reproducible test with three acceptable flow-volume curves.

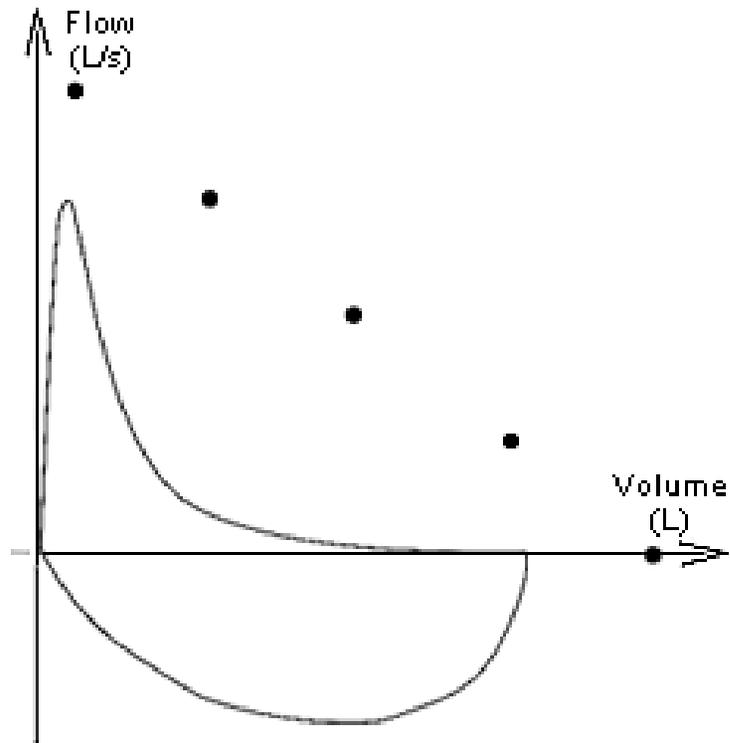
Curvas Obstruictivas



Curvas Restrictivas



Curvas Mixtas



Assessment of exhaled nitric oxide kinetics in healthy infants

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Submitted 19 August 2002; accepted in final form 22 January 2003

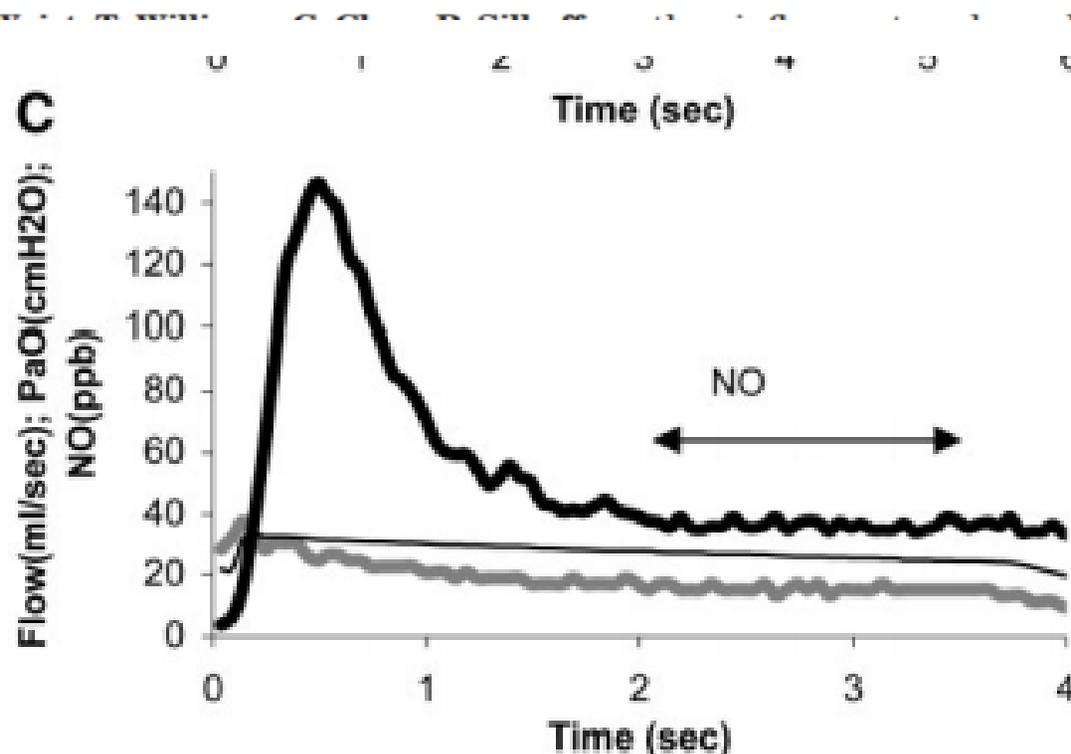


Fig. 2. Single-breath tracings of exhaled NO, mouth pressure (PaO), and expiratory flow obtained from a healthy infant at flows of 50 (A), 25 (B), and 15 ml/s (C) (see text).

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Eur Respir J. 2015 January ; 45(1): 98–106. doi:10.1183/09031936.00034614.

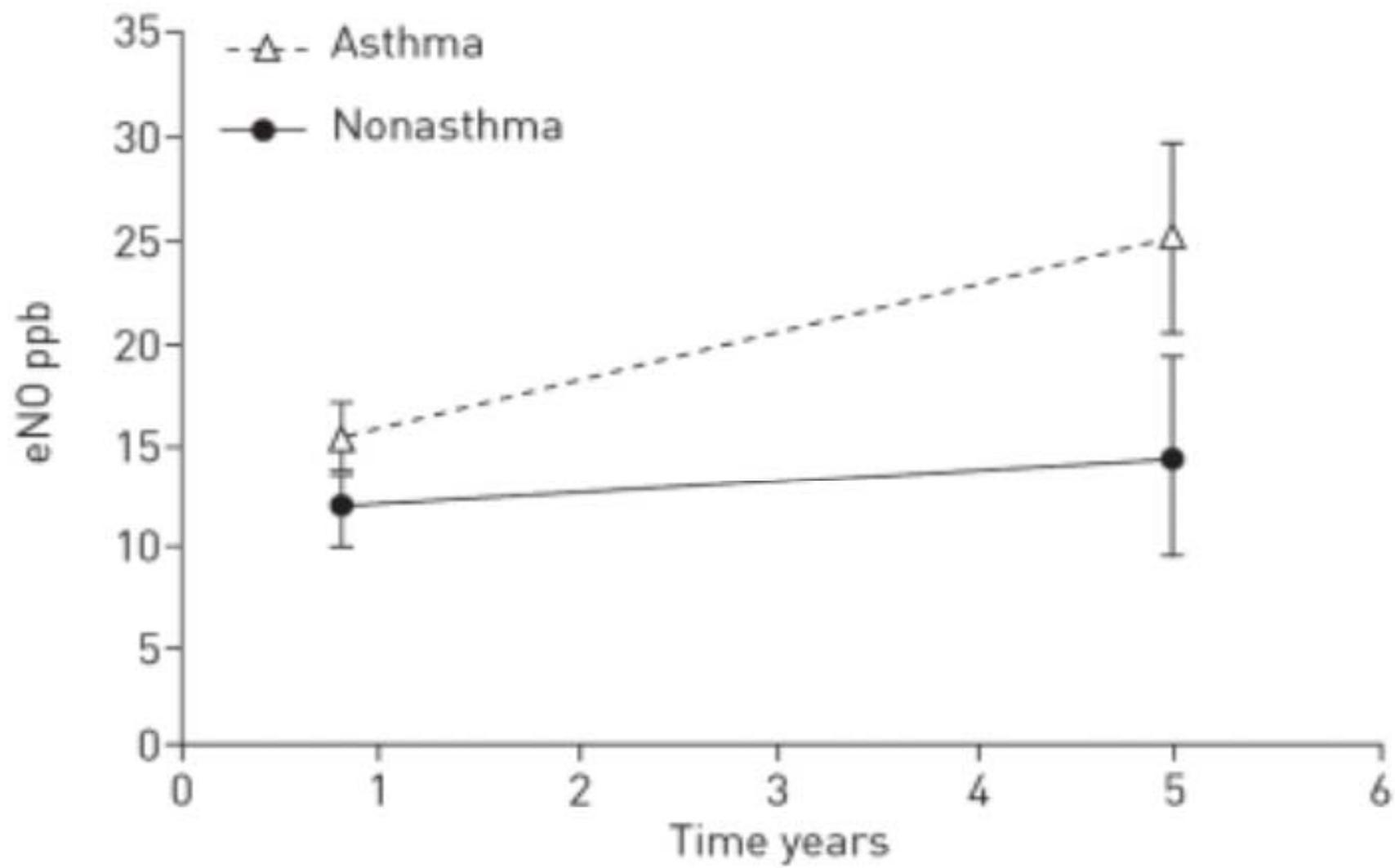
Exhaled nitric oxide during infancy as a risk factor for asthma and airway hyperreactivity

