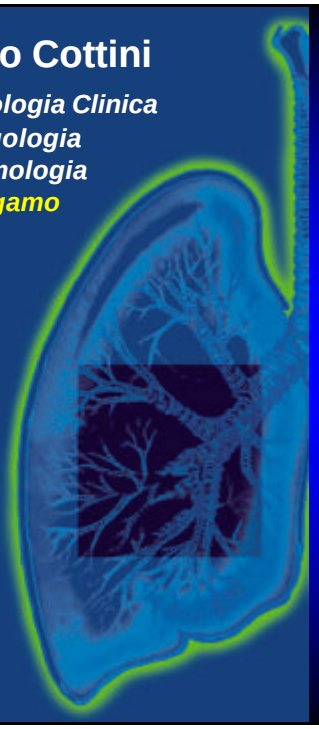
Marcello Cottini

Sp. Immunologia Clinica
Allergologia
Pneumologia
Bergamo



Asma da esercizio fisico

CORSO DI AGGIORNAMENTO

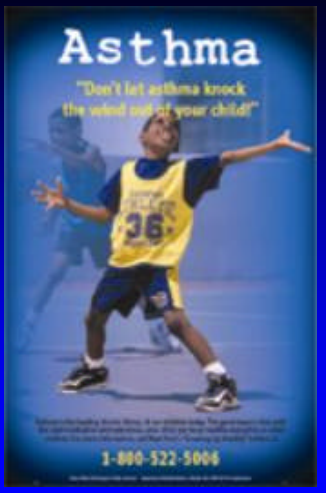
"I FENOTIPI DELL'ASMA' "

Arenzano 16 Febbraio 2008

Exercise-induced bronchospasm: a different phenotype?

EIA è presente in circa il 70-80% dei bambini non in terapia con steroidi inalatori

L’asma da sforzo allontana i bambini dallo sport!



Exercise training on disease control and quality of life in asthmatic children

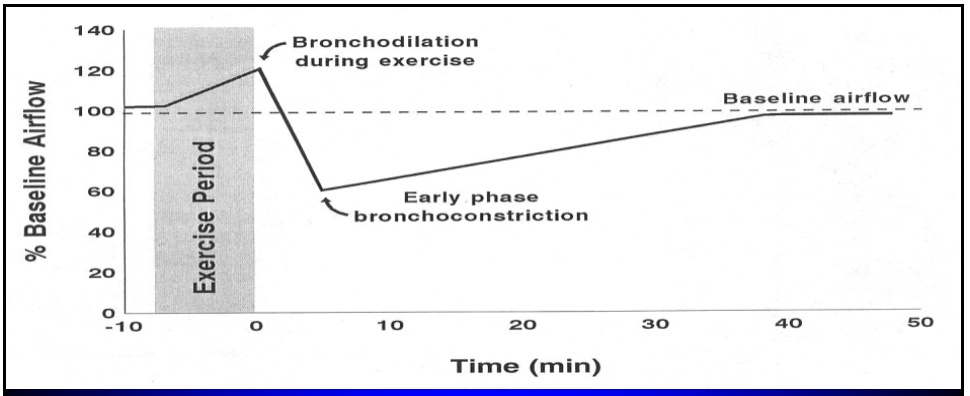
Fanelli A, Med Sci Sports Exerc 2007

Thirty-eight children with moderate to severe persistent asthma : control (N=17) training (N=21) groups

In trained children:

- ↑ physiological variables at peak and submaximal exercise
- ↓ Severity of exercise-induced bronchoconstriction (EIB) and postexercise breathlessness
- ↑ Pediatric Asthma Quality of Life Questionnaire (PAQLQ) scores
- ↓ Daily doses of inhaled steroids

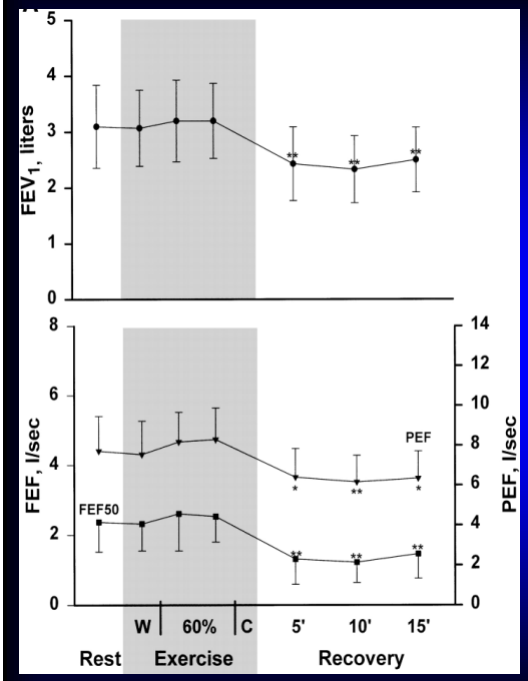
Exercise-induced asthma (EIA), connotes transient airflow obstruction associated with physical exertion.



1962 : **Jones and collegues reported that the effect of exercise on the asthmatic airway was dependent on the duration of activity.**

Prolonged exercise of 5-to 10-min duration created bronchoconstriction

Jones RS, Br J Dis Chest 1962



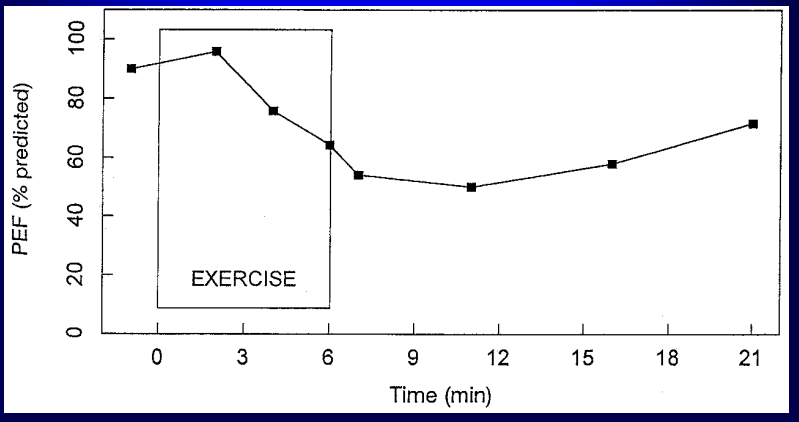
Asma da esercizio fisico

Riduzione dei flussi espiratori **dopo, ma non durante**, esercizio fisico breve (6 min) preceduto da warm-up (W)

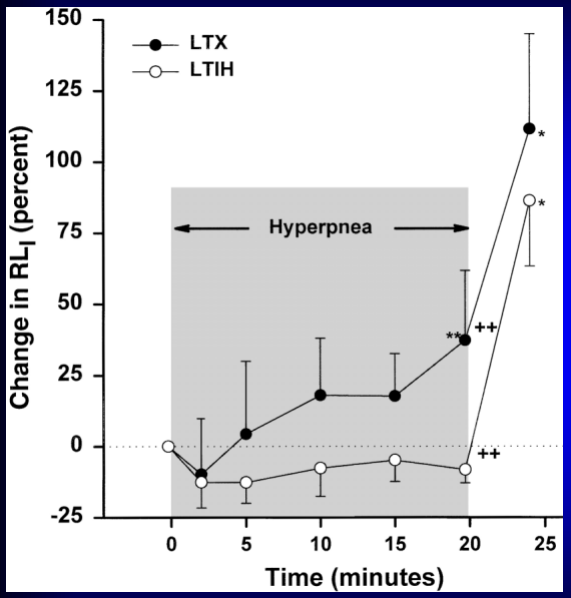
Beck et al., JAP 1999

DURING or AFTER ???

The bronchospasm can occur also **during the exercise**, especially during prolonged exertion



Godfrey S, Bar-Yishay E, Exercise induced asthma revised, Respiratory Medicine 1993



Asma da esercizio fisico

Aumento della resistenza inspiratoria (RL_I) **durante e dopo** esercizio prolungato

Suman et al., JAP 1999

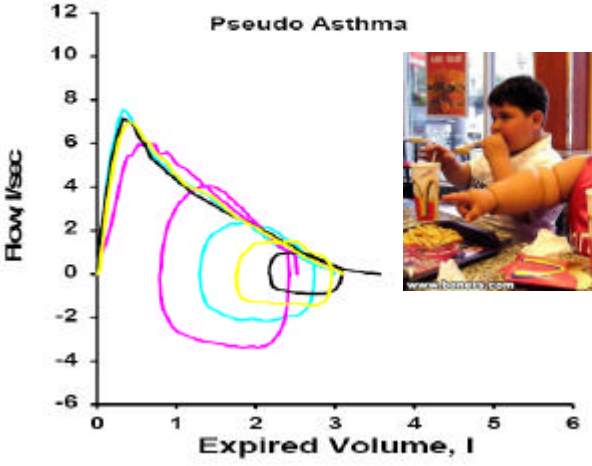
Mistaken Diagnosis of EIB

- Being unfit
- Breathlessness in the overweight / obese
- Vocal cord dysfunction
- Exercise hyperventilation syndrome

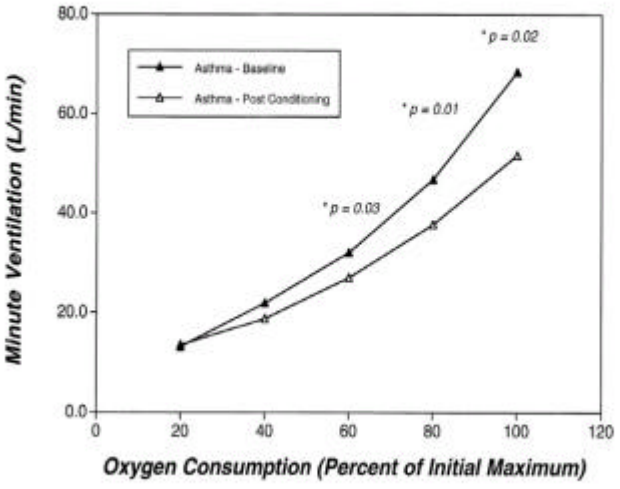
Are all often incorrectly diagnosed as EIB.

For these disorders the symptoms occur DURING rather than AFTER exercise.

