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# XXVIII CONGRESSO NAZIONALE SIMRI

*Il respiro: scienza e terapia per la salute del bambino*

Programma



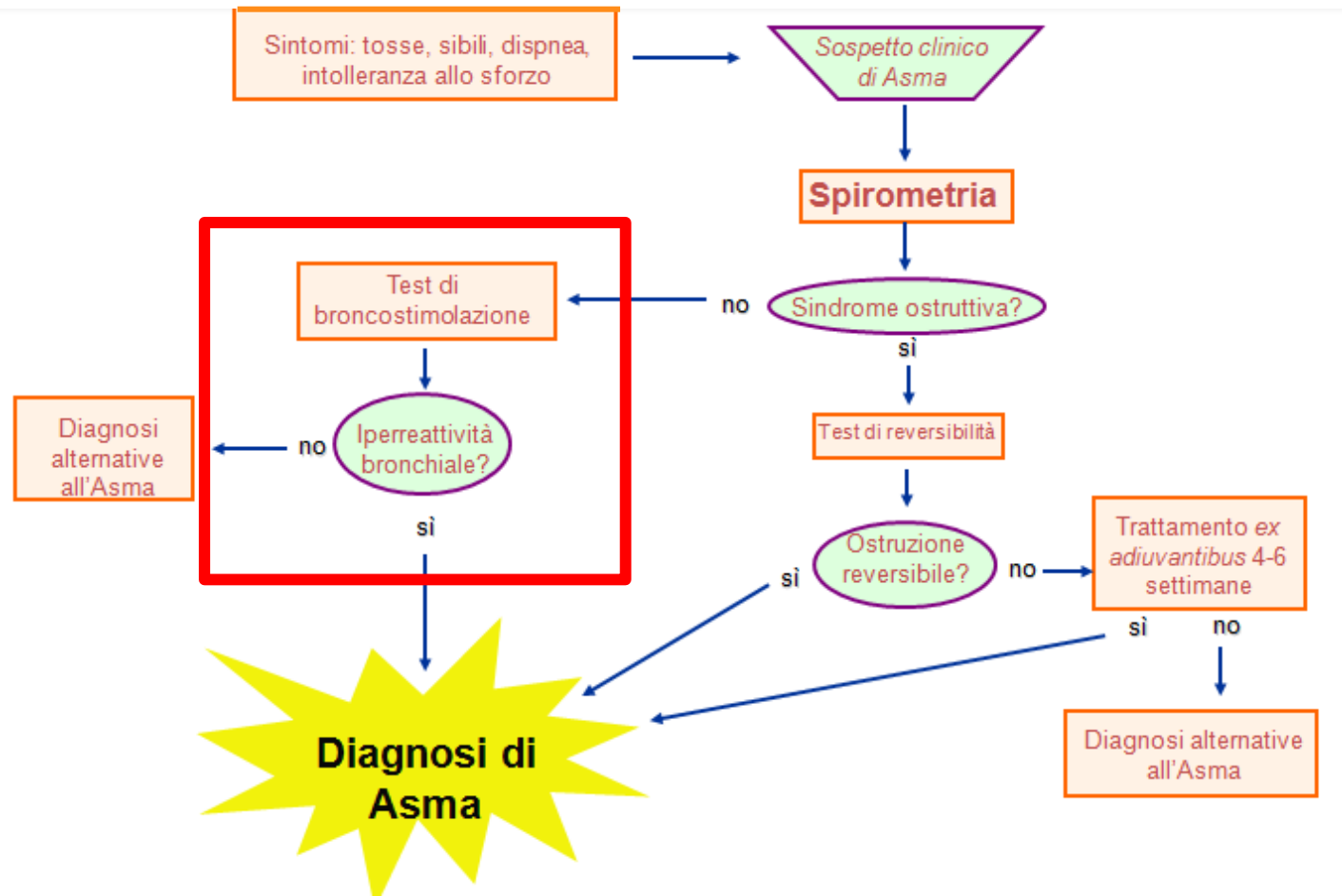
## Test di provocazione bronchiale: a che punto siamo?

*Dott. Michele Ghezzi*

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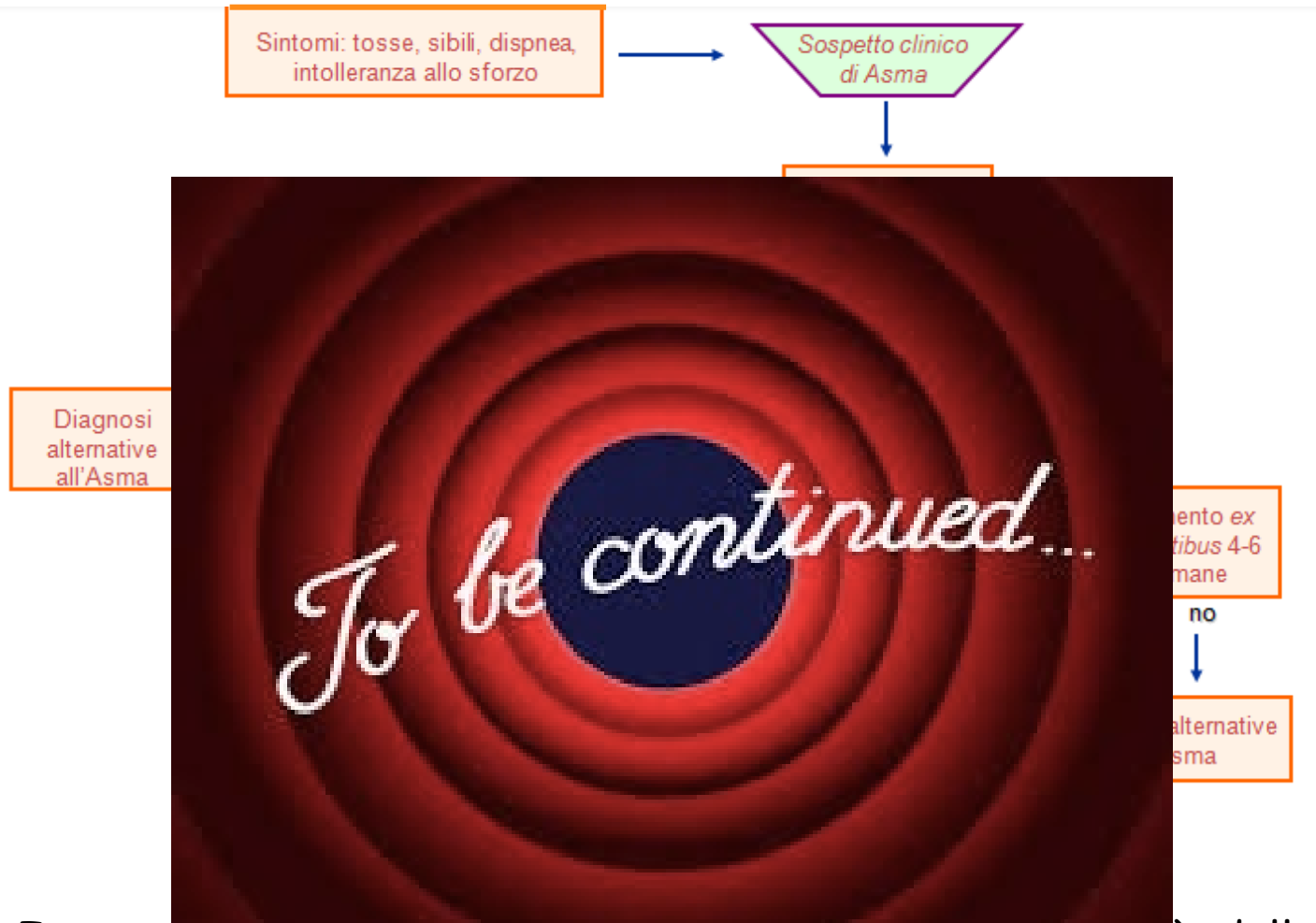