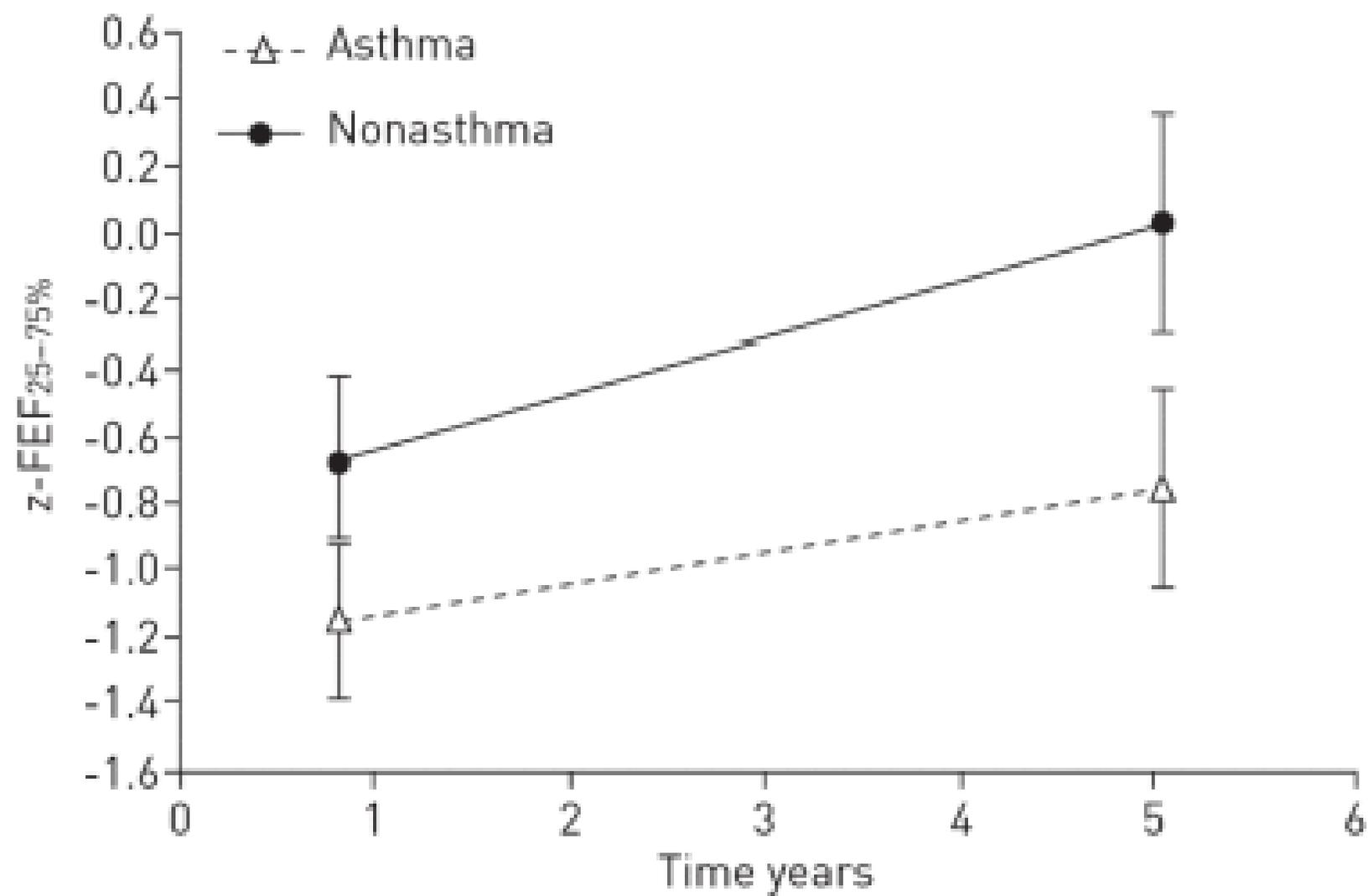
Daniel Chang¹, Weiguo Yao¹, Christina J. Tiller¹, Jeffrey Kisling¹, James E. Slaven², Zhangsheng Yu², Mark H. Kaplan^{1,3}, and Robert S. Tepper¹

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Técnica de Oscilación Forzada

DuBois 1956

No invasiva – Mínima cooperación

Técnica Volumen Corriente

Neonatos y Niños pequeños

Impedancia: Fuerza para mover el aire adentro y afuera del sistema respiratorio

Mecánica Respiratoria (Resistencia y Reactancia)