Obesity Pseudo Asthma



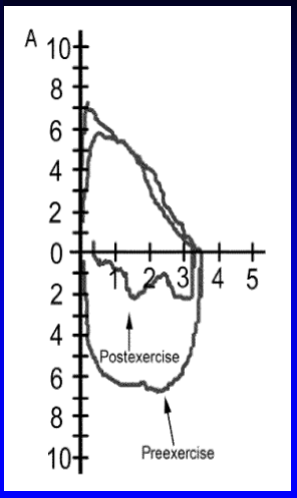
Being fit reduces ventilation for a given exercise task so being fit will mean feeling less breathless



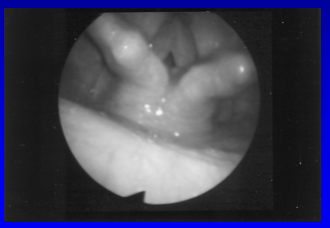
Hallstrand, T. S. et al. Chest 2000;118:1460-1469

Pseudo-asthma: when cough, wheezing, and dyspnea are not asthma.

Weinberger, Pediatrics Oct 2007



Exercise-induced vocal cord dysfunction



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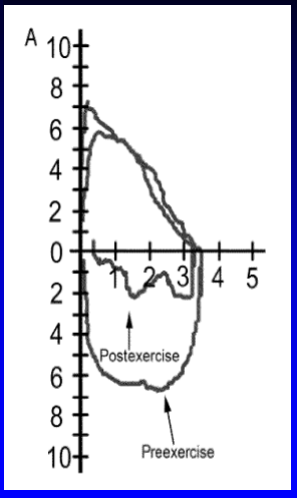
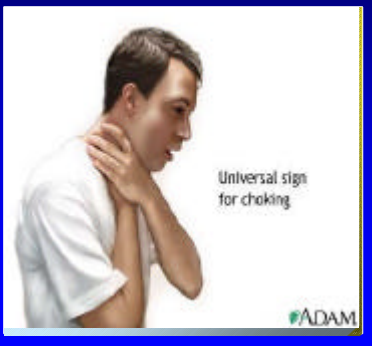
Weinberger, Pediatrics Oct 2007



Exercise-induced vocal cord dysfunction



Although most exacerbations are self-limited or subside readily with medication, sudden fatal asthma exacerbations occur in both competitive and recreational athletes, and can be precipitated by sporting activity

Becker JM, Rogers J, Rossini G, et al. Asthma deaths during sports: report of a 7-year experience.

J Allergy Clin Immunol 2004

Rashidi Wheeler morto per asma sul campo 03.08.01

Becker JM, Rogers J, Rossini G, et al. Asthma deaths during sports: report of a 7-year experience.

J Allergy Clin Immunol 2004

61 deaths over a 7-y period

81% < 21 y

57% elite athletes

Becker JM, Rogers J, Rossini G, et al. Asthma deaths during sports: report of a 7-year experience.

J Allergy Clin Immunol 2004

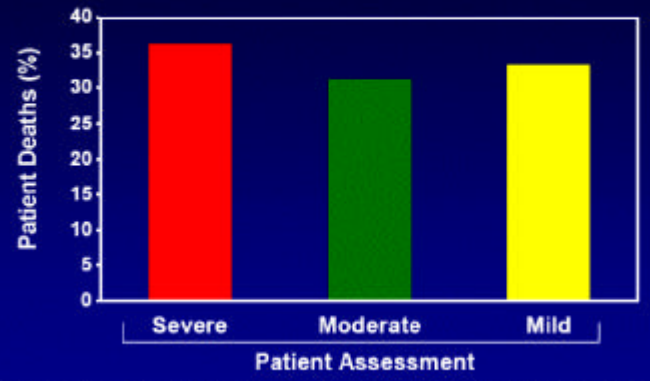
- Adolescenti a rischio: 10-14 anni fascia prevalente!
- Non solo sport agonistico.

Becker JM, Rogers J, Rossini G, et al. Asthma deaths during sports: report of a 7-year experience.

J Allergy Clin Immunol 2004

- Adolescenti a rischio: 10-14 anni fascia prevalente!
- Non solo sport agonistico.
- **Molti con asma lieve.**

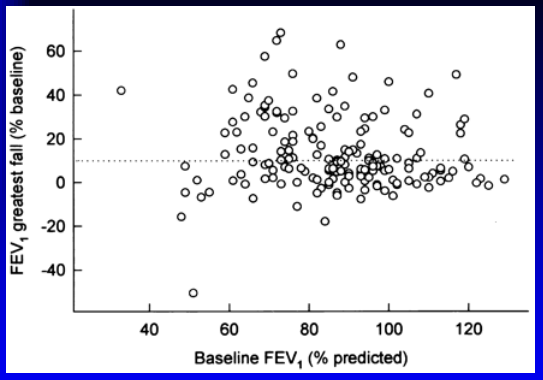
Asthma Deaths: Patients With Mild Asthma Are Also at Risk



Findings from a cohort study reviewing all pediatric asthma-related deaths (n=51) in the Australian state of Victoria from 1986 to 1989.

Robertson et al. *Pediatr Pulmonol.* 1992;13:95-100.

Exercise-induced bronchospasm in children: effects of asthma severity



The prevalence of EIB is greater in children with more severe asthma, and the intensity of response to exercise is not consistently related to the clinical severity of asthma.

Cabral, AJRCCM 1999

Becker JM, Rogers J, Rossini G, et al. Asthma deaths during sports: report of a 7-year experience.

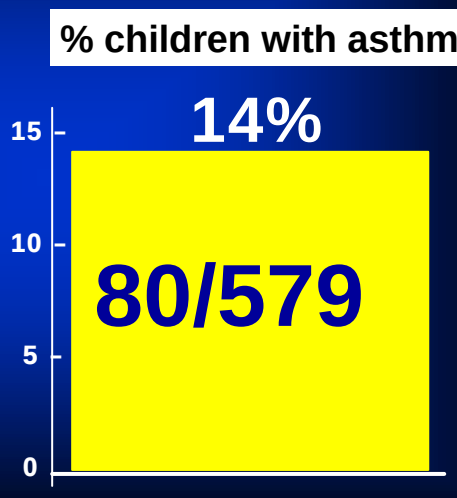
J Allergy Clin Immunol 2004

- Adolescenti a rischio: 10-14 anni fascia prevalente!
- Non solo sport agonistico.
- Molti con asma lieve.
- **77% non in terapia di fondo per asma!**

A PILOT SURVEY OF ß$_2$-AGONIST INHALER AVAILABILITY FOR CHILDREN WITH ASTHMA DURING ORGANIZED SPORTING EVENTS

Cardona Ann. Allergy Asthma Immunol. 2004; 92: 340

- ✓579 ch.<12 yrs playing baseball or soccer
- ✓Parents reported asthma



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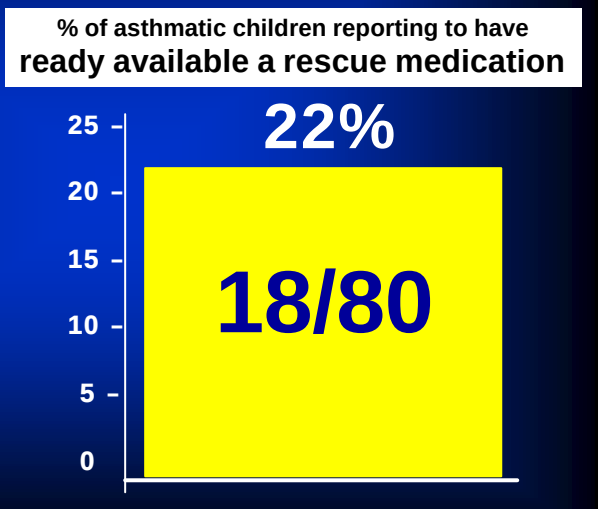


History


THE
PREFACE
TO THE
TREATISE
OF THE
ASTHMA.

Sir John Floyer, who was himself asthmatic, first described the adverse effects of physical exercise on his asthma, noting that <u>different types of exercise</u> had greater or lesser adverse effects

Floyer J, Sir. A treatise of the asthma. R Wilkin & W Innis, London, 1698

EFFECT OF EXERCISE TYPE

Frequency and Severity of EIA

Free-range running (↓ 47% PEF)

Running on a treadmill (↓ 33%)

Cycling (↓ 25%)

Swimming,kayaking,walking (↓ 15%)

Anderson, Br J Dis Chest 1975 ; Fitch, JAMA 1976

Original article

Swimming pool attendance and hay fever rates later in life

Allergy 2006: 61: 1305–1309

Higher rates of hay fever.

Pulmonary Epithelial Integrity in Children: Relationship to Ambient Ozone Exposure and Swimming Pool Attendance

Birgitta Json Lagerkvist,[1] Alfred Bernard,[2] Anders Blomberg,[3] Erik Bergstrom,[4] Bertil Forsberg,[1] Karin Holmstrom,[5] Kjell Karp,[5] Nils-Goran Lundstrom,[1] Bo Segerstedt,[1] Mona Svensson,[1] and Gunnar Nordberg[1]

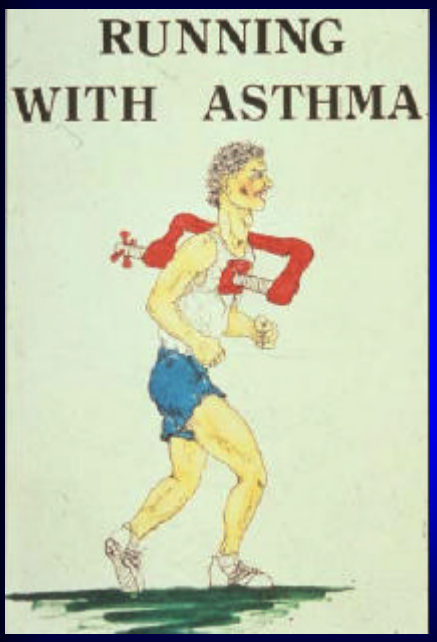
Environmental Health Perspectives • VOLUME 112 | NUMBER 17 | December 2004

Adverse effects on the Clara cell function

Indoor swimming pools, water chlorination and respiratory health

During training and competition, higly trained swimmers inhale large amounts of air that floats just above the water surface.

Therefore they are repetedly and stongly exposed to chlorine derivatives.