# Test di provocazione bronchiale: a che punto siamo?



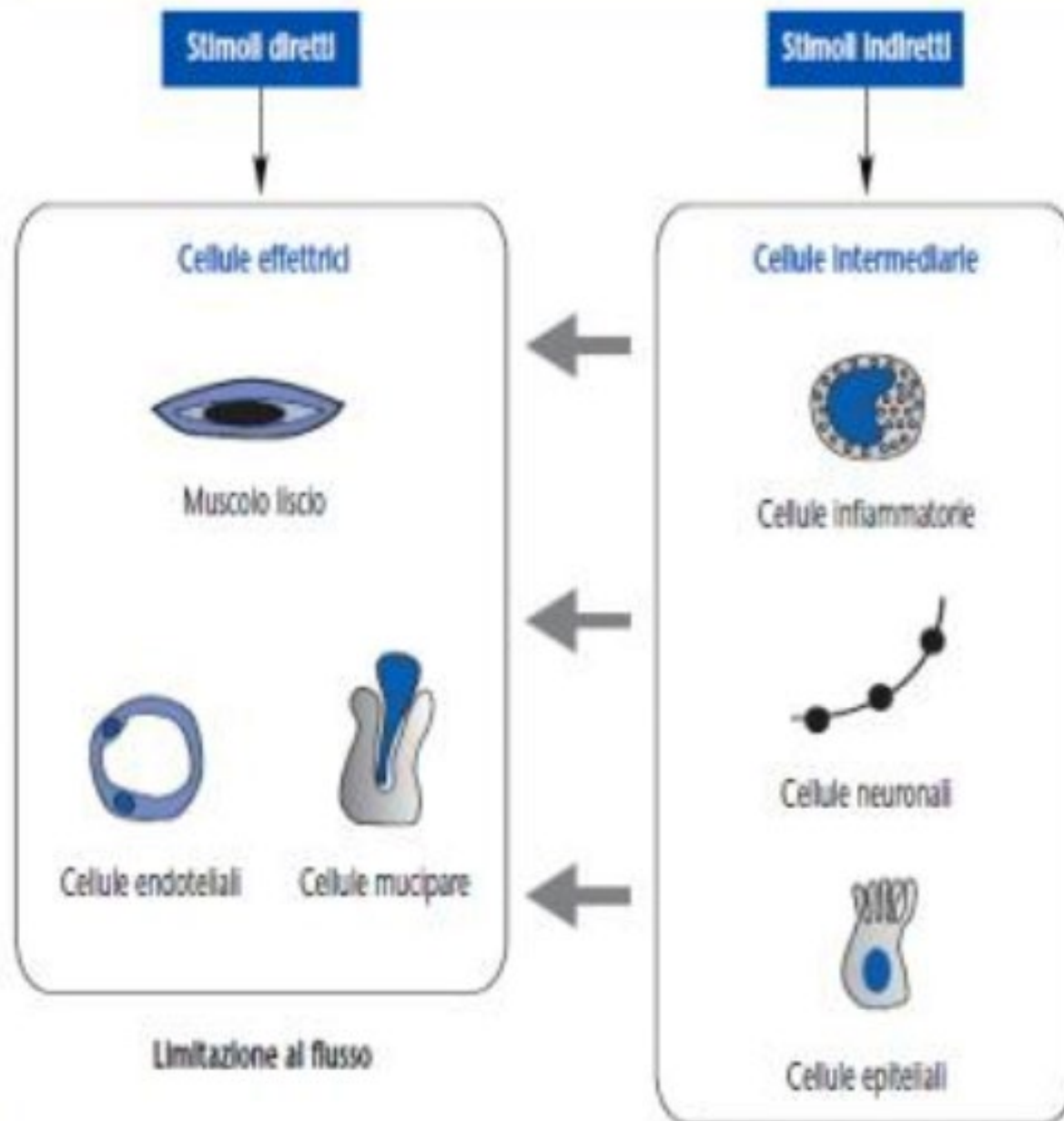
➤ I test di broncostimolazione esprimono la sensibilità delle vie aeree a fattori in grado di scatenare sintomi e broncocostrizione. Sono utili nella diagnosi di asma in pazienti sintomatici, ma con normale spirometria.

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# Test di provocazione bronchiale: a che punto siamo?



# Test di provocazione bronchiale: a che punto siamo?



## DIRETTI

- Test alla Metacolina



## INDIRETTI

- **Single Strong Stimulus Test**
  - Test da Sforzo
  - Test di iperpnea eucapnica
  - Test con aria fredda
- **Incremental Challenge Test**
  - Aerosol con soluzione ipertonica
  - Test al Mannitolo
  - Test all'Adenosina

# Test di provocazione bronchiale: a che punto siamo?

	Challenge diretti	Challenge indiretti
Meccanismo	Effetto diretto sui recettori delle vie aeree	Determinano rilascio di mediatori
Esempi	Istamina, Metacolina	Esercizio fisico, Ipertonica salina, EVI, Mannitolo, cAMP
<i>Dipendenza da:</i> Funz. Muscolo liscio vie aeree Calibro vie aeree Flogosi vie aeree	++++ +++ ++	++ Nessuno o Minimo ++++
Dose massima richiesta	Bassa (1,0 mg)	Alta (Mannitolo: 635 mg – cAMP: 100 mg)
Sensibilità	Alta	Bassa
Specificità	Bassa	Alta
Valore Diagnostico	Esclusione Asma	Conferma Asma

# ERS technical standard on bronchial challenge testing: general considerations and performance of methacholine challenge tests

*Coates, Eur Respir J 2017*

## Indications

- Bronchial challenge, or bronchoprovocation, testing is used to assess **airway hyperresponsiveness (AHR)**, defined as an increased sensitivity and exaggerated response to nonallergenic stimuli that cause airway narrowing.
- While most commonly associated with asthma, AHR is also seen in other diseases associated with airway inflammation or obstruction and is common among athletes, especially in winter sports.
- **Methacholine** mimics the neurotransmitter acetylcholine to directly interact with muscarinic receptors on airway smooth muscle, resulting in contraction and airway narrowing.



# ERS technical standard on bronchial challenge testing: general considerations and performance of methacholine challenge tests

*Coates, Eur Respir J 2017*

## Contraindications

TABLE 1 Contraindications for bronchial challenge testing

### Airflow limitation

FEV<sub>1</sub> <60% predicted (adults or children) or 1.5 L (adults)

FEV<sub>1</sub> <75% predicted (adults or children) for exercise or eucapnic voluntary hyperpnoea challenge

### Spirometry quality

Inability to perform acceptable and repeatable spirometry manoeuvres throughout the test procedure

### Cardiovascular problems

Myocardial infarction or stroke in last 3 months

Uncontrolled hypertension

Known aortic aneurysm

Recent eye surgery or intracranial pressure elevation risk

### General

Inability to perform any of the testing manoeuvres, such as inhaling the challenge agent consistently or difficulty with exercise on treadmill or bike; most commonly in young children or elderly patients

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FEV<sub>1</sub>: forced expiratory volume in 1 s.

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# ERS technical standard on bronchial challenge testing: general considerations and performance of methacholine challenge tests

*Coates, Eur Respir J 2017*

## Preparation

- Avoid prior to the test **alcohol (4 h)** and **smoking (1 h)** before the test



# ERS technical standard on bronchial challenge testing: general considerations and performance of methacholine challenge tests

Coates, *Eur Respir J* 2017

## Preparation

### ➤ Stop medication

TABLE 3 Medications which may decrease airway hyperresponsiveness and withholding time

Medication	Minimum time interval from last dose to MCT h	Reference(s)
Short-acting $\beta$ -agonists in conventional inhaled doses (e.g. albuterol 200 $\mu$ g)	6	[21, 22]
Long-acting $\beta$ -agonists (e.g. salmeterol)	36	[23, 24]
Ultra-long-acting $\beta$ -agonists (e.g. indacaterol, vilanterol, olodaterol)	48	[25]
Ipratropium (Atrovent 40 $\mu$ g)	12	[26–28]
Long-acting anti-muscarinic agents	$\geq 168$	[29, 30]
Oral theophylline	12–24	[3]

MCT: methacholine challenge test.



# ERS technical standard on bronchial challenge testing: general considerations and performance of methacholine challenge tests

*Coates, Eur Respir J 2017*

## Preparation

- Explain the test
- Obtain informed consent

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### SAMPLE METHACHOLINE CHALLENGE TEST CONSENT FORM

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**PROCEDURE.** The purpose of a methacholine challenge test is to determine the amount of airway irritability of a patient. You (or your child) will be asked to inhale a mist that contains different concentrations of methacholine. The mist is produced by a device called a nebulizer and inhaled through a mouthpiece or facemask. Before the test begins, and after each period of inhalation, you or your child will be asked to blow forcefully into a spirometer. The test usually takes about an hour.