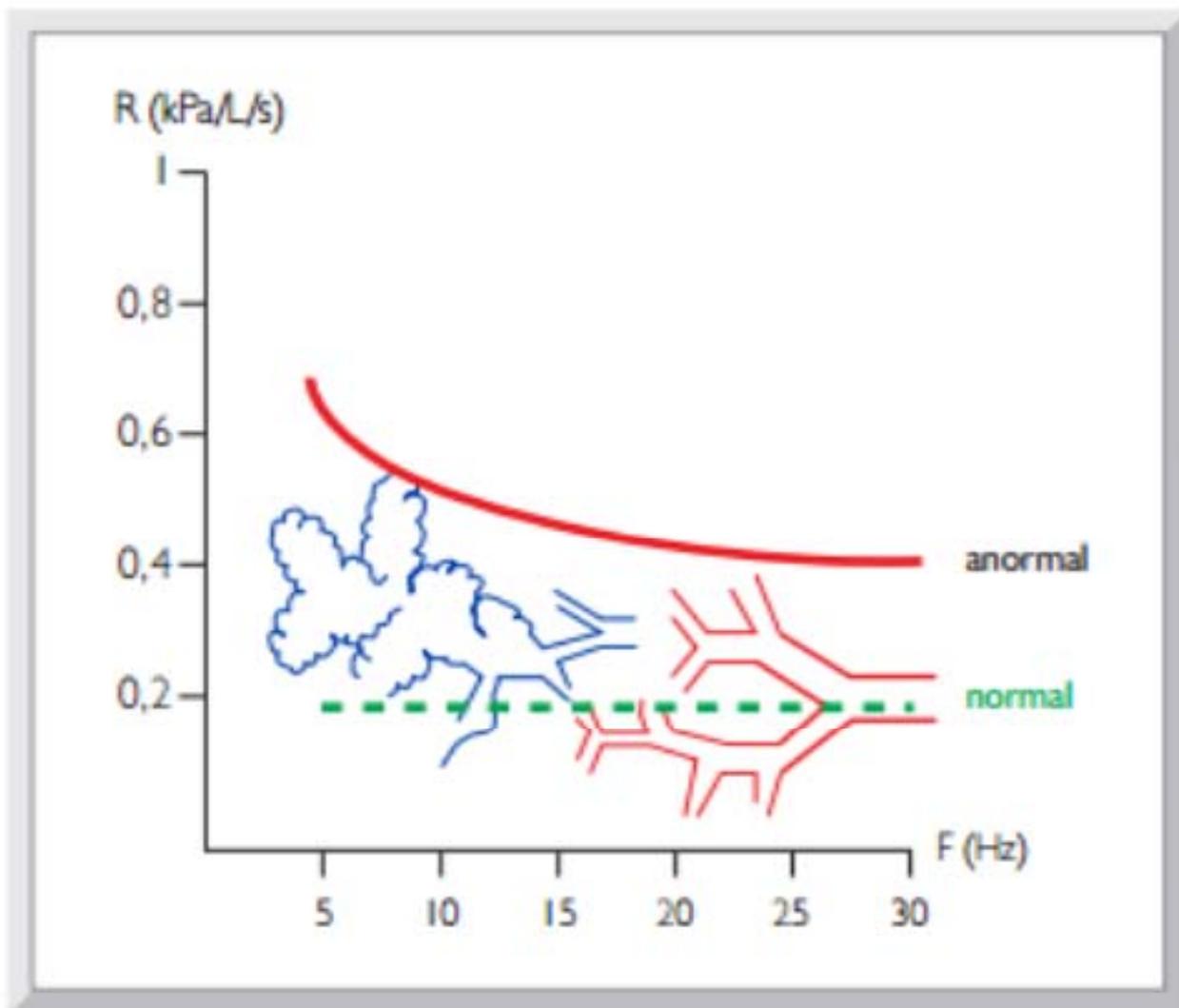


Figura 2.- Gráfico que muestra en el eje vertical el nivel de resistencia (R) de la vía aérea medida en función de una escala de frecuencia (F) con valores normales (línea verde) y anormales (línea roja), que puede ser el caso de un niño asmático con respuesta al broncodilatador. De fondo se ilustra la relación entre la escala de frecuencia y el sitio de resistencia de la vía aérea, a menor frecuencia evalúa vía aérea periférica y viceversa.

PAEDIATRIC LUNG DISEASE

Respiratory function in healthy young children using forced oscillations

Graham L Hall, Peter D Sly, Takayoshi Fukushima, Merci M Kusel, Peter J Franklin, Friedrich Horak Jr, Hilary Patterson, Catherine Gangell, Stephen M Stick

Thorax 2007;62:521–526. doi: 10.1136/thx.2006.067835

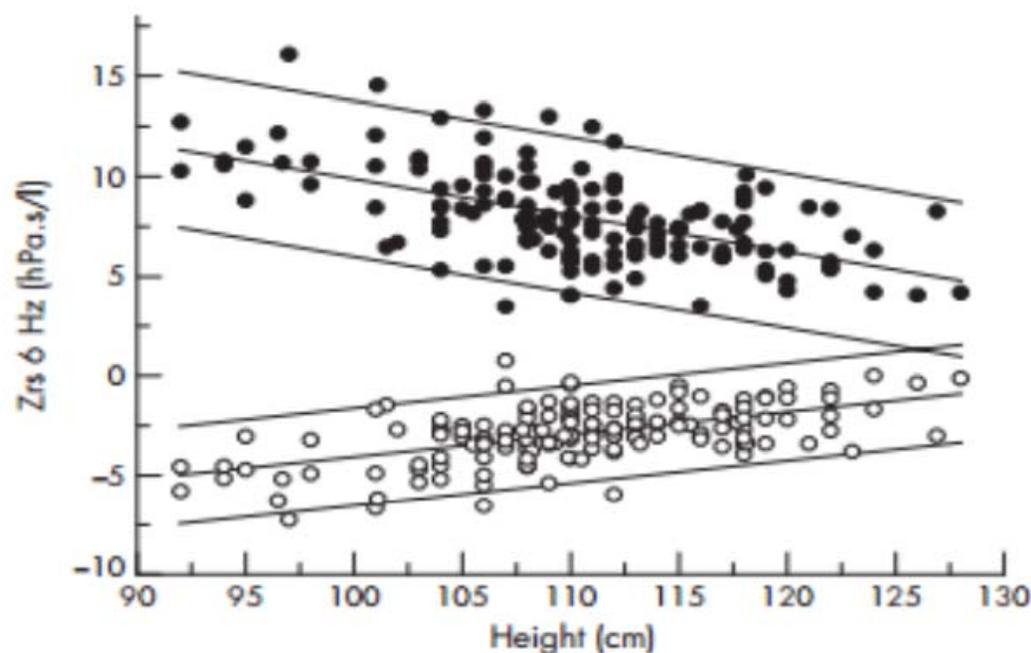


Figure 1 Respiratory input impedance at 6 Hz against height in 149 healthy young children plotted as individual measurements of mean respiratory resistance at 6 Hz (R_{rs6} , closed circles) and respiratory reactance at 6 Hz (X_{rs6} , open circles). Predicted and 95% confidence intervals of R_{rs6} and X_{rs6} are plotted as solid lines.



Forced oscillations in the clinical setting in young children with neonatal lung disease

K. Udomittipong^{*,#}, P.D. Sly^{*,†}, H.J. Patterson^{*}, C.L. Gangell⁺,
S.M. Stick^{†,+} and G.L. Hall^{†,+}

ABSTRACT: The extent of respiratory dysfunction is not well characterised in children with neonatal chronic lung disease (nCLD) too young to perform spirometry. Forced oscillations are easily performed by healthy young children; however, they may be more difficult for those with nCLD. The present study aimed to describe the feasibility of using the forced oscillation technique in children with nCLD in a routine clinical setting and to investigate the influence of neonatal factors on subsequent lung function.

Respiratory function tests were attempted in 64 patients with nCLD aged 3.2–6.6 yrs. Respiratory resistance and reactance at 6, 8 and 10 Hz were expressed as z-scores derived from a healthy reference population. The within-test variation and between-test repeatability were also assessed.

Technically, satisfactory data were obtained from 77% of children. On grouped data, z-scores for all oscillatory indices were different from zero and related to hospital oxygen administration in the neonatal period.

In conclusion, the forced oscillation technique was feasible in preschool children with neonatal chronic lung disease in the clinical outpatient setting. These children had lung function significantly worse than that predicted from healthy children. Respiratory function assessed using forced oscillations appeared to reflect the severity of lung disease during the neonatal period.

AFFILIATIONS

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Tucson Children`s Respiratory Study

- Iniciado en 1982 Fernando Martínez
- Incluyeron 826 niños desde el nacimiento hasta la actualidad
- Evaluados por Cuestionarios
- Dosajes de IgE, Test Cutáneos
- Estudios de Función Pulmonar