Exercise-induced Asthma : Symptoms

Symptoms of EIA

Typical	Atypical
Cough: during or after exercise	Stomach cramps
Wheezing	Headache
Shortness of breath during or after exercise	"Being out of shape"

Symptoms of EIA

Typical	Atypical
Cough: during or after exercise Wheezing Shortness of breath during or after exercise	Stomach cramps Headache "Being out of shape"

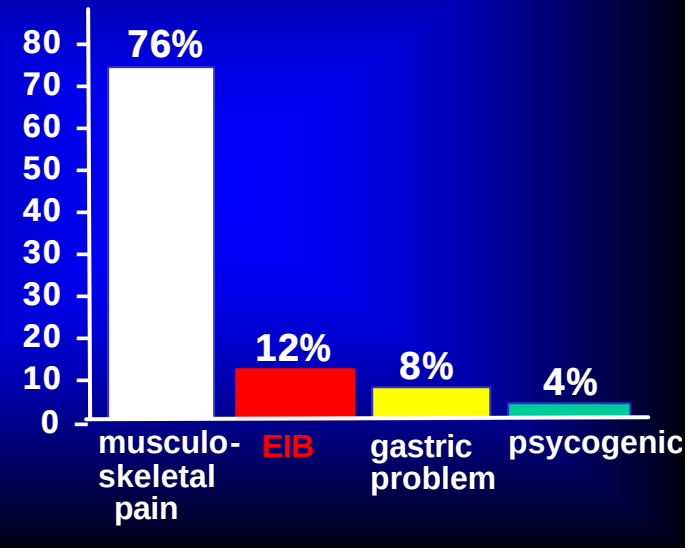
può manifestarsi come dolore toracico

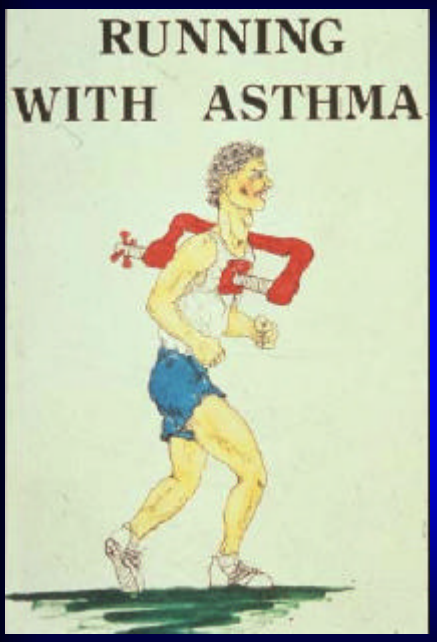
Nudel Clin. Pediatr. 1987; 26: 388

CHEST PAIN IN CHILDREN: DIAGNOSIS THROUGH HISTORY AND PHYSICAL EXAMINATION

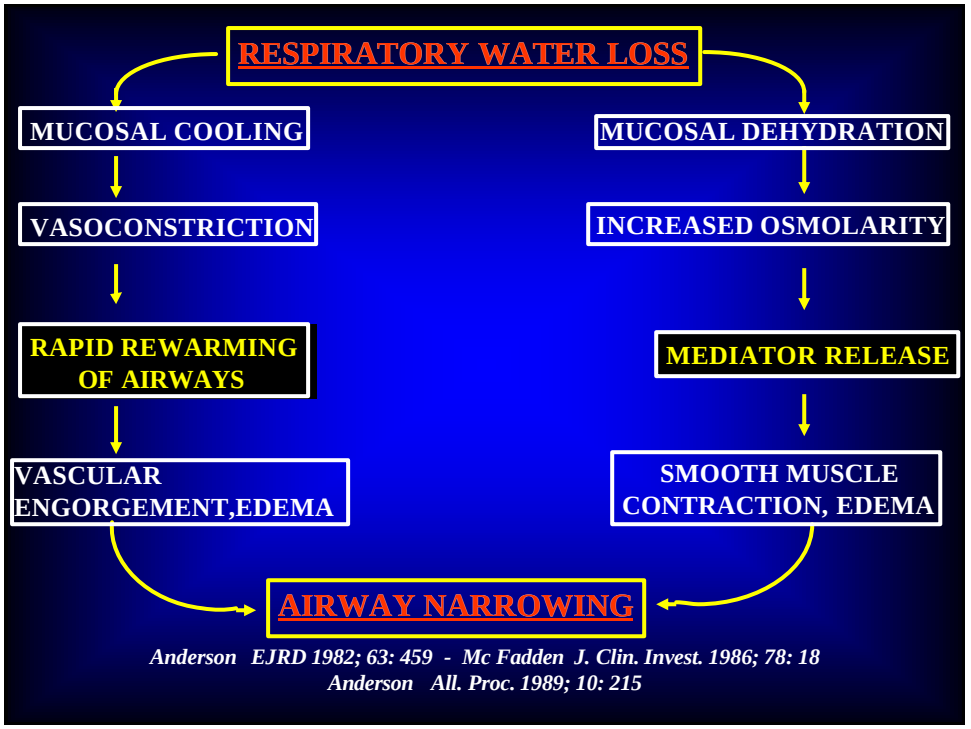
Evangelista JA, JPHC 2000; 14: 3

- ✓ 50 ch. referred for chest pain
- ✓ Physical examination and ECG



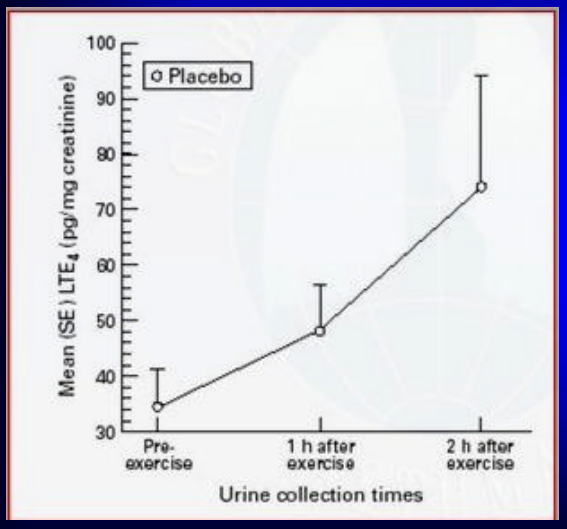


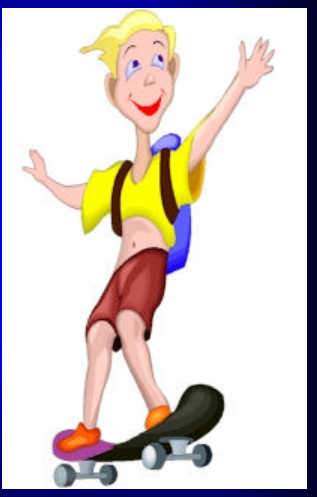
Exercise-induced Asthma : Pathophysiology



Anderson EJRD 1982; 63: 459 - Mc Fadden J. Clin. Invest. 1986; 78: 18
Anderson All. Proc. 1989; 10: 215

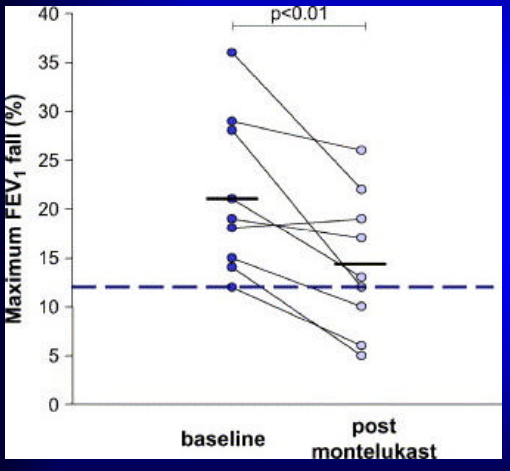
Increased urinary excretion of LTE4 after exercise





Reiss TF, Thorax 1997

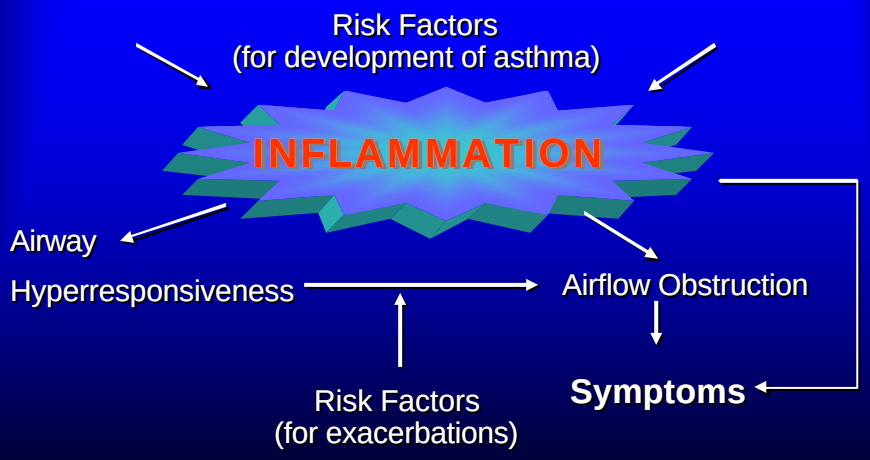
Exhaled breath condensate cysteinyl leukotrienes are increased in children with exercise-induced bronchoconstriction



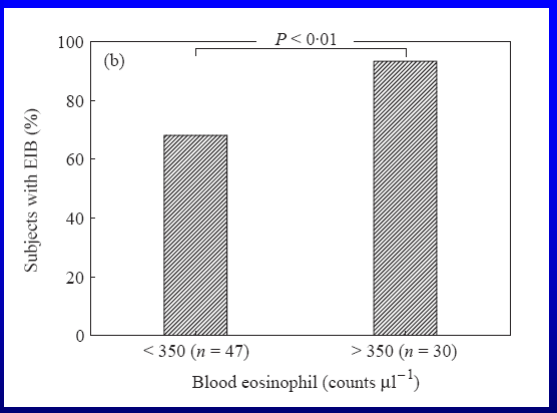
Maximal FEV_1 decrease after exercise in asthmatic children with EIB at baseline and after 3 days of treatment with **montelukast**

Carraro S, JACI 2005

Mechanisms Underlying the Definition of Asthma



Blood eosinophil counts for the prediction of the severity of exercise-induced bronchospasm in asthma



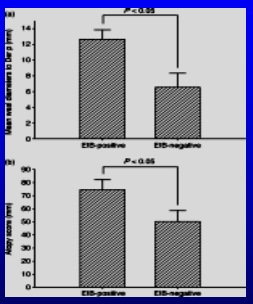
Percentages of subjects with EIB according to the degree of blood eosinophils