**DISCOMFORTS AND RISKS.** This test does not cause an asthma attack but the inhalation of aerosols may be associated with mild shortness of breath, cough, chest tightness, wheezing, chest soreness, or headache. Many subjects do not have any symptoms at all. These symptoms (if they occur) are mild, last for only a few minutes, and disappear following the inhalation of a bronchodilator medication. There is a very small possibility of severe narrowing of your airways. This could cause severe shortness of breath. If this occurs, you will be immediately treated.

I have read the above information and understand the purpose of the test and the associated risks. With this knowledge I agree to having this test performed on me or my child.

\_\_\_\_\_  
Patient or Guardian

\_\_\_\_\_  
Date

\_\_\_\_\_  
Witness

\_\_\_\_\_  
Date

---



# ERS technical standard on bronchial challenge testing: general considerations and performance of methacholine challenge tests

*Coates, Eur Respir J 2017*

## Preparation

- Explain the test
- Obtain informed consent
- Urinate before the test



# ERS technical standard on bronchial challenge testing: general considerations and performance of methacholine challenge tests

*Coates, Eur Respir J 2017*

## Delivery methods and dosing regimens

- Current technology has made it easier to calculate a delivered dose for any combination of device and inhalation protocol.
- **Methods requiring deep inhalations to TLC during aerosol delivery are no longer recommended** because of the bronchodilating or bronchoprotective effect of a maximal inspiratory manoeuvre with a breathhold at TLC.
- We recommend **tidal breathing with an inhalation period of 1 min (or more)** when using a breath-actuated or continuous nebuliser; when using a dosimeter, a breath count is calculated to deliver appropriate dose steps.



# ERS technical standard on bronchial challenge testing: general considerations and performance of methacholine challenge tests

*Coates, Eur Respir J 2017*

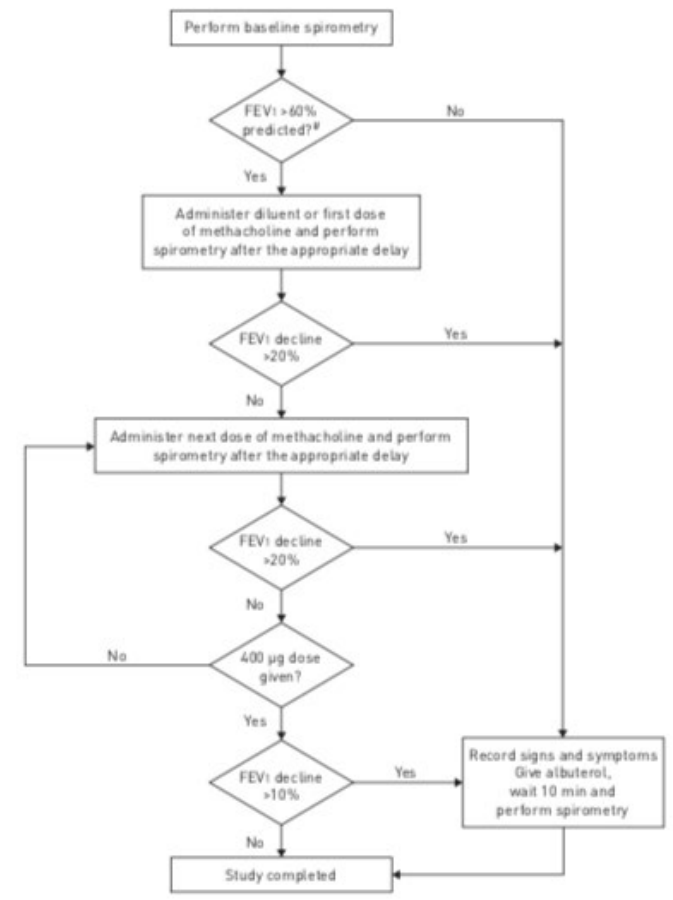
## Delivery methods and dosing regimens

- We recommend the calculation of stepwise delivered doses **starting at 1-3 µg** followed by either doubling or quadrupling steps

Doubling increments		Quadrupling increments	
Concentration mg·mL <sup>-1</sup>	Dose µg	Concentration mg·mL <sup>-1</sup>	Dose µg
0.0625	1.425	0.0625	1.425
0.125	2.969		
0.25	5.938	0.25	5.938
0.5	11.875		
1	23.75	1	23.75
2	47.5		
4	95	4	95
8	190		
16	380	16	380

Shown are the incremental doses at specific concentrations for both doubling and quadrupling increments.

- Standardising the time of the start of delivery with the time of spirometry is absolutely essential for consistency of test results.



# ERS technical standard on bronchial challenge testing: general considerations and performance of methacholine challenge tests

*Coates, Eur Respir J 2017*

- We recommend basing the result upon **the effective delivered dose of methacholine causing a 20% fall in FEV<sub>1</sub> (provocative dose (PD<sub>20</sub>))**. The PD<sub>20</sub> end-point allows comparable results from different devices or protocols.

TABLE 6 Categorisation of airway response to methacholine

PD <sub>20</sub> µmol (µg)	PC <sub>20</sub> mg·mL <sup>-1</sup>	Interpretation
>2 (>400)	>16	Normal
0.5–2.0 (100–400)	4–16	Borderline AHR
0.13–0.5 (25–100)	1–4	Mild AHR
0.03–0.13 (6–25)	0.25–1	Moderate AHR
<0.03 (<6)	<0.25	Marked AHR

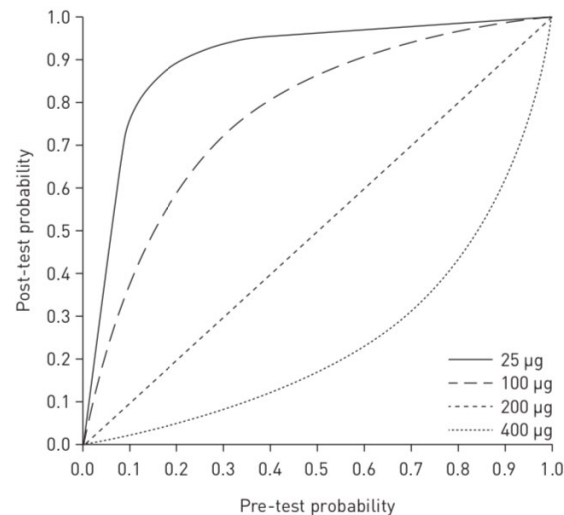
PD<sub>20</sub>: provocative dose causing a 20% fall in forced expiratory volume in 1 s (FEV<sub>1</sub>); PC<sub>20</sub>: provocative concentration causing a 20% fall in FEV<sub>1</sub>; AHR: airway hyperresponsiveness. Information from [3].