Resultados

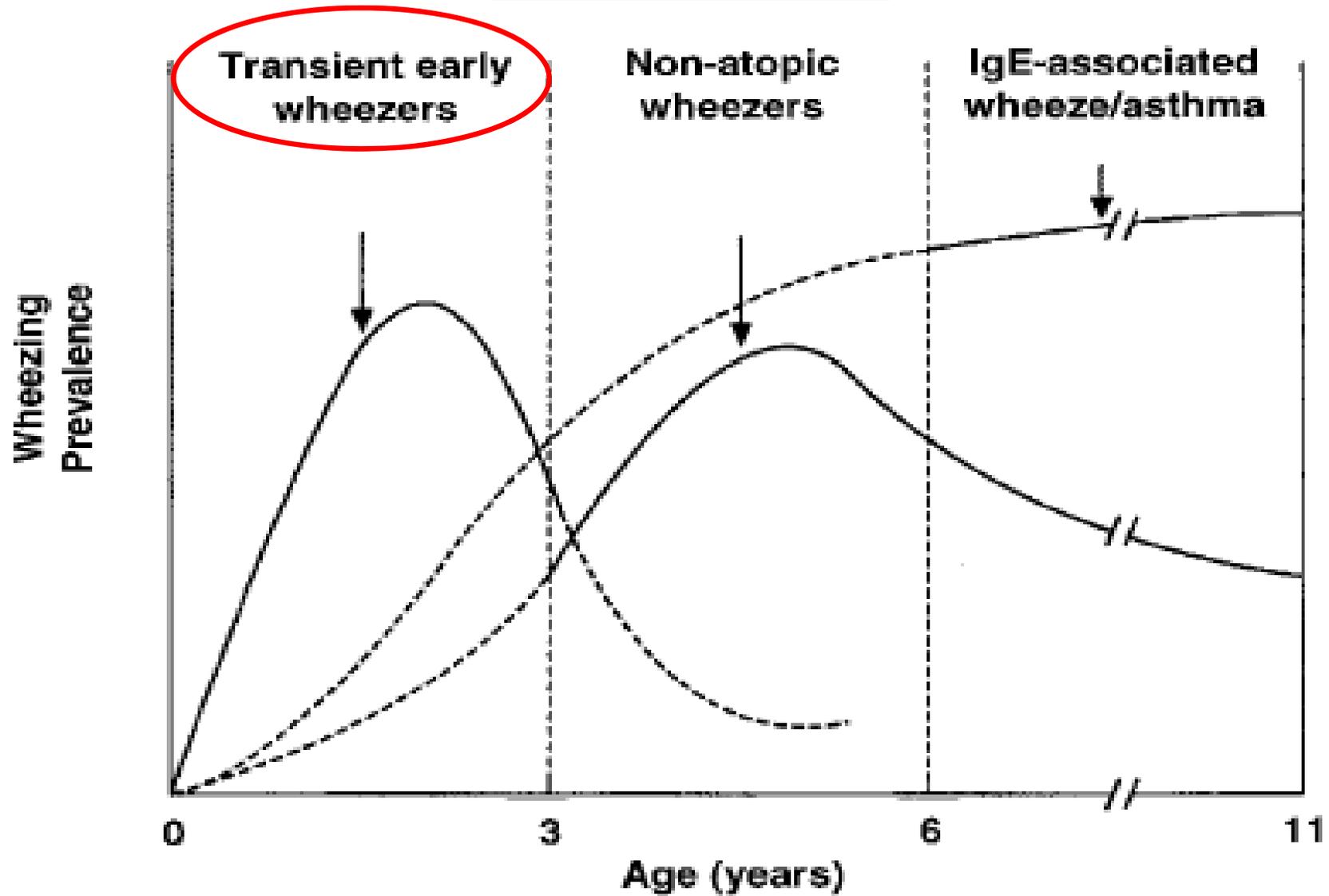
EL 51% NO PRESENTO SIBILANCIAS EN NINGUN MOMENTO

- NO SIBILANCIAS (51%)

EL 49% PRESENTO SIBILANCIAS (1 Ó + EPISODIOS)

- SIBILANCIAS TRANSITORIAS (20%)
- SIBILANCIAS INICIO TARDÍO (15%)
- SIBILANCIAS PERMANENTES (14%)

Fenotipos

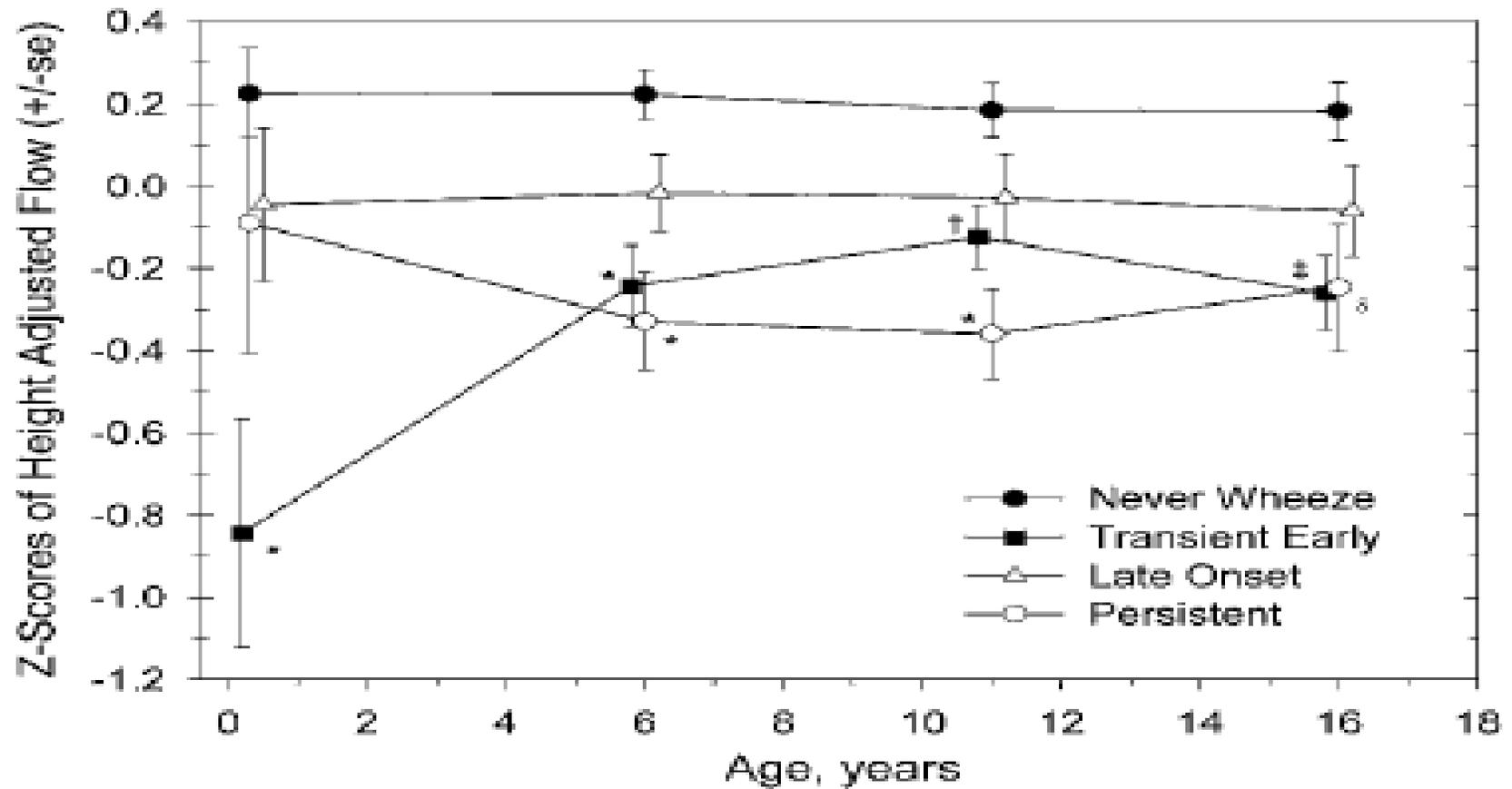


Sibilantes Atópicos/Asma

Sibila antes de los 3 años y a los 6 años

- > 50% empieza antes de los 3 años
- Eosinofilia, IgE, y Atopía
- Inicio Temprano se asocia con mayor severidad y mayor hiperreactividad bronquial.