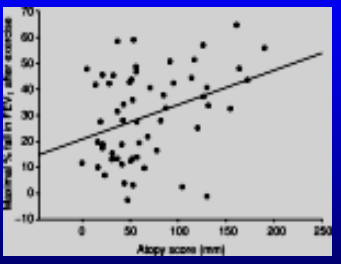
Eosinophils play a major role in the severity of exercise-induced bronchoconstriction in children with asthma

Pediatr Pulmonol 2006

Atopy may be related to exercise-induced bronchospasm in asthma

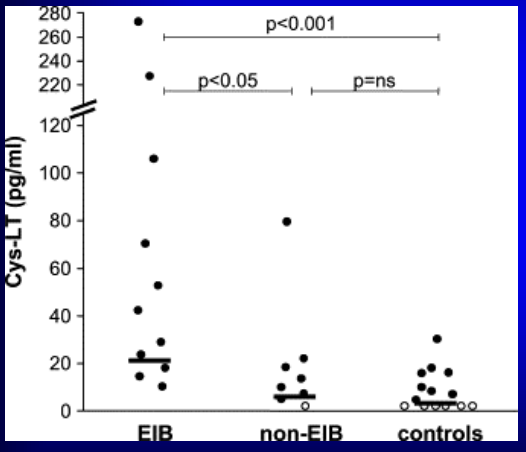
Koh YI, Clin Exp Allergy 2002





Atopy defined as skin test reactivity may contribute to the development of EIB in asthma, indipendently of AHR to metacholine

Exhaled breath condensate cysteinyl leukotrienes are increased in children with exercise-induced bronchoconstriction

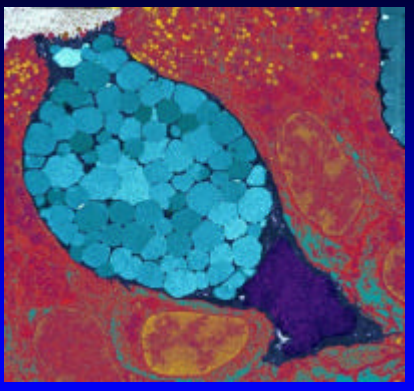


Cys-LT levels in EBC of asthmatic children with EIB, asthmatic children without EIB, and healthy control children

Carraro S, JACI 2005

Emerging evidence indicates that injury to the airway epithelium is a key susceptibility factor for EIB.

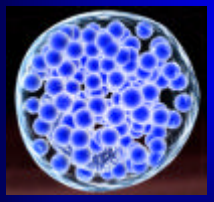
One consequence of epithelial injury is replacement of ciliated epithelial cells by mucin secreting cells.

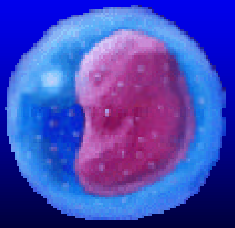


Anderson SD, *Curr Allergy Asthma Rep.* 2005 Hallstrand TS, *J Allergy Clin Immunol.* 2005

Athletes and exercise-induced bronchoconstriction

Same inflammation ??





*Work Group Report**

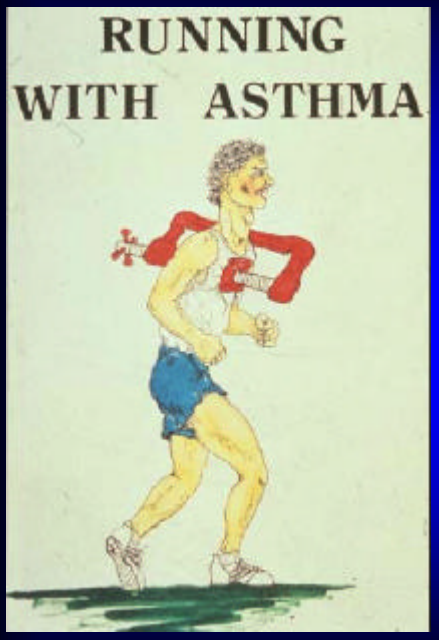
JACI , June 2007

American Academy of Allergy, Asthma & Immunology Work Group Report: Exercise-induced asthma

John M. Weiler, MD,[a] Sergio Bonini, MD,[b] Robert Coifman, MD,[c] Timothy Craig, DO,[d] Luis Delgado, MD,[e,j] Miguel Capão-Filipe, MD,[e] Desiderio Passali, MD,[f] Christopher Randolph, MD,[h] and William Storms, MD[i] *Iowa City, Iowa, Rome and Siena, Italy, Millville, NJ, Hershey, Pa, Porto, Portugal, and Colorado Springs, Colo*

EIA and EIB: different phenotypes?

"We use the term ***exercise-induced bronchospasm*** (EIB) to describe the airway obstruction that occurs in association with exercise without regard to the presence of chronic asthma".



Exercise-induced Asthma : Prevalence

Up to 90% of subjects with asthma will have EIB

Mc Fadden ER, NEJM 1994

Factors that Exacerbate Asthma

- Allergens
- Air Pollutants
- Respiratory infections
- **Exercise and hyperventilation**
- Weather changes
- Sulfur dioxide
- Food, additives, drugs

Prevalence of EIA

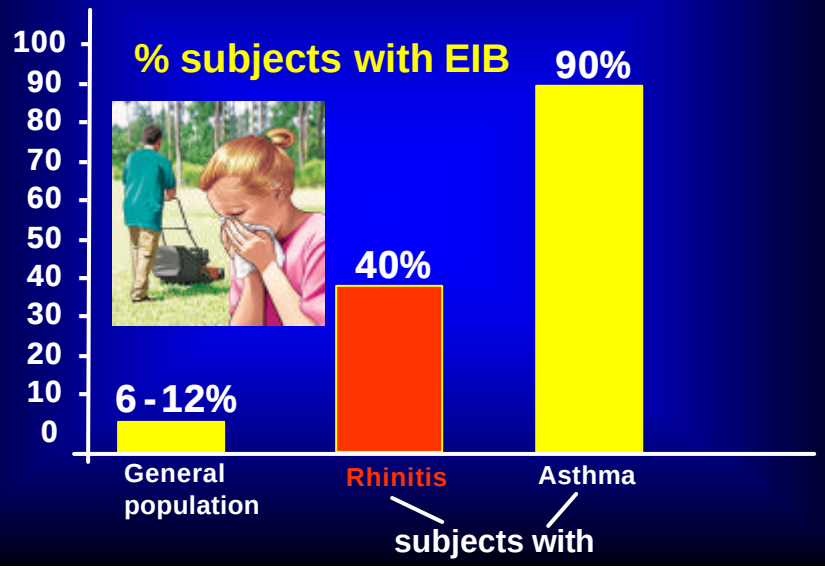
✓ **Hallstrand found 9% of school children had EIA**
Hallstrand TS, J Pediatr 2002

✓ **Rupp found 12% of school children had EIA**
Rupp NT, Ann Allergy 1993

Method: sport-specific challenge testing in nonathletes

KEEPING CHILDREN WITH EXERCISE-INDUCED ASTHMA ACTIVE

Milgrom H Pediatrics 1999; 104 :38



British study: EIA (>15% fall in FEV1) in 29/100 sequentially referred potential recruits with a history suggestive of asthma in childhood but no asthma symptoms or therapy in the last 4 years.

Sinclair DG etal. Eur Respir et J 1995;8:1314-17

Prevalence of EIA

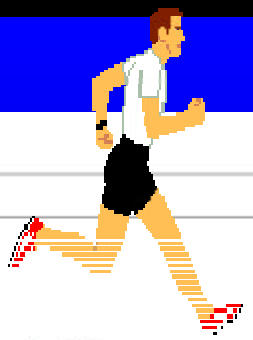


TABLE 1. Incidence ofEIA.

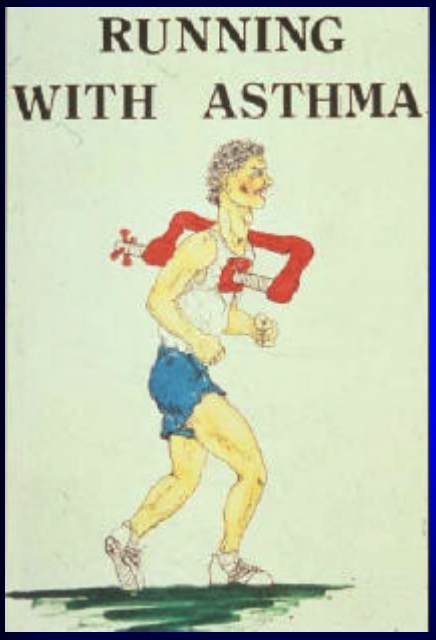
Sport	%
Cross-country skiers	50
Ice hockey	35
Speed skaters	43
Figure skaters	35
Summer and winter Olympic athletes	17
School children	12

Delaying Decline in Pulmonary Function with Physical Activity

A 25-Year Follow-up

Physical activity is associated with a slower decline in pulmonary function and with lower mortality

Pelkonen M, AJRCCM 2003



Exercise-induced Asthma : diagnosis

ASTHMA SCREENING OF HIGH SCHOOL ATHLETES: IDENTIFYING THE UNDIAGNOSED AND POORLY CONTROLLED WITH FREE-RUNNING CHALLENGE

Ann All Asthma Imm 2002; 88: 380

- ✓ 801 student athletes
- ✓ questionnaire and free running exercise challenge

Total 801 student athletes → Asthma and EIA identified by questionnaire 46 (5.7%)

Asthma and EIA identified by questionnaire 46 (5.7%) → remaining 755

Asthma and EIA identified by questionnaire 46 (5.7%) → 49 (6.5%) → Identified by free running test