# ERS technical standard on bronchial challenge testing: general considerations and performance of methacholine challenge tests

*Coates, Eur Respir J 2017*

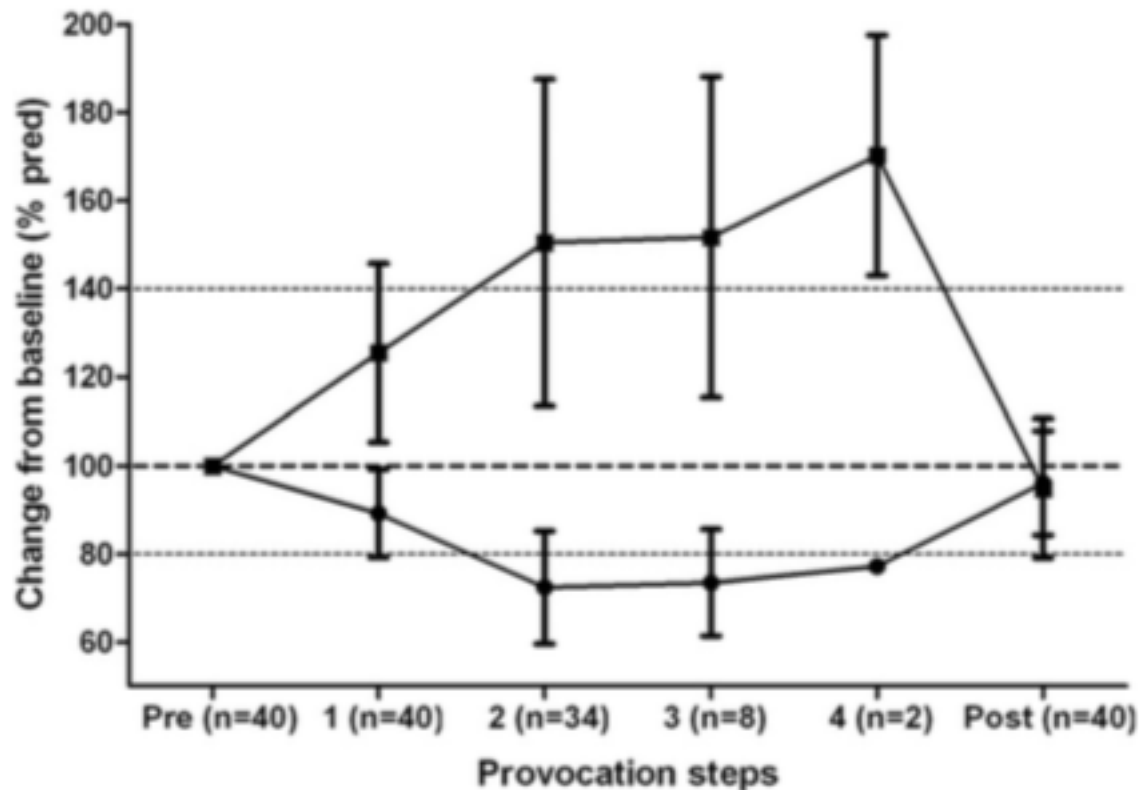
- The optimal diagnostic value of methacholine challenge testing occurs when the pre-test probability of asthma is 30-70%. Current symptoms consistent with asthma increase the pre-test probability of this diagnosis.
- **Methacholine challenge testing is more useful in excluding a diagnosis of asthma**
- Airway responsiveness may have been suppressed if the patient was taking medications
- In patients without current symptoms, the season for aeroallergen exposure may have passed



# Methacholine challenge in young children as evaluated by spirometry and impulse oscillometry

*Schulze, Resp Med 2012*

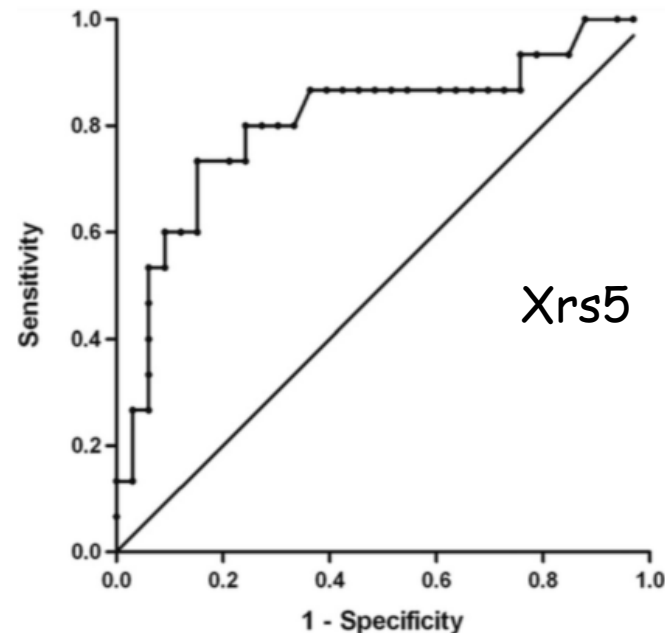
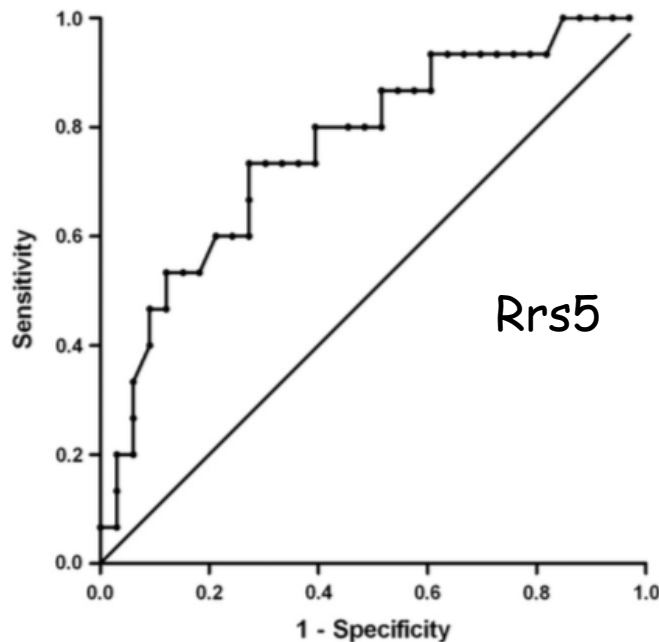
- 48 children : 29 male and 19 female, mean age 5.3 years
- The mean maximal reduction in FEV1 was 29.8% ( $p < 0.0001$ )
- The mean increase in Rsr5 was 55.3%, and the mean decrease in Xrs5 was  $0.37 \text{ kPa s L}^{-1} \cdot 0.23$  ( $p < 0.001$ )



# Methacholine challenge in young children as evaluated by spirometry and impulse oscillometry

*Schulze, Resp Med 2012*

- To evaluate the sensitivity and specificity of Rrs5 and Xrs5 to detect a 20% drop in FEV1, we calculated the receiver-operator characteristic (ROC) curve (Figs. 2 and 3).
- An Rrs5 increase of 45.2% compared to the base-line showed the optimal combination of sensitivity and specificity. The area under the ROC (AUC) was 0.76 ( $p < 0.005$ ).
- An Xrs5 decrease of 0.69 kPa s L<sup>-1</sup> showed the optimal combination of sensitivity and specificity and the AUC was 0.81 ( $p < 0.001$ ).

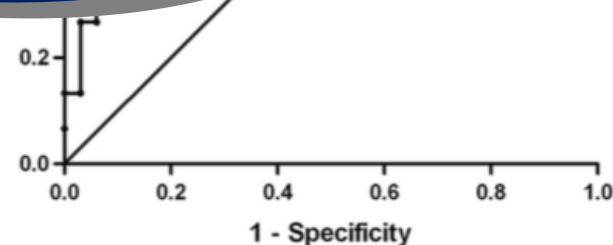
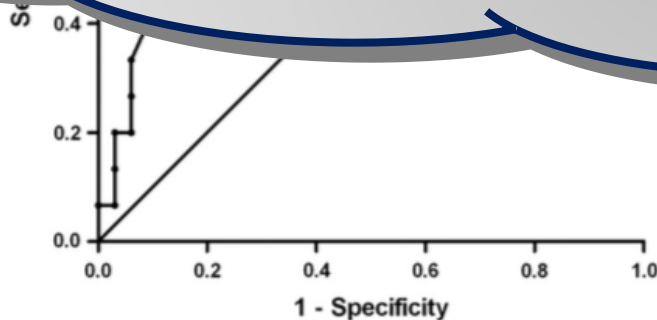


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significant increases in Rrs5 of >40% preceded the reactions in FEV1 at significantly lower doses of methacholine



# Test di provocazione bronchiale: a che punto siamo?

	Challenge diretti	Challenge indiretti
Meccanismo	Effetto diretto sui recettori delle vie aeree	Determinano rilascio di mediatori
Esempi	Istamina, Metacolina	Esercizio fisico, Ipertonica salina, EVI, Mannitolo, cAMP
<i>Dipendenza da:</i> Funz. Muscolo liscio vie aeree Calibro vie aeree Flogosi vie aeree	++++ +++ ++	++ Nessuno o Minimo ++++
Dose massima richiesta	Bassa (1,0 mg)	Alta (Mannitolo: 635 mg – cAMP: 100 mg)
Sensibilità	Alta	Bassa
Specificità	Bassa	Alta
Valore Diagnostico	Esclusione Asma	Conferma Asma