Función Pulmonar



A Clinical Index to Define Risk of Asthma in Young Children with Recurrent Wheezing

JOSÉ A. CASTRO-RODRÍGUEZ, CATHARINE J. HOLBERG, ANNE L. WRIGHT, and FERNANDO D. MARTINEZ

Respiratory Sciences Center, University of Arizona, College of Medicine, Tucson, Arizona

Because most cases of asthma begin during the first years of life, identification of young children at high risk of developing the disease is an important public health priority. We used data from the Tucson Children's Respiratory Study to develop two indices for the prediction of asthma. A stringent index included frequent wheezing during the first 3 yr of life and either one major risk factor (parental history of asthma or eczema) or two of three minor risk factors (eosinophilia, wheezing without colds, and allergic rhinitis). A loose index required any wheezing during the first 3 yr of life plus the same combination of risk factors described previously. Children with a positive loose index were 2.6 to 5.5 times more likely to have active asthma between ages 6 and 13 than children with a negative loose index. Risk of having subsequent asthma increased to 4.3 to 9.8 times when a stringent index was used. We found that 59% of children with a positive loose index and 76% of those with a positive stringent index had active asthma in at least one survey during the school years. Over 95% of children with a negative stringent index never had active asthma between ages 6 and 13. We conclude that the subsequent development of asthma can be predicted with reasonable accuracy using simple, clinically based

group of their peers who also wheeze in early life but whose symptoms are transient and usually subside during the preschool or early school years (7). Distinguishing these two asthmalike phenotypes during infancy and early childhood simply on the basis of their clinical presentation is problematic. There are still no reliable genetic markers available and the use of any single biochemical marker is still controversial (1). It is possible, however, that by use of both clinical data and simple, easily obtainable laboratory information, a combination of these parameters may be used to identify children at high risk of developing persistent symptoms in a clinical setting.

In the present study, we used the longitudinal data available in the Tucson Children's Respiratory Study to describe predictive indices for asthma during the school years among children having wheezing episodes during the first 3 yr of life.

METHODS

The Tucson Children's Respiratory Study is a large, longitudinal assessment of respiratory illnesses in children (8). Eligible participants

Criterios para Asma

- **CRITERIOS MAYORES:**
 - Dermatitis atópica
 - Asma en los padres

- **CRITERIOS MENORES:**
 - Sibilancias fuera de episodios virales
 - Rinitis fuera de episodios virales
 - Eosinofilia $\geq 4\%$

Resultados

- Sensibilidad: 42%
- Especificidad: 85%
- Valor Predictivo Positivo: 59%
- Valor Predictivo Negativo: 73%

Castro-Rodríguez, Holberg, Wright, *et al.*: Recognizing Early Asthma in Children

TABLE 5
SENSITIVITY, SPECIFICITY, POSITIVE PREDICTIVE VALUE, AND NEGATIVE
PREDICTIVE VALUE OF THE LOOSE INDEX FOR THE PREDICTION OF ASTHMA
FOR ACTIVE ASTHMA AT YR 6, YR 8, YR 11, AND YR 13 SURVEYS

Active Asthma	OR* (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive p Value % (95% CI)	Negative p Value % (95% CI)
At Yr 6 (n = 921)	5.5 (3.5–8.4)	56.6 (53.3–59.9)	80.8 (78.3–83.3)	26.2 (23.4–29.0)	93.9 (92.4–95.4)
At Yr 8 (n = 776)	4.4 (2.8–6.8)	50.5 (47.0–54.0)	81.1 (78.3–83.9)	29.4 (26.2–32.6)	91.3 (89.3–93.3)
At Yr 11 (n = 861)	2.6 (1.8–3.8)	40.1 (36.8–43.4)	79.6 (76.9–82.3)	27.1 (24.1–30.1)	87.5 (85.3–89.7)
At Yr 13 (n = 644)	3.0 (1.9–4.6)	39.3 (35.5–43.1)	82.1 (79.1–85.1)	31.7 (28.1–35.3)	86.5 (83.9–89.1)
In at least one survey (n = 651)	3.9 (2.7–5.7)	41.6 (37.8–45.4)	84.7 (81.9–87.5)	59.1 (55.3–62.9)	73.2 (69.8–76.6)

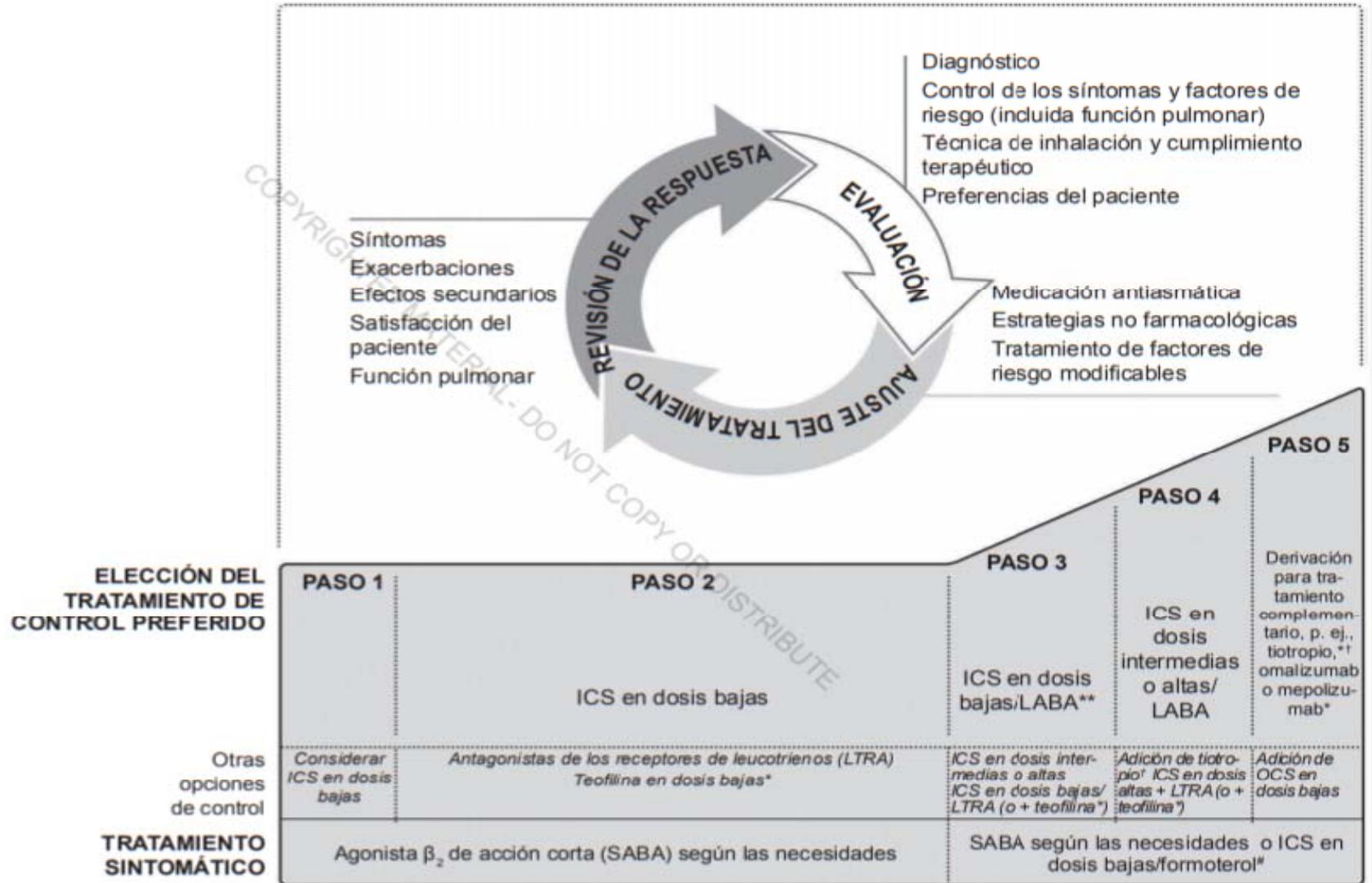
* $p < 0.00001$: between positive versus negative loose index for prediction of asthma for active asthma at each survey.