Perception of exercise induced asthma by children and their parents

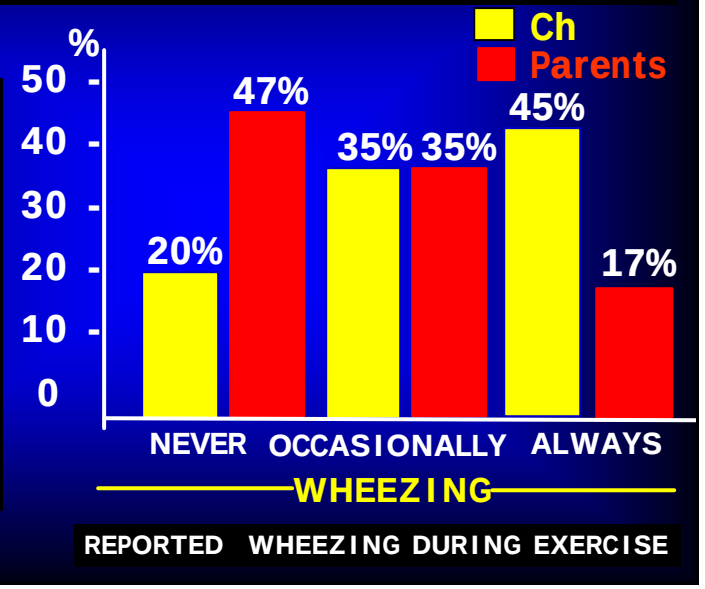
Modest specificity (82%) and low sensitivity (50%) of children's descriptions

Panditi S, ADC 2003

DIFFERENCES BETWEEN CHILD AND PARENT REPORTS OF SYMPTOMS AMONG CHILDREN WITH ASTHMA

Lara M Pediatrics 1998; 102 : E68

- ✓ 97 ch. with asthma
- ✓ child and parent interviews
- ✓ exercise test



History and/or p.e. compatible with EIA

↓

Spirometry (FEV1 reversibility > 12%)

Tan RA, Ann Allergy Asthma Immunol 2002

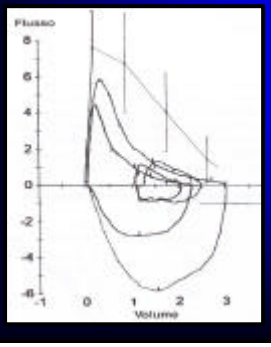
History and/or p.e. compatible with EIA

↓

Spirometry (FEV1 reversibility > 12%)

⊕

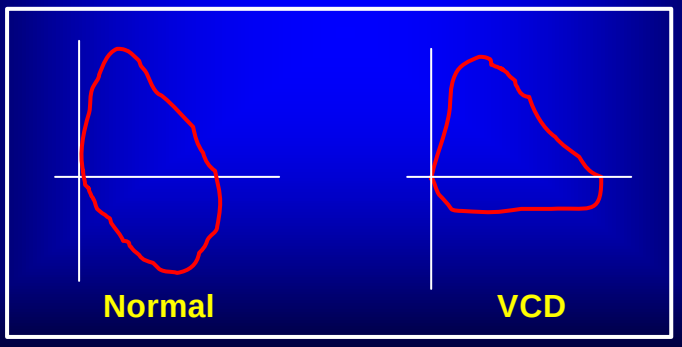
Treat as ASTHMA

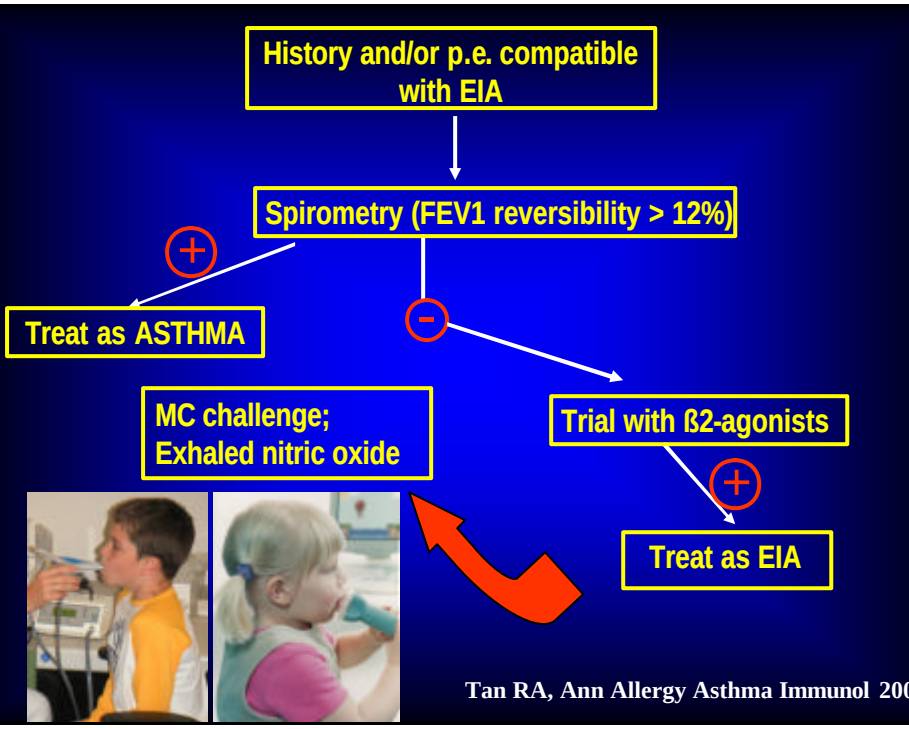


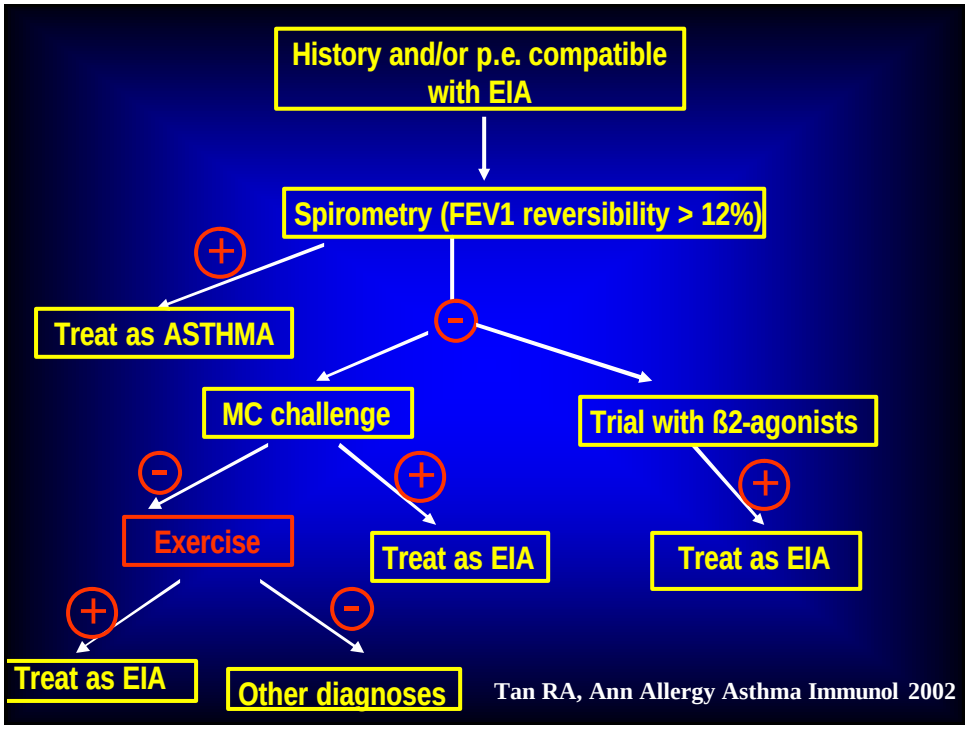
Tan RA, Ann Allergy Asthma Immunol 2002

Pulmonary Function Tests

- Flow-volume loop demonstrates flattened inspiratory loop when symptomatic.





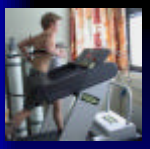

History and/or p.e. compatible with EIA
Spirometry (FEV1 reversibility > 12%)
+
Treat as ASTHMA
-
MC challenge
Trial with ß2-agonists
-
+
+
Exercise
Treat as EIA
Treat as EIA
+
-
Treat as EIA
Other diagnoses
Tan RA, Ann Allergy Asthma Immunol 2002


Per avviare il bambino asmatico allo sport
Valutare il bambino mediante test da sforzo

Il test da sforzo appare particolarmente adeguato in età pediatrica poiché rappresenta uno stimolo fisiologico che riproduce circostanze di "vita reale", quotidiane

ATS- Am J Respir Crit Care Med 2000;161:309-329

Test da sforzo eseguito in laboratorio



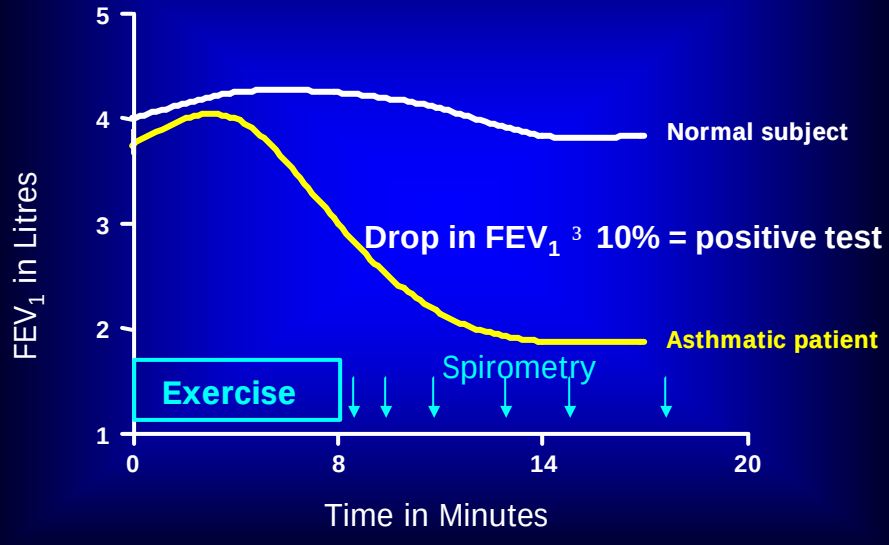
Tapis Roulant

- Ventilazione aumenta di più, bronco-ostruzione facile (V'O2 +10%)
- Per qualche paziente più facile da eseguire.
- Più difficile determinare intensità (watt)

Bicicletta

- Non ha velocità e inclinazione, solo carico di lavoro (workload)
- Preferibile per pazienti con difficoltà di camminare/ correre
- Facile determinare intensità (watt)

EXERCISE TESTING



ASMA DA SFORZO – PRECAUZIONI

- ✓ **non eseguire il test se:**
  - **il paziente presenta broncospasmo a riposo**
  - **PEFR o FEV_1 < 70 % del predetto**
    < 80 % dei valori usuali
    (in tal caso test di reversibilità)
- ✓ **presenza del medico per tutta la durata del test**
- ✓ **cardiomonitor**
- ✓ **somministrare b_2 stimolante spray e ossigeno se broncospasmo grave**