- Diagnosi EIB (con o senza asma)
- Valutazione della risposta alla terapia (EIB/asma)

# Exercise-Induced Bronchoconstriction in Children: State of the Art from Diagnosis to Treatment

*Grandinetti, J. Clin. Med. 2024*

## Definizione

- “**Exercise-Induced Asthma**” (EIA) indicated the narrowing of the airways occurring in **asthmatic patients** during or after physical exercise
- In **1970**, the term “**exercise-induced bronchoconstriction**” (EIB) replaced the term EIA since the narrowing of the airways after or during physical activity could **also occur in non asthmatic patients**
- American Thoracic Society (ATS) Clinical Practice Guideline proposed to differentiate EIB occurring in asthmatic patients (**EIBa—EIB with asthma**) and exercise-induced bronchoconstriction in patients without typical signs or symptoms of asthma (**EIBwa—EIB without asthma**)
- Common symptoms include cough, dyspnea, wheezing, chest tightness, increased mucus production, heightened respiratory effort, diminished performance, increased fatigue, or a sense of reduced fitness in physically fit patients
- EIB typically starts within 15 min after 5 - 8 min of high-intensity aerobic training. Symptoms spontaneously resolve within approximately 60 min.

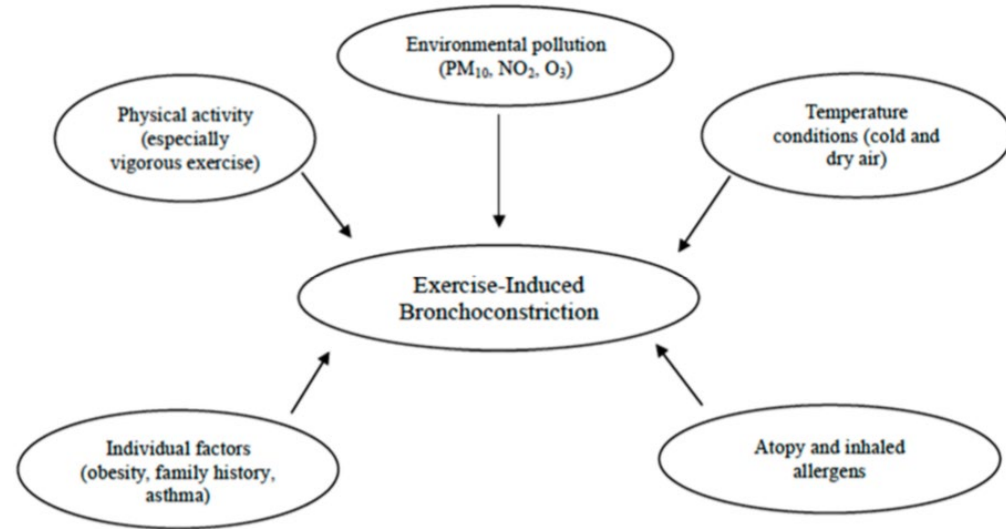


# Exercise-Induced Bronchoconstriction in Children: State of the Art from Diagnosis to Treatment

*Grandinetti, J. Clin. Med. 2024*

## The prevalence of EIB:

- One study found that **46.7% of children with asthma** experience symptoms of EIB, compared with only **7.4% of those without asthma**.
- This increased prevalence is indicative of **disease control**, since it is more present in severe or poorly controlled asthma patients



Higher occurrence in those engaged in endurance activities such as long- distance running, cycling, triathlon, and pentathlon.

EIB among general athletes is 23%, while for Olympic athletes the estimate is 8%

In sports with elevated risk factors, such as swimming and activities exposing athletes to cold air, the prevalence varies widely, ranging from 25% to 75%

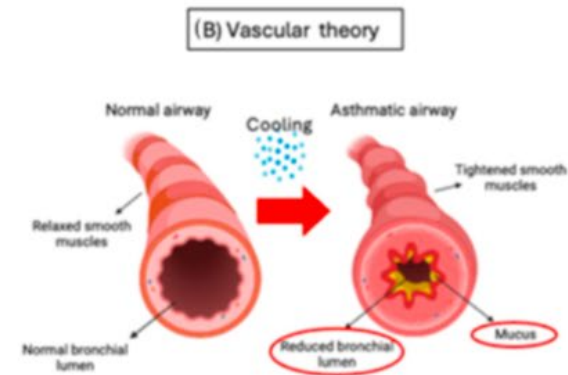
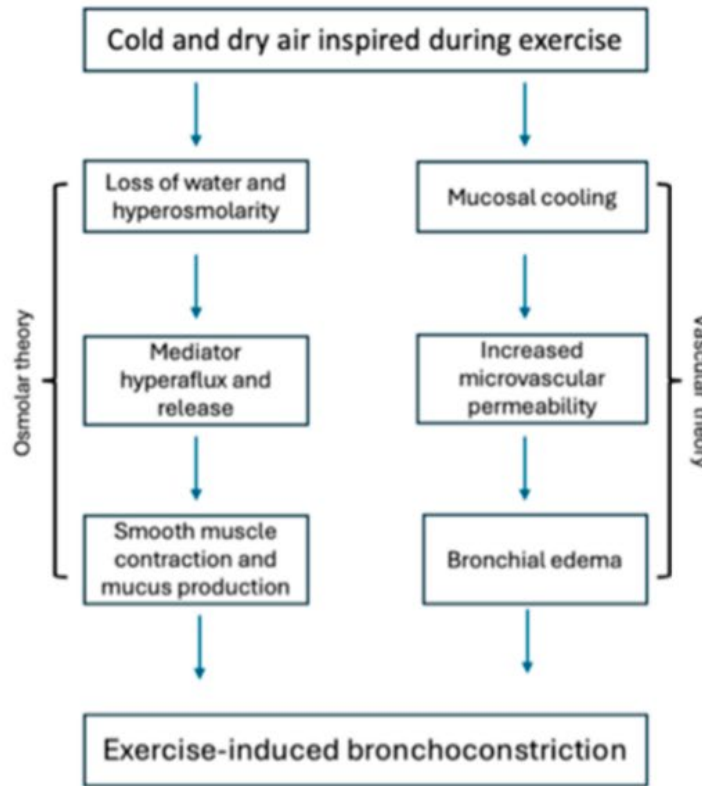
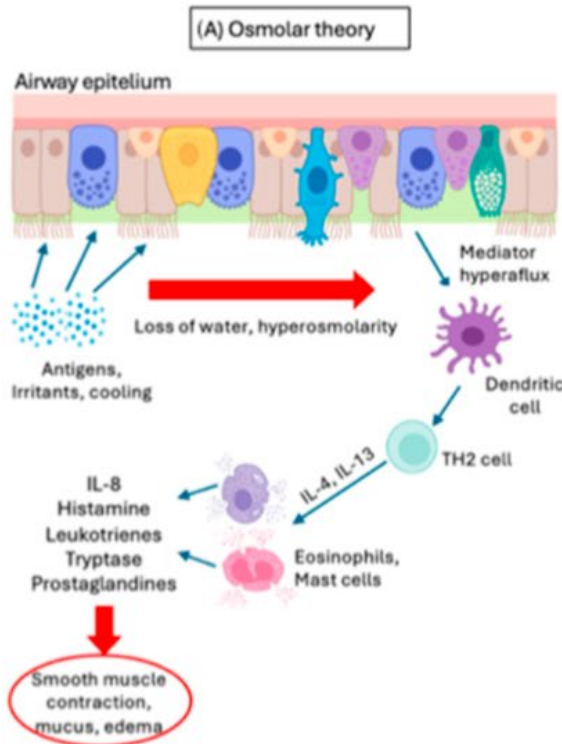
For summer sports, the reported prevalence of EIB is 23%, and in winter sports, this increases up to 55%.