Tratamiento No Farmacologico

- Ambientes limpios y ventilados
- No Tabaco
- Ejercicios

Tratamientos

Abordaje escalonado del tratamiento del asma



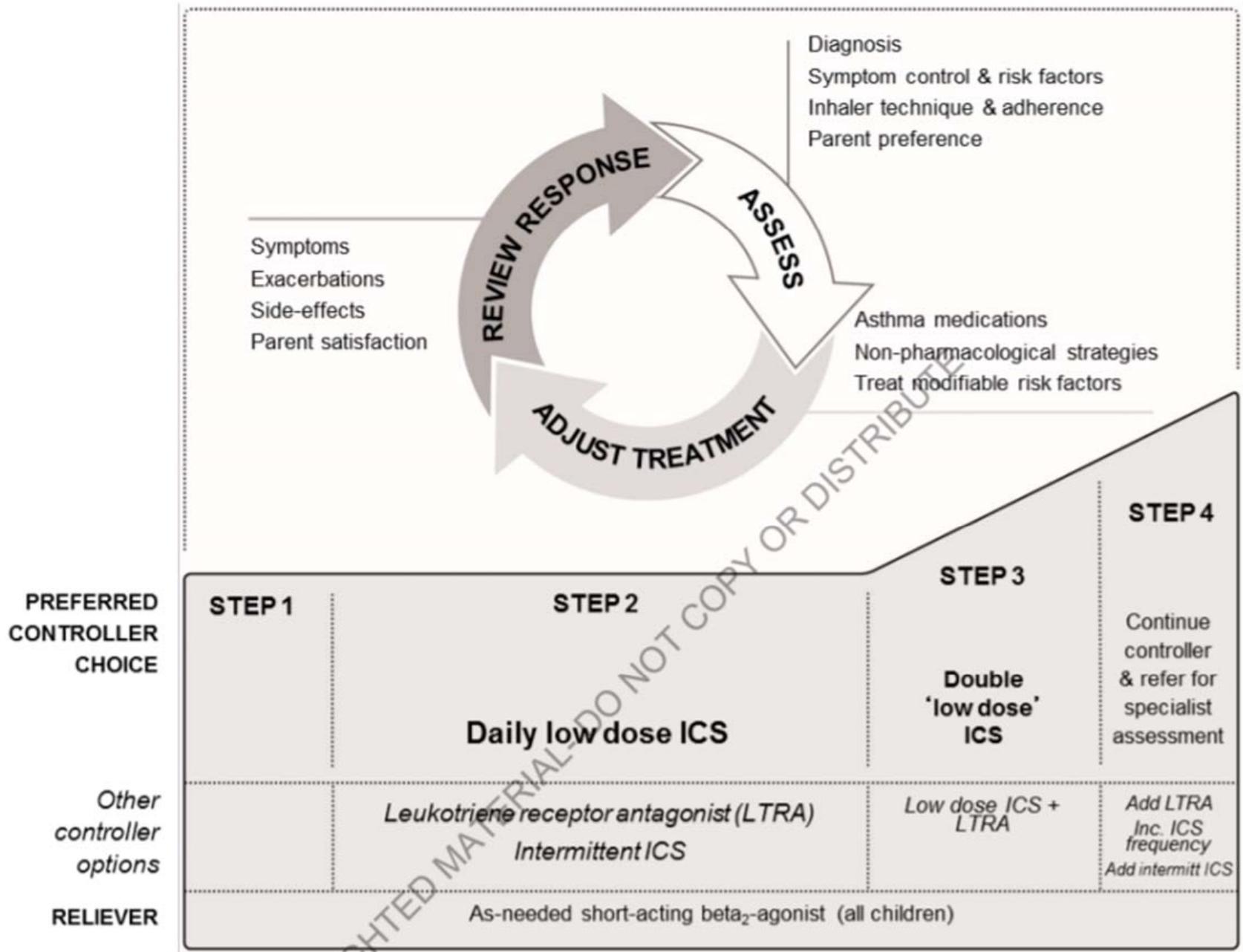
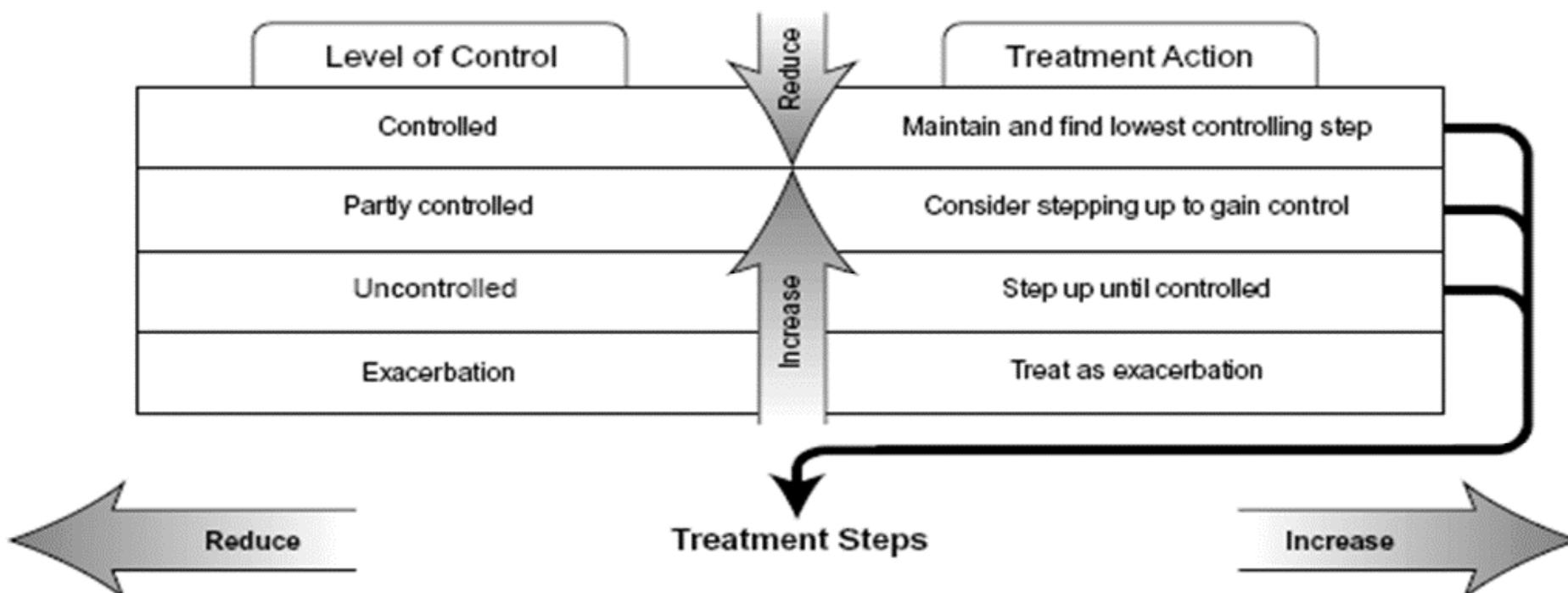


Figure 5. Management Approach Based On Control

For Children Older Than 5 Years, Adolescents and Adults





CrossMark

Medication adherence and the risk of severe asthma exacerbations: a systematic review

Marjolein Engelkes¹, Hettie M. Janssens², Johan C. de Jongste²,
Miriam C.J.M. Sturkenboom¹ and Katia M.C. Verhamme¹

ABSTRACT The benefits of drug therapy for asthma have been well established, but adherence to treatment is poor, and this might be associated with an increased risk of asthma exacerbations. The aim of this study was to review the literature on the association between adherence to asthma controller treatment and risk of severe asthma exacerbations in children and adults.

A systematic literature search was performed in PubMed, Embase and Web of Science, from inception until January 2014. Studies were included if data on the association between medication adherence and severe asthma exacerbations were presented. Quality was assessed using a modified version of the Newcastle–Ottawa Scale.