Anche il test della corsa libera è risultato valido e ripetibile, con il limite delle condizioni ambientali (temp. 20-24°C,umidità relativa < 40%)

ATS- Am J Respir Crit Care Med 2000;161:309-329

Exercise-induced bronchospasm in children: comparison of FEV1 and FEF25-75% responses

FEF(25-75%) can decrease in response to exercise without changes in FEV(1), mainly in children with mild asthma

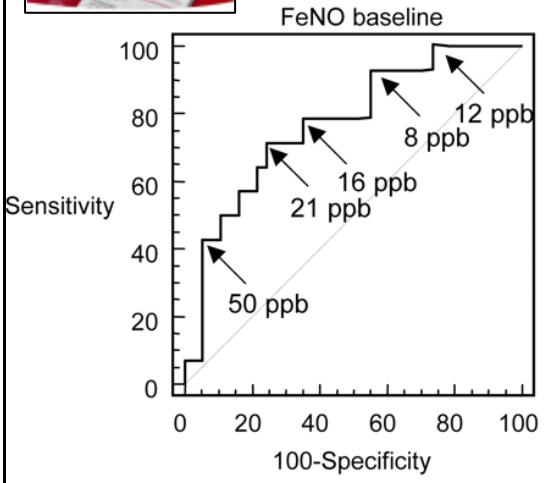
Fonsega-Guedes, Pediatr Pulmonol 2003

Exhaled Nitric Oxide Predicts Exercise-Induced Bronchoconstriction in Asthmatic School Children

Frederik Buchvald, Mette N. Hermansen, Kim G. Nielsen and Hans Bisgaard

Chest 2005;128;1964-1967

DOI: 10.1378/chest.128.4.1964



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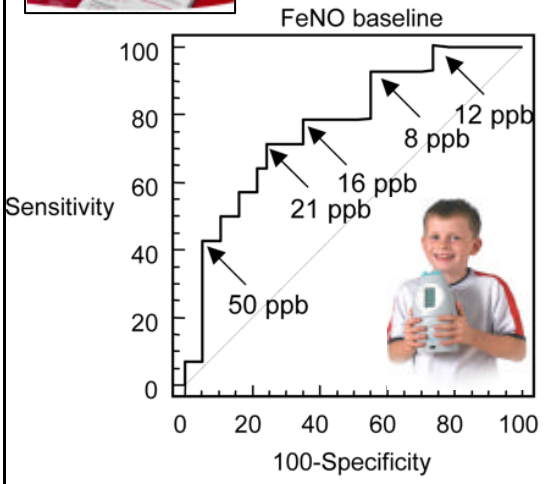
DOI: 10.1378/chest.128.4.1964



EIB could be excluded with a probability of 90% in asthmatic children with FeNO levels < 20 parts per billion (ppb) without current inhaled corticosteroid treatment, and < 12 ppb in children with current inhaled corticosteroid treatment.

Value of surrogate tests to predict exercise-induced bronchoconstriction in atopic childhood asthma

Lex, Pediatr Pulmonol 2007

All children with normal eNO levels (< or = 25 ppb) had normal lung function results after exercise; hence the negative predictive value (NPV) of eNO levels for prediction of EIB was 100%.

Exhaled nitric oxide and exercise-induced bronchospasm assessed by FEV1, FEF25-75% in childhood asthma

Nishio K,J Asthma 2007

Not only FEV1 but FEF25-75% can be used to evaluate the correlations between BHR (EIB) and airway inflammation (eNO) in asthmatic children.

A low eNO is useful for a negative predictor for EIB

Asma bronchiale negli atleti

Percorso diagnostico per le Olimpiadi di Atene

Test di broncostimolazione positivo

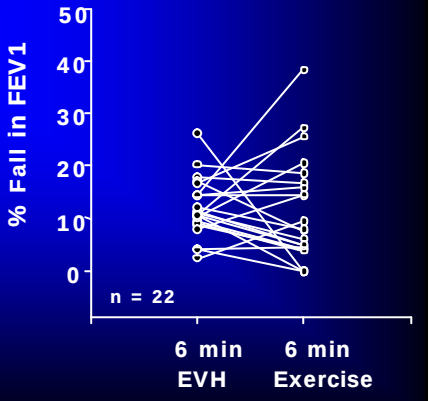
1) test metacolina:PD20 < 200 mcg
2) test sforzo- < 10 % FEV1 v. b.
3) test iperpnea vol. isocapnica < 10% FEV1 v.b.
4) Aerosol ipertonico < 15% FEV1 v.b.

Diagnosi di Iperreattività bronchiale

→ Asma bronchiale -→ Terapia - Prevenzione

EUCAPNIC VOLUNTARY HYPERVENTILATION

- 6min of hyperpnoea
  - dry air
  - 4.9% CO_2
- 10% fall in FEV_1
- Specific for diagnosis of EIA *(Rundell et al. 2004)*
- Recommended by the IOC



IBAs USE SYDNEY vs ATHENS

	SYDNEY 2000 (notified)		ATHENS 2004 (approved)	
• NOC	IBAs	PERCENT	IBAs	PERCENT
• NZL	31	21.1%	11	11.3%
• AUS	128	20.7%	65	13.7%
• UK	62	19.9%	62	23.3%
• USA	112	18.9%	50	9.1%
• CAN	55	18.6%	11	4.1%
• FIN	10	14.3%	4	6.6%

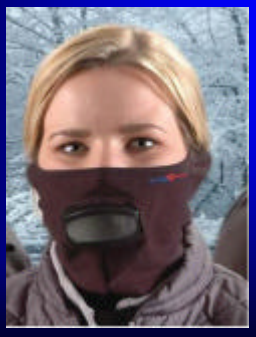
Anderson et al. submitted

Per avviare il bambino asmatico allo sport

EIA:terapia non farmacologica

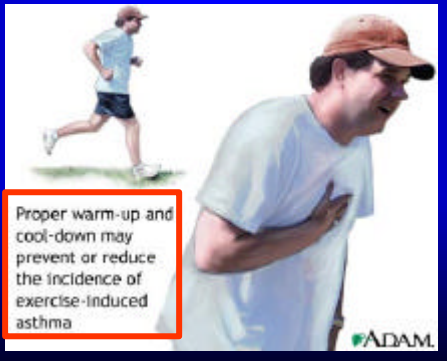
SCHACHTER, E. N., E. LACH, and M. LEE.
The protective effect of a cold weather mask on exercised-induced asthma.

***Ann. Allergy* 46:12–16, 1981.**



EIA:terapia non farmacologica

A special warm-up routine has been shown to reduce the severity of EIA



EIA:terapia non farmacologica

TRAINING OF AEROBIC AND ANAEROBIC FITNESS IN CHILDREN WITH ASTHMA

FRANÇOIS-PIERRE COUNIL, MD, PHD, ALAIN VARRAY, PHD, STEPHAN MATECKI, MD, PHD, ALAIN BEUREY, MD, PATRICK MARCHAL, MD, MICHEL VOISIN, MD, AND CHRISTIAN PRÉFAUT, MD

ALLENAMENTO INTERMITTENTE

Esecuzione,durante il preriscaldamento,di sprint brevi(10-12),della durata di 20-30 secondi,intercalati da periodi di recupero di 1-2 min,per indurre refrattarietà all'EIA senza provocare broncoostruzione clinicamente significativa

FRANÇOIS-PIERRE COUNIL, *J Pediatr 2003*

ASMA DA SFORZO (EIA) - ALLERGIA

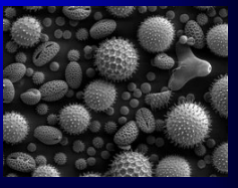
esposizione allergeni

aumento EIA

- infiammazione

sforzo

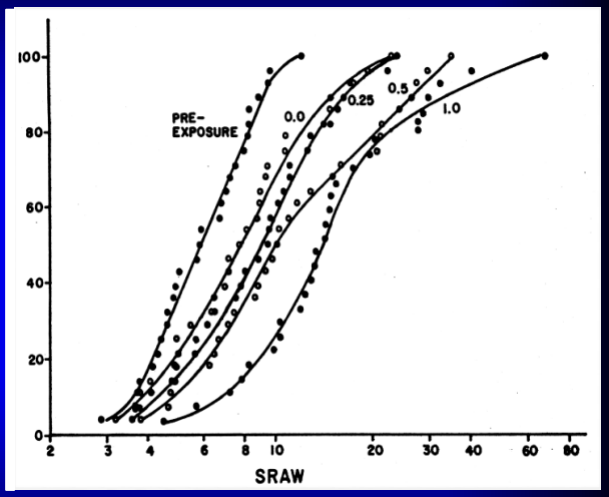
- reattività bronchiale aspecifica



ASMA DA SFORZO ED INQUINAMENTO ATMOSFERICO

Bronchoconstriction in asthmatics exposed to sulfur dioxide during repeated exercise.

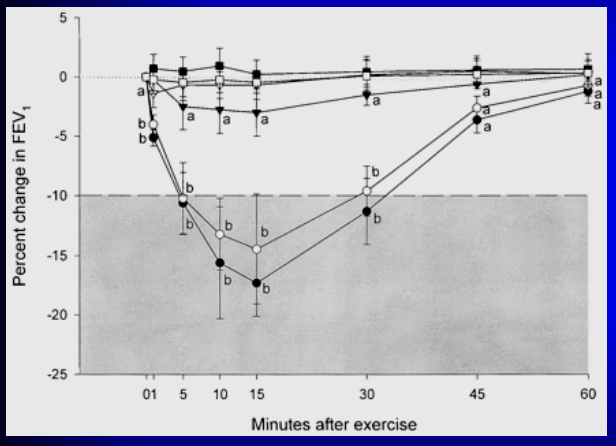
Roger
J.Appl.Physiol. 1985



Distribution of specific airway resistance (sRaw; cm H_2O - s) in asthmatic subjects exposed, during exercise, to air (0.0 ppm) or SO_2 (0.25, 0.5, and 1.0 ppm)

Fish Oil Supplementation Reduces Severity of Exercise-induced Bronchoconstriction in Elite Athletes

Mickleborough, *American Journal of Respiratory and Critical Care Medicine* 2003



Supplementing the dietwith n-3 PUFA represents a potentially beneficial treatment for elite athletes with EIB.