# Exercise-Induced Bronchoconstriction in Children: State of the Art from Diagnosis to Treatment

*Grandinetti, J. Clin. Med. 2024*

## The pathogenesis of EIB:



# ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing

*Hallstrand TS Eur Respir J 2018*

## Exercise challenge test

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### Preliminary Assessments and Environmental Settings

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- Check standard environmental conditions: temperature (20–25 °C), humidity ( $\leq 50\%$ ), air quality (minimal pollutants)
  - Informed consent signed by at least one parent
  - Monitor heart rate and SpO<sub>2</sub>
  - **Nose clip**
- 



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  - **Nose clip**
- 

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### Contraindications

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- Dyspnoea at rest, FEV<sub>1</sub> < 75%
  - SpO<sub>2</sub> < 85% in air
  - Fever
  - Pericarditis, myocarditis, uncontrolled hypertension, uncontrolled heart failure
  - Acute kidney disease, acute hepatitis, uncontrolled diabetes
  - **Recent pneumothorax/pneumomediastinum, recent thoracic surgery**
-

# ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing

Hallstrand TS *Eur Respir J* 2018

TABLE 1 Withholding times prior to indirect challenge testing

	Withholding time	Maximum duration of protection <sup>#</sup>
SABA (albuterol, terbutaline)	8 h	<6 h
LABA (salmeterol, eformoterol)	36 h	12 h
LABA in combination with an ICS (salmeterol/fluticasone, formoterol/budesonide)	36 h	NA
Ultra-LABAs (indacaterol, olodaterol, vilanterol)	48 h	NA
ICS (budesonide, fluticasone propionate, beclomethasone)	6 h	NA
Long-acting ICS (fluticasone furoate, ciclesonide)	24 h	NA
Leukotriene receptor antagonists (montelukast, zafirlukast)	4 days	24 h
Leukotriene synthesis inhibitors (zileuton/slow-release zileuton)	12 h/16 h	4 h
Antihistamines (loratadine, cetirzine, fexofenadine)	72 h	<2 h
Short-acting muscarinic acetylcholine antagonist (ipratropium bromide)	12 h	<0.5 h
Long-acting muscarinic acetylcholine antagonist (tiotropium bromide, aclidinium bromide, glycopyrronium)	72 h	NA
Cromones (sodium cromoglycate, nedocromil sodium)	4 h	2 h
Xanthines (theophylline)	24 h	NA
Caffeine	24 h	NA
Vigorous exercise	4 h	<4 h

Examples of specific medications within the class are provided in parenthesis. The withholding times recommended for short- and long-acting  $\beta_2$ -agonists differs from the recommendation in the original reference, reflecting the recommendations of this task force and the uncertainty in the precise duration of the inhibitory effect of these medications on indirect airway hyperresponsiveness. SABA: short-acting  $\beta_2$ -agonist; LABA: long-acting  $\beta_2$ -agonist; ICS: inhaled corticosteroid; NA: not available. <sup>#</sup>: refers to the potential effects of a single dose and may not apply to chronic dosing. Reproduced and modified from [7] with permission from the publisher.

# ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing

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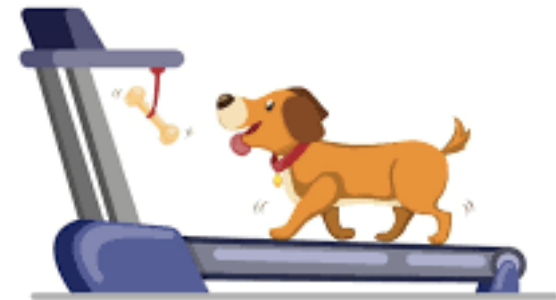
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## Procedure

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- Avoid physical exercise in the previous 6 h
  - Avoid eating for 4 h prior the test
  - Perform basal spirometry (a basal FEV<sub>1</sub> of at least 75% is required)
  - Adjust speed and grade of the treadmill to achieve within 2–3 min: 1) 85% (95% in children and elite athletes) of the maximum heart rate (220—age in years or 208—0.7 × age in years)
  - Maintain this level of intensity for at least 6 min
  - Spirometry after 5, 10, 15 and 30 min (additional measurements depending on patient's clinical history)
- 

- The rapid rise in work rate is needed because a warm-up period or prolonged lower-level exercise may decrease the severity of EIB
- it is preferable to achieve a ventilation target
- An acceptable alternative is a **target heart rate of >85% of the predicted maximum** (calculated as 220 - age in years)



# ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing

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## Treadmill Protocol



### *Treadmill protocol*

On the treadmill, speed and grade are progressively advanced during the first 2–3 min of exercise until the target level is obtained. The degree of physical fitness and body weight will strongly influence the grade and speed necessary to obtain the desired ventilation or heart rate. A reasonable procedure is to quickly advance to a rapid, but comfortable speed at a treadmill incline of 5.5% (3°) then, raise the slope until the desired heart rate or ventilation is obtained, up to an incline of 10%. Nomograms have been proposed to predict speed and grade that will elicit the desired heart rate, but they have not been validated extensively [60]. Another approach is to use a nomogram relating oxygen consumption per kilogram to speed and slope of the treadmill; however, the relationship between oxygen consumption and the percentage of maximum ventilation is variable [60]. The test ends when the patient has exercised at the target ventilation or heart rate for 6 min. The treadmill challenge protocol has a high degree of repeatability [87–89].

## Bicycle ergometer protocol



### *Bicycle ergometer protocol*

For cycle ergometer exercise, work rate is rapidly increased using the electromagnetic braking system to achieve the target ventilation. Direct measurement of ventilation is easier with the stable position on an ergometer and is the preferred target. The target heart rate or ventilation should be reached within 2–3 min. A valid test requires the target exercise intensity to be sustained for 6 min, although sustained exercise of  $\geq 4$  min may be acceptable if the subject becomes fatigued. Although the repeatability of the bicycle protocol has not received extensive study, the repeatability in a limited number of individuals was excellent [60, 90].

# ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing

*Hallstrand TS Eur Respir J 2018*

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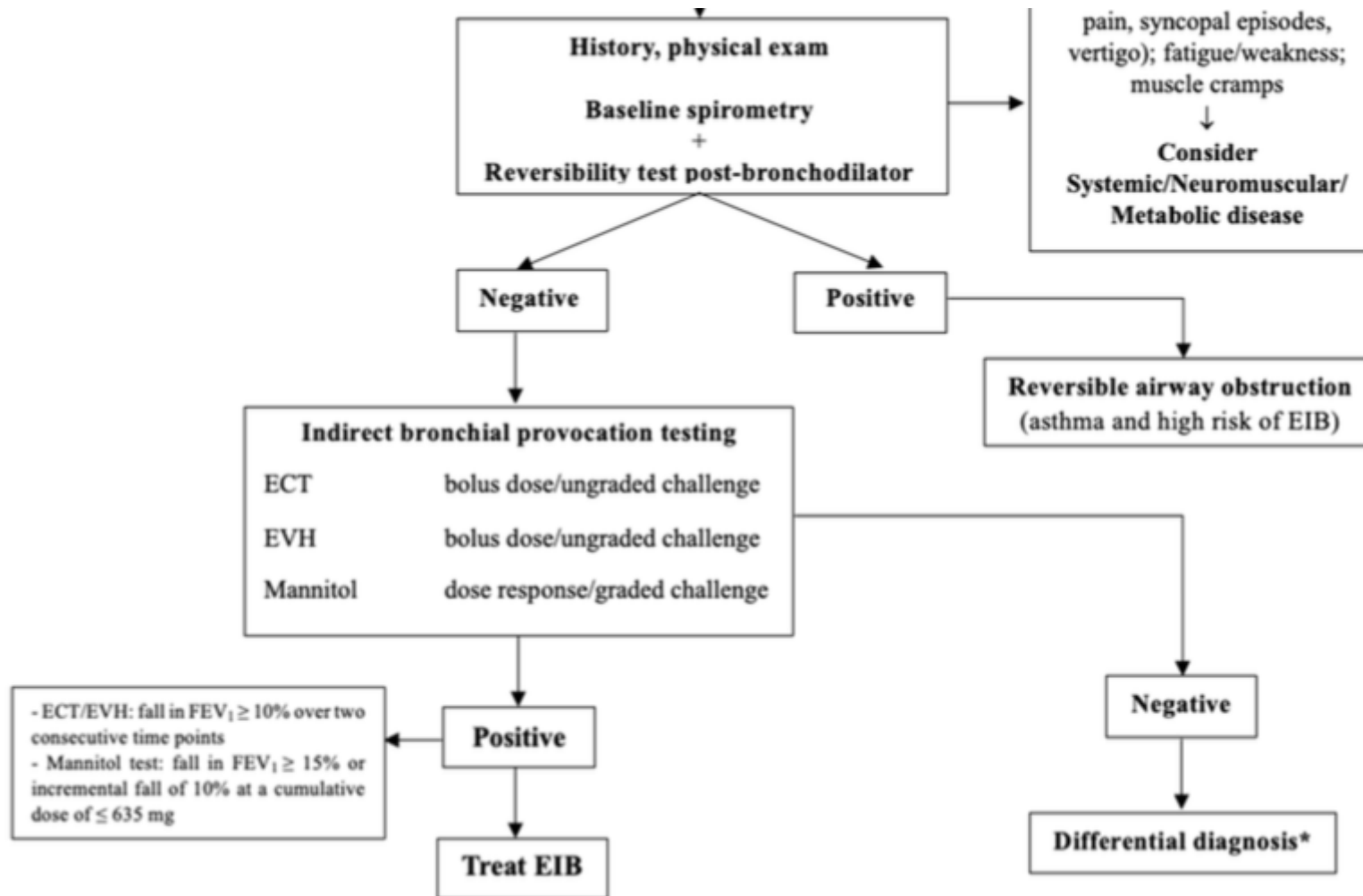
## Diagnosis