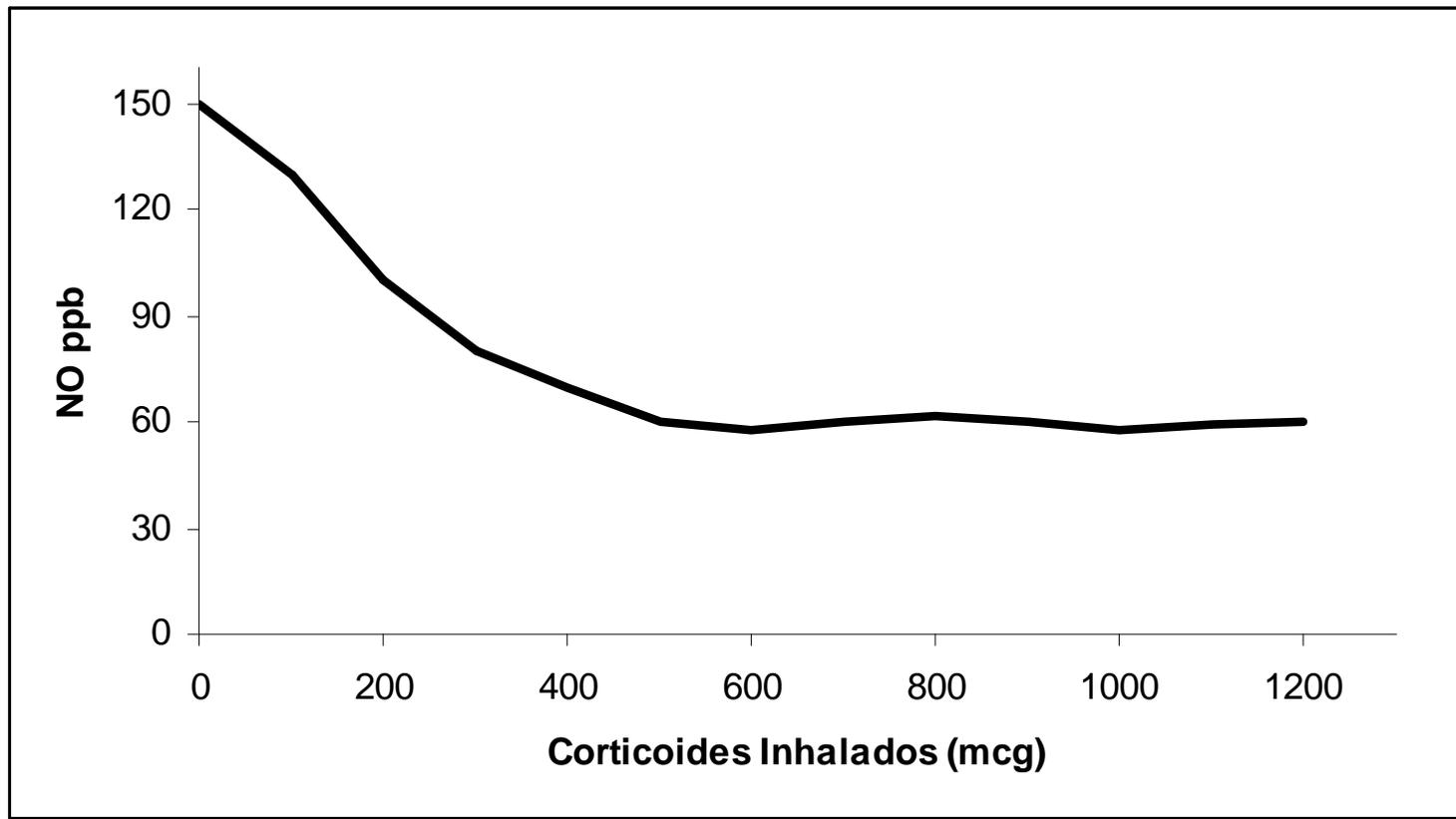
The search yielded 2319 unique publications, of which 23 met the inclusion criteria and underwent data extraction and quality scoring. High levels of heterogeneity across studies with regard to adherence and exacerbation measurements, designs and analysis precluded a formal meta-analysis. Although effect measures varied widely, good adherence was associated with fewer severe asthma exacerbations in high-quality studies.

Good adherence tended to be associated with lower risk of severe asthma exacerbations. Future studies should use standardised methodology to assess adherence and exacerbations, and should consider inhaler competence.

Corticoides Inhalados

- Se los considera generalmente seguros
- No dosis altas por periodos prolongados
- Retraso en el crecimiento
- Supresión del eje adrenal
- Osteopenia

Corticoides Inhalados



Box 3-6. Low, medium and high daily doses of inhaled corticosteroids

Adults and adolescents (12 years and older)			
Drug	Daily dose (mcg)		
	Low	Medium	High
Beclometasone dipropionate (CFC)*	200–500	>500–1000	>1000
Beclometasone dipropionate (HFA)	100–200	>200–400	>400
Budesonide (DPI)	200–400	>400–800	>800
Ciclesonide (HFA)	80–160	>160–320	>320
Fluticasone furoate (DPI)	100	n.a.	200
Fluticasone propionate(DPI)	100–250	>250–500	>500
Fluticasone propionate (HFA)	100–250	>250–500	>500
Mometasone furoate	110–220	>220–440	>440
Triamcinolone acetonide	400–1000	>1000–2000	>2000
Children 6–11 years (for children 5 years and younger, see Box 6-6, p.112)			
Beclometasone dipropionate (CFC)*	100–200	>200–400	>400
Beclometasone dipropionate (HFA)	50-100	>100-200	>200
Budesonide (DPI)	100–200	>200–400	>400
Budesonide (nebules)	250–500	>500–1000	>1000
Ciclesonide	80	>80-160	>160
Fluticasone furoate (DPI)	n.a.	n.a.	n.a.
Fluticasone propionate (DPI)	100–200	>200–400	>400
Fluticasone propionate (HFA)	100–200	>200–500	>500
Mometasone furoate	110	≥220–<440	≥440
Triamcinolone acetonide	400–800	>800–1200	>1200

Quien Necesita Tratamiento Combinado

Pacientes Con Mal Control del Asma

PERSISTENCIA DE SINTOMAS A PESAR DEL
TRATAMIENTO ADECUADO

- Reciben el Tratamiento?
- Técnica Correcta?
- No Fuman en Casa?

Diferentes Tipos de Tratamientos Combinados

Long Acting B₂ Agonists (LABA): 12 hs

Salmeterol-Fluticasona

Formoterol-Budesonide

Antileucotrienos:

Montelukast

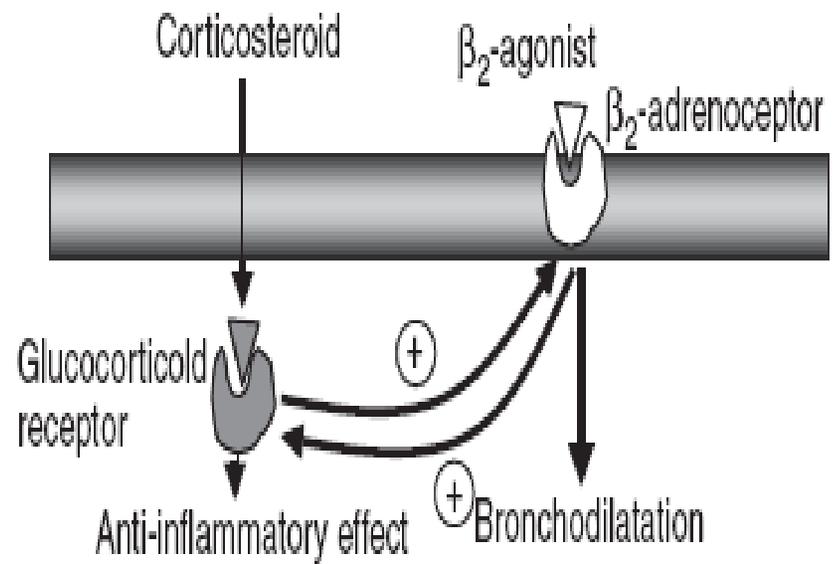
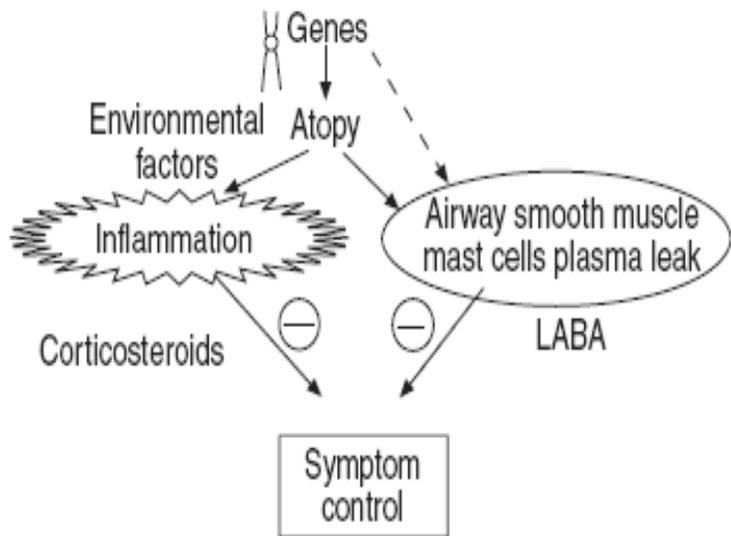
Anti IgE: Omalizumav