TERAPIA E PREVENZIONE DELL'ASMA DA SFORZO

1. Premedicazione

- ß2-agonisti
- Cromoni
- Montelukast

TERAPIA E PREVENZIONE DELL'ASMA DA SFORZO

2. Terapia di fondo

- Steroidi inalatori
- Montelukast

TERAPIA E PREVENZIONE DELL'ASMA DA SFORZO

1. Premedicazione

- **ß2-agonisti**
- Cromoni
- Montelukast

Long-acting beta-agonists

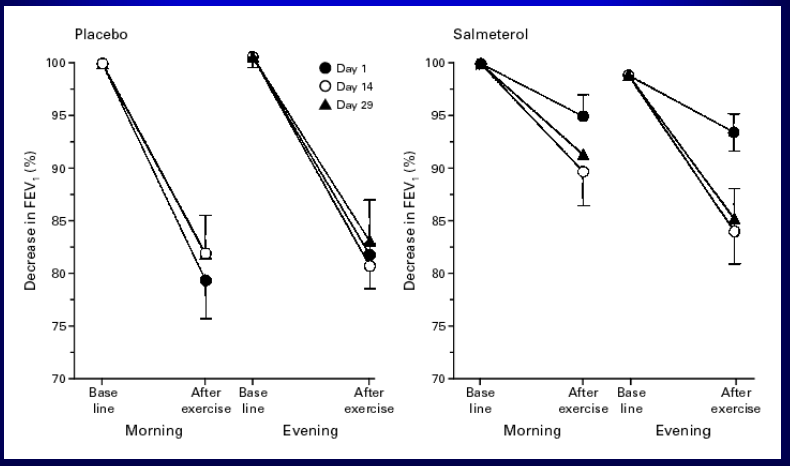
- ✓ Prevention of EIA in pediatric asthma patients: a comparison of two salmeterol powder delivery devices.
  Bronsky,Pediatrics 1999
- ✓ Evidence of the rapid protective effect of formoterol dry-powder inhalation against EIA in athletes with asthma.
  Ferrari, Respiration 2000

ß2-Agonist Tolerance and EIB

- Hancox RJ, AJRCCM 2002 (salbutamol)
- Nelson JA, NEJM 1998 (salmeterol)
- Garcia R, J Invest All Clin Immunol 2001 (formoterol)

Asma da esercizio fisico

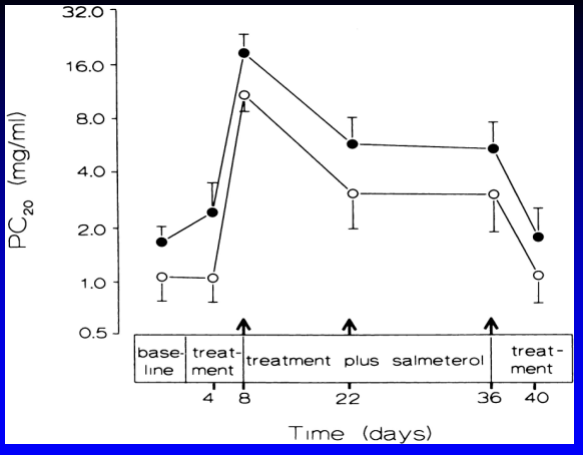
L'effetto del salmeterolo e la sua durata si attenuano col trattamento cronico



Nelson et al., NEJM 1998

Risposta alla metacolina

L'effetto protettivo del salmeterolo si riduce nel tempo



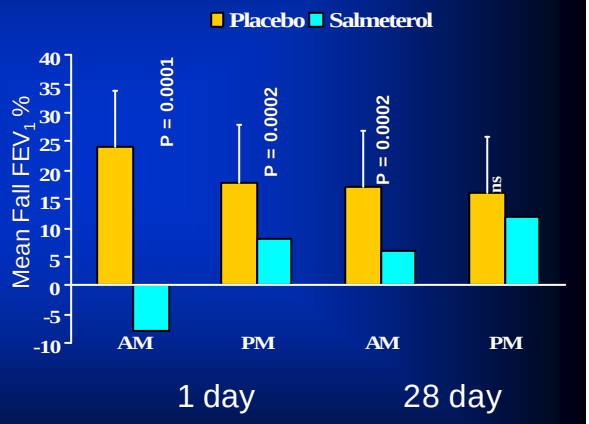
Cheung et al AJRCCM 1998

Tolerance to the bronchoprotective effect of salmeterol in adolescents with exercise induced asthma

Simons, Pediatrics 1997;99:665

- SLM 50 mcg once daily vs PL+ daily inhaled steroids therapy
- Exercise at 1 and 12 hours after drug, on day 1 and 28

The duration of the broncho-protective effect decreases during regular treatment with salmeterol despite concomitant use of inhaled steroids



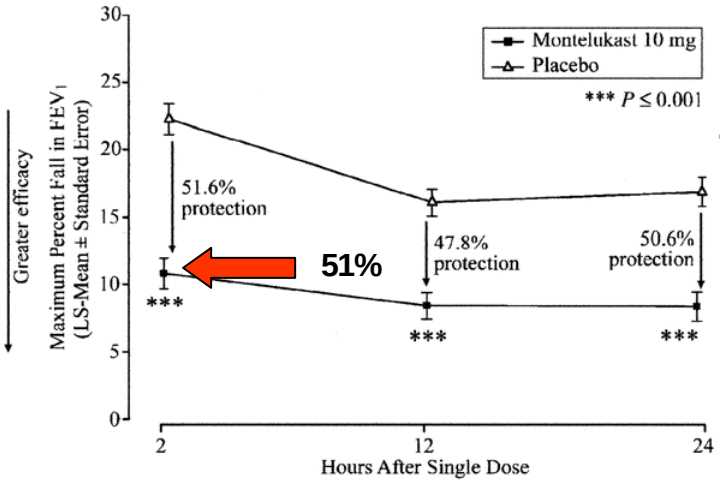
TERAPIA E PREVENZIONE DELL'ASMA DA SFORZO

1. **Premedicazione**

- ß2-agonisti
- Cromoni
- **Montelukast**

Onset and duration of protection against exercise-induced bronchoconstriction by a single oral dose of montelukast

David S. Pearlman, MD*; Janet van Adelsberg, MD†; George Philip, MD†; Stephen A. Tilles, MD‡; William Busse, MD§; Leslie Hendeles, PharmD‖; Thomas Loeys, PhD†; S. Balachandra Dass, PhD†; and Theodore F. Reiss, MD†



Ann Allergy Asthma Immunol. 2006;97:98–104.

TERAPIA E PREVENZIONE DELL'ASMA DA SFORZO

2. Terapia di fondo

- Steroidi inalatori
- Montelukast

Bambini con broncostruzione indotta da esercizio fisico

- La broncostruzione indotta dall'esercizio fisico è espressione di asma non adeguatamente controllato.
- Bambini con broncostruzione indotta dall'esercizio fisico dovrebbero essere trattati come pazienti con **asma persistente**.

Inhaled corticosteroids compared to placebo for prevention of exercise induced bronchoconstriction

Koh, *Cochrane Database of Systematic Reviews* 2007

four trials involving children

Inhaled corticosteroids used for 4 weeks or more before exercise testing significantly attenuated exercise-induced bronchoconstriction

Treatment of airway inflammation improves exercise pulmonary gas exchange and performance in asthmatic subjects

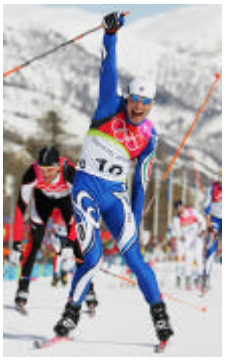
Hans C. Haverkamp, PhD,[a,b] Jerome A. Dempsey, PhD,[b] David F. Pegelow, MS,[b] Jordan D. Miller, PhD,[b,c] Lee M. Romer, PhD,[b,d] Marcus Santana, MD,[b] and Marlowe W. Eldridge, MD[b,e] *Burlington, Vt, Madison, Wis, Iowa City, Iowa, and Middlesex, United Kingdom*

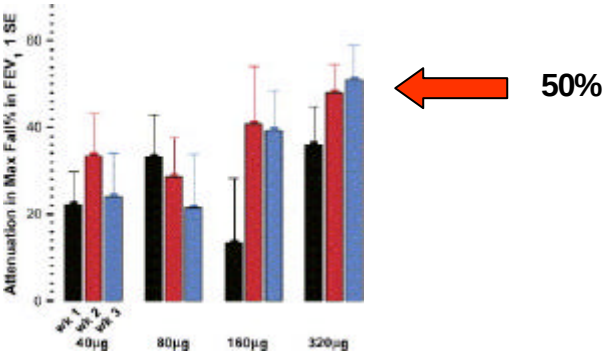
In asthmatic patients ICSs not only attenuate exercise-induced bronchospasm but also improve arterial blood oxygenation during exercise

JACI 2007

Effect of ciclesonide dose and duration of therapy on exercise-induced bronchoconstriction in patients with asthma

Padmaja Subbarao, MD, MSc,[a,b] Mylinh Duong, MD,[b] Ellinor Adelroth, MD, PhD,[c] Joceline Otis,[b] George Obminski, BSc,[b] Mark Inman, MD, PhD,[b] Soren Pedersen, MD, PhD,[d] and Paul M. O'Byrne, MB[b] *Toronto and Hamilton, Ontario, Canada, Umea, Sweden, and Kolding, Denmark*