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- Mild EIB: FEV<sub>1</sub> decrease  $\geq 10\%$  but  $< 25\%$
  - Moderate EIB: FEV<sub>1</sub> decrease  $> 25\%$  but  $< 50\%$
  - Severe EIB: FEV<sub>1</sub> decrease  $\geq 50\%$  (for steroid-naïve patients decrease in FEV<sub>1</sub>  $\geq 50\%$ ); for steroid-treated patients decrease in FEV<sub>1</sub>  $\geq 30\%$ )
-

# Exercise-Induced Bronchoconstriction in Children: State of the Art from Diagnosis to Treatment

*Grandinetti, J. Clin. Med. 2024*



# Exercise-Induced Bronchoconstriction in Children: State of the Art from Diagnosis to Treatment

*Grandinetti, J. Clin. Med. 2024*

## Differential Diagnosis:

Causes	Alternative Diagn
<i>Respiratory</i>	<ul style="list-style-type: none"><li>- Asthma without EIB</li><li>- EILO, dysfunctional breathing disorders</li><li>- Vascular malformations (vascular rings, pulmo</li><li>- Tracheobronchomalacia</li><li>- Infectious diseases</li><li>- Foreign body inhalation</li><li>- Tumors</li><li>- Interstitial diseases</li></ul>
<i>Cardiac</i>	<ul style="list-style-type: none"><li>- Arrhythmias (EIVT, SVT)</li><li>- Pericarditis/Myocarditis</li><li>- Shunting, vascular malformations</li><li>- Cardiomyopathies</li><li>- Pulmonary hypertension</li><li>- Valvular abnormalities</li></ul>



# Exercise-Induced Bronchoconstriction in Children: State of the Art from Diagnosis to Treatment

*Grandinetti, J. Clin. Med. 2024*

## Differential Diagnosis:

*Metabolic/  
Neuromuscular*

- Mitochondrial disorders, mitochondrial enzym
- Storage diseases (glycogenosis, sphingolipidos
- Motor neuron diseases
- Myopathies
- Myasthenia gravis spectrum disorder

*Psychological*

- Anxiety, hyperventilation syndrome

*Others*

- Physiologic limitation
- Physical deconditioning
- Obesity
- Exercise-associated gastroesophageal reflux
- Anemia
- Severe pectus



# Exercise-Induced Bronchoconstriction Identified Using the Forced Oscillation Technique

Seccombe LM, *Front. Physiol.* 10:1411

**TABLE 1** | Subject baseline characteristics.

Category	Asthma	Healthy normal
Male:female	8:11	5:5
Age (years)	28 ± 6	31 ± 5
Height (cm)	169 ± 11	170 ± 9
BMI (kg/cm <sup>2</sup> )	23.8 ± 3.1	24.0 ± 2.9
FEV <sub>1</sub> (L)	3.46 ± 0.75	3.51 ± 0.65
FEV <sub>1</sub> (%predicted)	93 ± 11	99 ± 13
FEV <sub>1</sub> /FVC ratio	0.77 ± 0.07*	0.85 ± 0.04
R <sub>5</sub> (cm H <sub>2</sub> O s L <sup>-1</sup> )	3.49 ± 1.21	2.90 ± 1.02
X <sub>5</sub> (cm H <sub>2</sub> O s L <sup>-1</sup> )	-1.20 ± 0.50	-1.00 ± 0.35



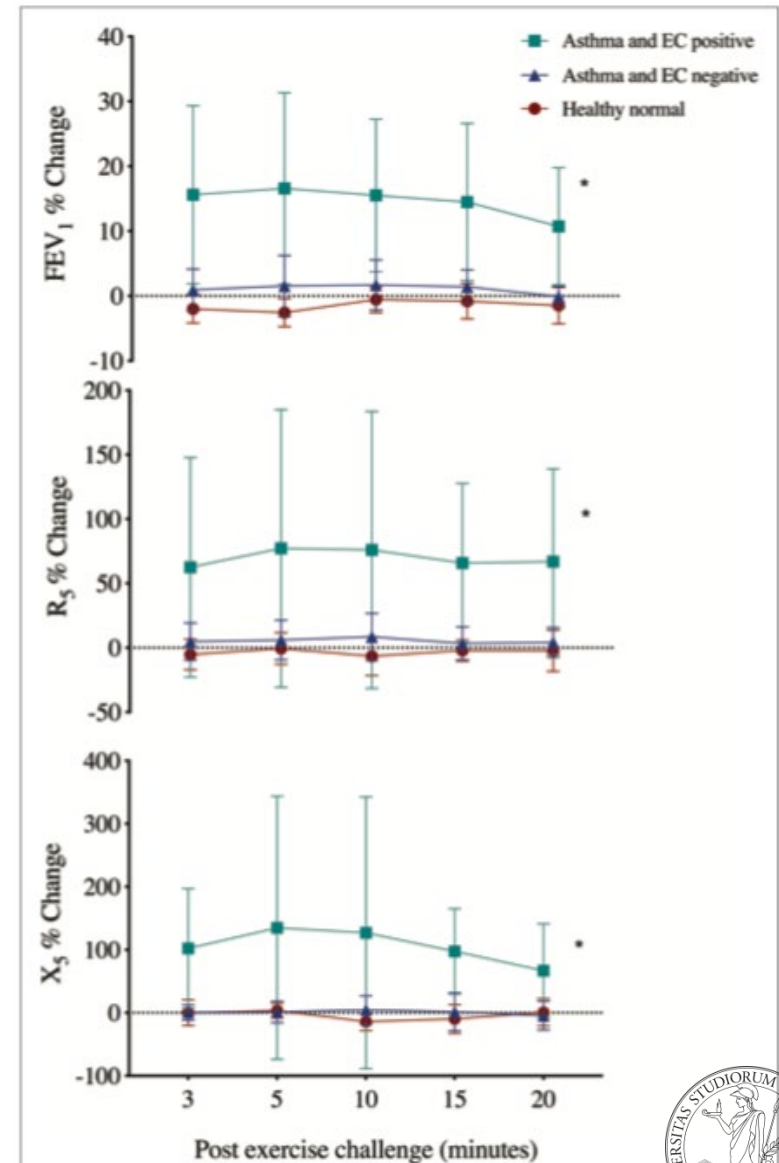
- Airway resistance (R<sub>5</sub>) and reactance (X<sub>5</sub>) at 5 Hz and VE were measured prior to forced expiratory volume in 1 s (FEV<sub>1</sub>) before and up to 20 min after a standard **Exercise Challenge** in people with asthma and healthy controls.
- Subjects with current asthma (n = 19, mean ± SD age 28 ± 6 years) and controls (n = 10, 31 ± 5 years) were studied