Anti IL5: Mepolizumab

- SABA vs. LABA
- SABA Hidrofílico acción directa sobre el receptor beta 2
- LABA Salmeterol: Lipofílico difunde bicapa lipídica (cel ML) actúa en el receptor beta2
- Formoterol Menos lipofílico rápido inicio de acción

Mecanismo de Acción de los LABA

- Relaja el Musculo Liso
- Inhiben liberacion de Histamina y Cisteinyl leucotrienos (SABA)
- Exudacion Plasmatica



COCHRANE

Long-acting beta2-agonists versus placebo in addition to inhaled corticosteroids in children and adults with chronic asthma (Review)

Ni Chroinin M, Greenstone IR, Danish A, Magdolinos H, Masse V, Zhang X, Ducharme FM



**THE COCHRANE
COLLABORATION®**

Criterios de Revisión

- Estudios Randomizados Controlados
- Adultos y Niños
- LABA administrado diariamente por al menos 30 días.
- La dosis de corticoides tenía que ser la misma entre el grupo control y el grupo de intervención.

citas encontradas solo 49 cumplían con los
criterios para ser incluidas en este análisis

Resultados

- Menos necesidad de corticoides sistémicos en exacerbaciones
- Mejoría en el FEV1
- Mayor número de días libres de síntomas
- Mayor número de días libres de rescates
- No presento mayores efectos adversos (mas que temblores) comparados con el grupo de corticoides solo.

PEDIATRIA

Los datos son insuficientes para sacar conclusiones en pacientes pediatricos en edad escolar y preescolar.

COCHRANE

Addition of anti-leukotriene agents to inhaled corticosteroids for chronic asthma (Review)

Ducharme F, Schwartz Z, Kakuma R



OBJETIVOS

Evaluar la seguridad y eficacia de Anti-leucotrienos mas corticoides inhalados vs. Corticoides inhalados solamente.

Criterios de Revisión

- Estudios Randomizados Controlados
- Adultos y Niños mayores de 2 años
- Tratamiento administrado diariamente durante por lo menos 30 días.
- Se evaluaron trabajos con misma dosis de corticoides entre el grupo control y el grupo de intervención o mayor en el grupo control.

Estudios

De 587 citas, solo 27 cumplían con los criterios de inclusión.

Tratamientos

Corticoides Inhalados

Anti-Leucotrienos

Mayor Dosis
Corticoides

Resultados

CI + AL (dosis aprobadas)

- No ↓ Riesgo de Exacerbaciones
- Modesta mejoría en el peak flow y N° de Eosinofilos

CI + AL (dosis altas)

- 66% Reducción de exacerbaciones
- Mejoría de VEF1 y PEF
- Menos Síntomas
- Menos Uso de Beta 2

Efectos Colaterales fueron comparables al Placebo

- Pacientes duplico dosis de CI vs. Pacientes en los que se agregó Anti-Leucotrienos a dosis altas. Similares resultados

Combination formoterol and budesonide as maintenance and reliever therapy versus current best practice (including inhaled steroid maintenance), for chronic asthma in adults and children (Review)

Cates CJ, Karner C



**THE COCHRANE
COLLABORATION®**

Objetivos

- Evaluar Eficacia y Seguridad de budesonide/formoterol en un single inhalador (SiT) para ser usado como mantenimiento y y en exacerbaciones en comparación con tratamiento de mantenimiento con inhaladores combinados con una dosis mayor de corticoides ya sean (fluticasone/salmeterol or budesonide/formoterol), Usando beta2-agonistas de rapida accion ante la presencia de sintomas

Main Results

- Four studies randomly assigning 9130 people with asthma were included; two were six-month double-blind studies, and two were 12-month open-label studies.
- Compared with higher fixed-dose combination inhalers, fewer people using SiT had exacerbations requiring hospitalisation or a visit to the ER (odds ratio (OR) 0.72, 95% confidence interval (CI) 0.57 to 0.90; I² = 0%, P = 0.66), and fewer had exacerbations requiring a course of oral

Authors' conclusions

- SiT reduces the number of people having asthma exacerbations requiring oral steroids and the number requiring hospitalisation or an ER visit compared with fixed-dose combination inhalers. Evidence for serious adverse events was unclear. The mean daily dose of inhaled corticosteroids (ICS) in SiT, including the total dose administered with reliever use, was always lower than that of the other combination groups.

Quintupling Inhaled Glucocorticoids to Prevent Childhood Asthma Exacerbations

METHODS

We studied 254 children, 5 to 11 years of age, who had mild-to-moderate persistent asthma and had had at least one asthma exacerbation treated with systemic glucocorticoids in the previous year. Children were treated for 48 weeks with maintenance low-dose inhaled glucocorticoids (fluticasone propionate at a dose of 44 μg per inhalation, two inhalations twice daily) and were randomly assigned to either continue the same dose (low-dose group) or use a quintupled dose (high-dose group; fluticasone at a dose of 220 μg per inhalation, two inhalations twice daily) for 7 days at the early signs of loss of asthma control (“yellow zone”). Treatment was provided in a double-blind fashion. The primary outcome was the rate of severe asthma exacerbations treated with systemic glucocorticoids.

RESULTS

The rate of severe asthma exacerbations treated with systemic glucocorticoids did not differ significantly between groups (0.48 exacerbations per year in the high-dose group and 0.37 exacerbations per year in the low-dose group; relative rate, 1.3; 95% confidence interval, 0.8 to 2.1; $P=0.30$). The time to the first exacerbation, the rate of treatment failure, symptom scores, and albuterol use during yellow-zone episodes did not differ significantly between groups. The total glucocorticoid exposure was 16% higher in the high-dose group than in the low-dose group. The difference in linear growth between the high-dose group and the low-dose group

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Quintupling Inhaled Glucocorticoids to Prevent Childhood
Asthma Exacerbations

CONCLUSIONS

In children with mild-to-moderate persistent asthma treated with daily inhaled glucocorticoids, quintupling the dose at the early signs of loss of asthma control did not reduce the rate of severe asthma exacerbations or improve other asthma outcomes and may be associated with diminished linear growth. (Funded by the National Heart, Lung, and Blood Institute; STICS ClinicalTrials.gov number, NCT02066129.)

N ENGL J MED 378;10 NEJM.ORG MARCH 8, 2018

Resumen

- Diagnostico esta basado en Anamnesis y Examen Clínico principalmente.
- Cuidar Medioambiente
- Revisar Adherencia, Adherencia y Adherencia
- Usar la menor dosis de Corticoides inhalados con la que el paciente pueda controlar sus síntomas.

MUCHAS GRACIAS