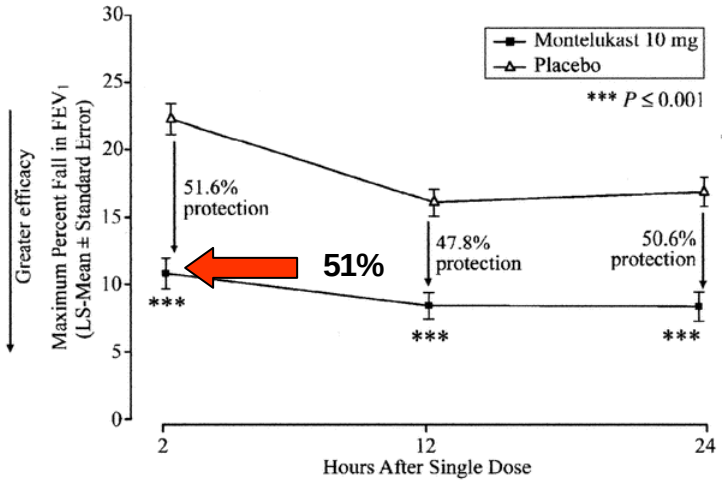




J ALLERGY CLIN IMMUNOL MAY 2006

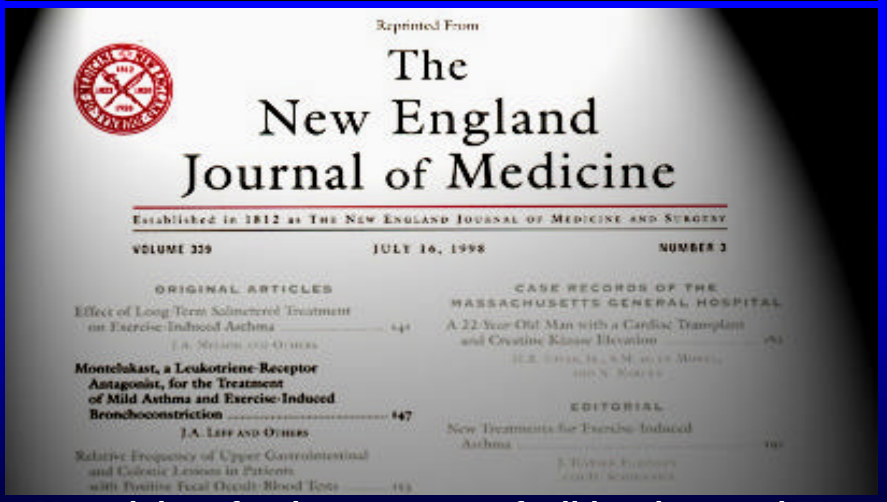
Onset and duration of protection against exercise-induced bronchoconstriction by a single oral dose of montelukast

David S. Pearlman, MD*; Janet van Adelsberg, MD†; George Philip, MD†; Stephen A. Tilles, MD‡; William Busse, MD§; Leslie Hendeles, PharmD‖; Thomas Loeys, PhD†; S. Balachandra Dass, PhD†; and Theodore F. Reiss, MD†



Ann Allergy Asthma Immunol. 2006;97:98–104.

New Treatments for Exercise-induced Asthma : MONTELUKAST



Montelukast for the treatment of mild asthma and EIB

Leff, NEJM 1998

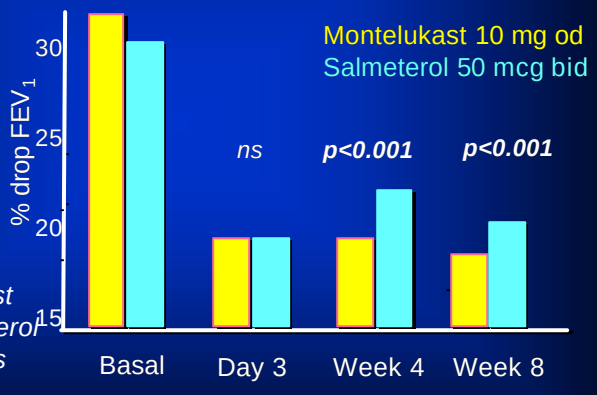
- **Montelukast for the treatment of mild asthma and EIB**
  Leff, NEJM 1998
- **Montelukast inhibits EIB in 6-to 14-year-old children with asthma**
  Kemp, J Pediatr 1998
- **Montelukast versus salmeterol in patients with asthma and EIB**
  Villaran, JACI 1999
- **Comparison of montelukast versus budesonide in the treatment of EIA**
  Vidal, AAAI 2001
- **Montelukast compared with salmeterol to prevent EIB**
  Edelman,Ann Intern Med 2000
- **Comparative effects of LABA and INI-LT on EIB**
  Coreno, JACI 2000

Montelukast *vs* salmeterol in patients with asthma and exercise-induced bronchoconstriction

Villaran, J Allergy Clin Immunol 1999;104:547

- 197 patients, 15-45 yrs
- Mild asthma
- MNT or SLM for 8 wks
- Exercise challenge at definite times 20-24 h after dosing

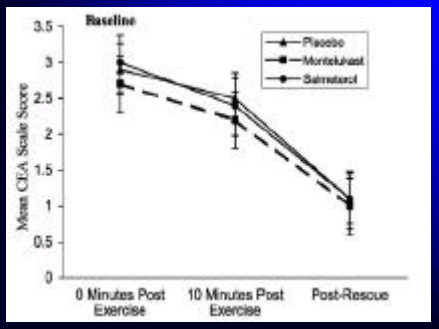
The effect of montelukast was greater than salmeterol over a period of 8 weeks

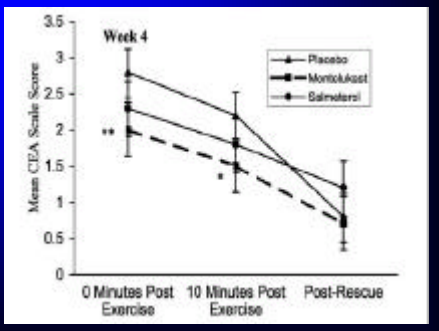


A comparison of the effects of oral montelukast and inhaled salmeterol on response to rescue bronchodilation after challenge

Respiratory Medicine (2004) 98, 1051–1062

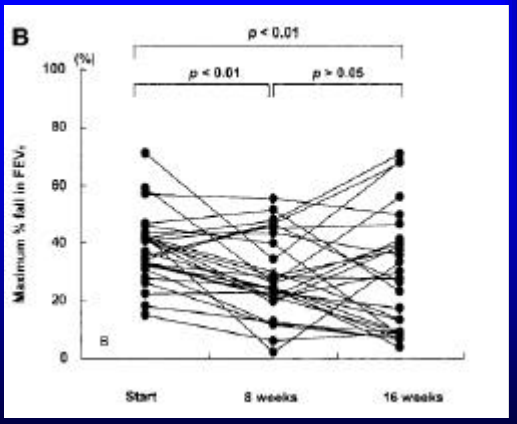
William Storms[a], Paul Chervinsky[b], Asma F. Ghannam[c], Steven Bird[c], Carolyn M. Hustad[c], Jonathan M. Edelman[c,*], for the Challenge–Rescue Study Group[†]





Prolonged Effect of Montelukast in Asthmatic Children With EIB, Pediatr Pulmonol, 2005

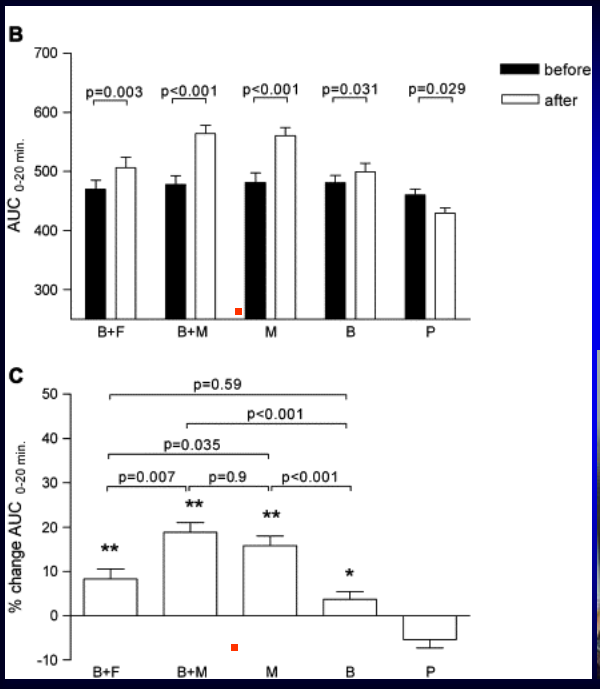
- Studio in doppio cieco (n=64) Montelukast contro placebo per 8 settimane, seguito da crossover di parte del gruppo trattato (28/40) per ulteriori 8 settimane



Prolonged Effect of Montelukast in Asthmatic Children With EIB

Kim Pediatr Pulmonol, 2005

- Miglioramento significativo per tutti i parametri considerati
  - Massima caduta di FEV1
  - Score sintomatologico
  - Tempo di recupero
- Nel gruppo crossover, dopo 8 settimane di washout, tutti i parametri rimanevano persistentemente e significativamente migliorati rispetto ai valori basali



Effect of different antiasthmatic treatments on exercise-induced bronchoconstriction in children with asthma

Stelmach, JACI in Press

Montelukast administered in the morning or evening to prevent exercise-induced bronchoconstriction in children

Montelukast, taken for 2 weeks, is equally effective in exercise-induced bronchoconstriction when dosing either in the morning or in the evening

Pajaron-Fernandez, Pediatr Pulmonol 2006

A recent study reported that montelukast provided greater protection against bronchoconstriction after exercise during high PM1 than low PM1 exposure (approximately 90% vs. approximately 35%)

Rundell KW, Spiering BA, Baumann JM, Evans TM. Bronchoconstriction provoked by exercise in a high-particulate-matter environment is attenuated by montelukast. *Inhal Toxicol* 2005;17:99–105.

Montelukast does not affect exercise performance at subfreezing temperature in highly trained non-asthmatic endurance athletes

Sue-Chu Int. J. Sports. Med. 2000; 21: 424

Compared to placebo, montelukast did not increase physiologic performance variables, or increase the mean running time to exhaustion

these findings do not suggest the need for disallowing the use of this drug by asthmatic athletes.

Concentrazioni urinarie al di sopra delle quali un laboratorio accreditato dal CIO deve dichiarare i risultati

• Salbutamolo	>	1000 ng/ml
• Efedrina	>	10 ng/ml
• Metilefedrina	>	10 ng/ml
• Catina	>	5 ng/ml
• Pseudoefedrina	>	25 ng/ml
• Fenilpropanolamina	>	25 ng/ml

- ***Dal 2004 pseudoefedrina e fenilpropalanina non sono proibite ma incluse nel programma di monitoraggio WADA**

Corticosteroidi
Norme WADA - CIO

Assolutamente vietati
per via sistemica

Ammessi solamente per via inalatoria per la terapia dell'asma bronchiale e delle allergopatie

CONTROINDICAZIONI

- Uso di respiratori subacquei
- Attività fisica in alta quota
- Sport motoristici
- Asma grave persistente

What About More Information?

- **macottini@alice.it**