# Exercise-Induced Bronchoconstriction Identified Using the Forced Oscillation Technique

Seccombe LM, *Front. Physiol.* 10:1411

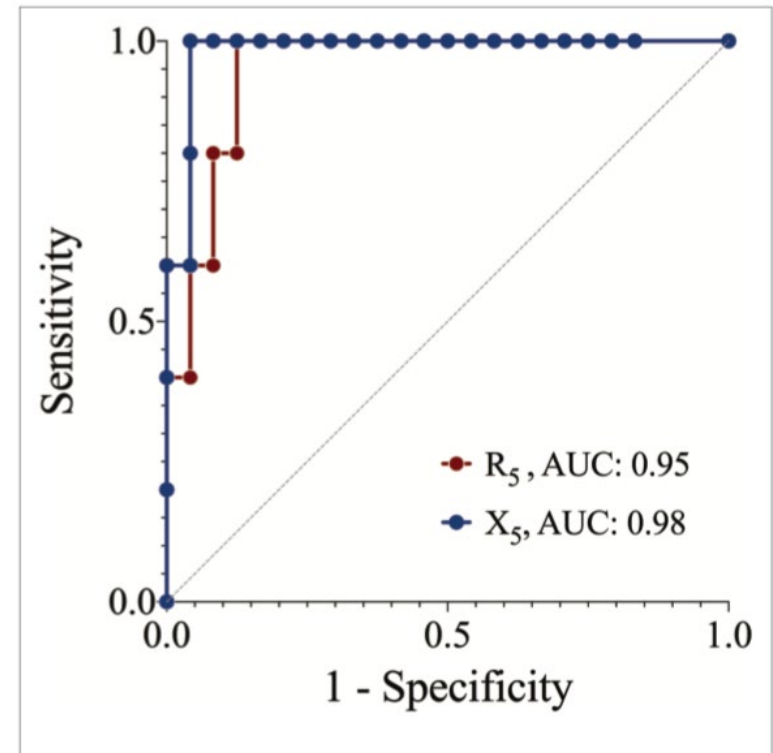
- Five of the 19 subjects with asthma were EC positive (fall in FEV1 >10%).
- The R5 and X5 responses following EC were different in this group as compared to EC-negative asthma and healthy normal subjects
- The % recovery to baseline from maximum change at 20 min post EC was greater for X5 (p = 0.03) but similar between R5 and FEV1.
- Following EC, max % change FEV1 correlated with R5 (r = 0.92, p = 0.001) and X5 (r = 0.91, p = 0.001) across all subjects.



# Exercise-Induced Bronchoconstriction Identified Using the Forced Oscillation Technique

*Seccombe LM, Front. Physiol. 10:1411*

- R5 had a sensitivity and specificity of 80 and 86%, X5 had a sensitivity and specificity of 80 and 93%, respectively.
- A cut-off of 27% increase in R5 and 47% decrease in X5 yielded optimal sensitivity and specificity for a positive response as detected using FEV1.



The sensitivity and specificity of R5 and X5 to detect a positive response to the EC as determined by FEV1



# Indications and outcomes of exercise challenge tests performed in children before and during COVID-19 pandemic

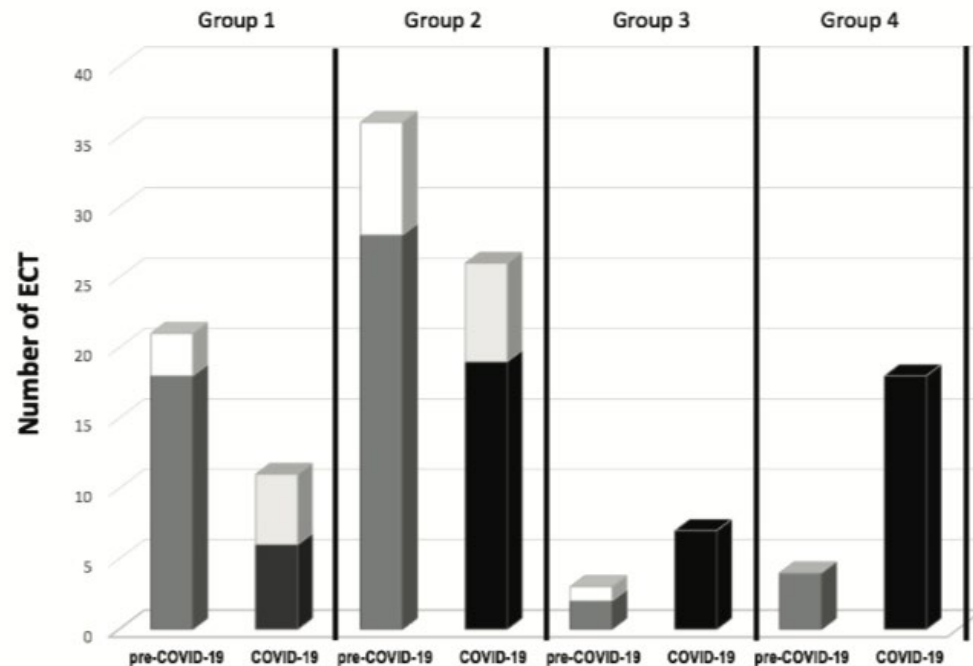
*De Bernardo, PRJ 2024*

Gr1. asthmatic patients who reported exercise-induced respiratory symptoms

Gr2. patients with no previous diagnosis of asthma who reported respiratory symptoms only with exercise

Gr3. patients with no previous diagnosis of asthma who reported both exercise-related and at rest respiratory symptoms;

Gr4. patients with no previous diagnosis of asthma who reported exercise-related subjective respiratory symptoms



# Indications and outcomes of exercise challenge tests performed in children before and during COVID-19 pandemic

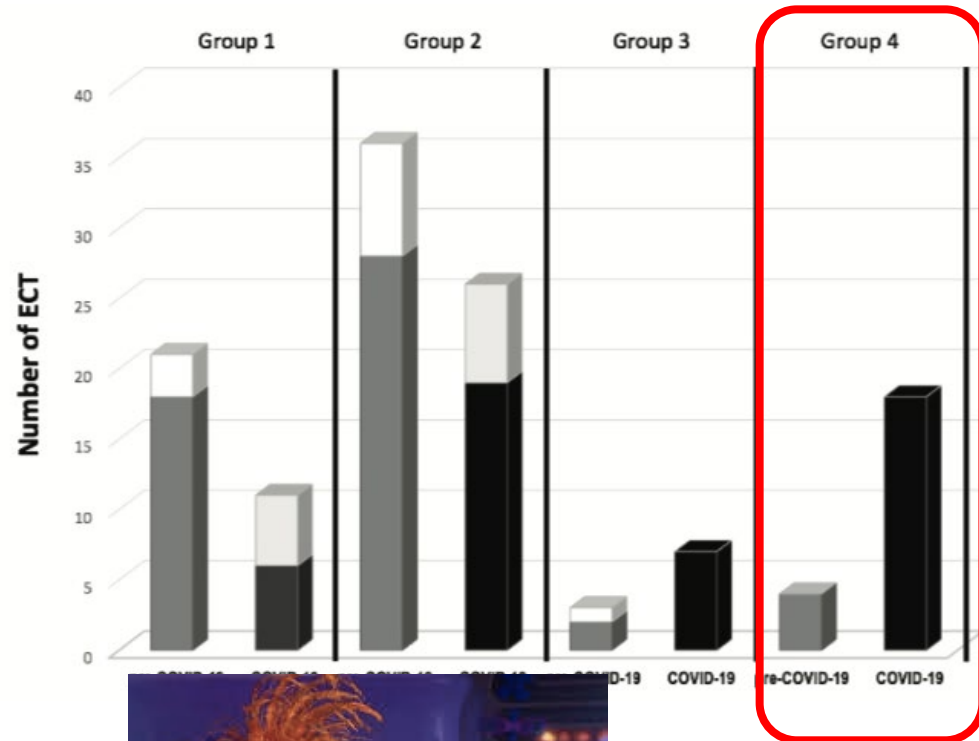
*De Bernardo, PRJ 2024*

Gr1. asthmatic patients who reported exercise-induced respiratory symptoms

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Gr3. patients with no previous diagnosis of asthma who reported both exercise-related and at rest respiratory symptoms;

Gr4. patients with no previous diagnosis of asthma who reported exercise-related subjective respiratory symptoms



# Test di provocazione bronchiale: a che punto siamo?



## DIRETTI

- Test alla Metacolina

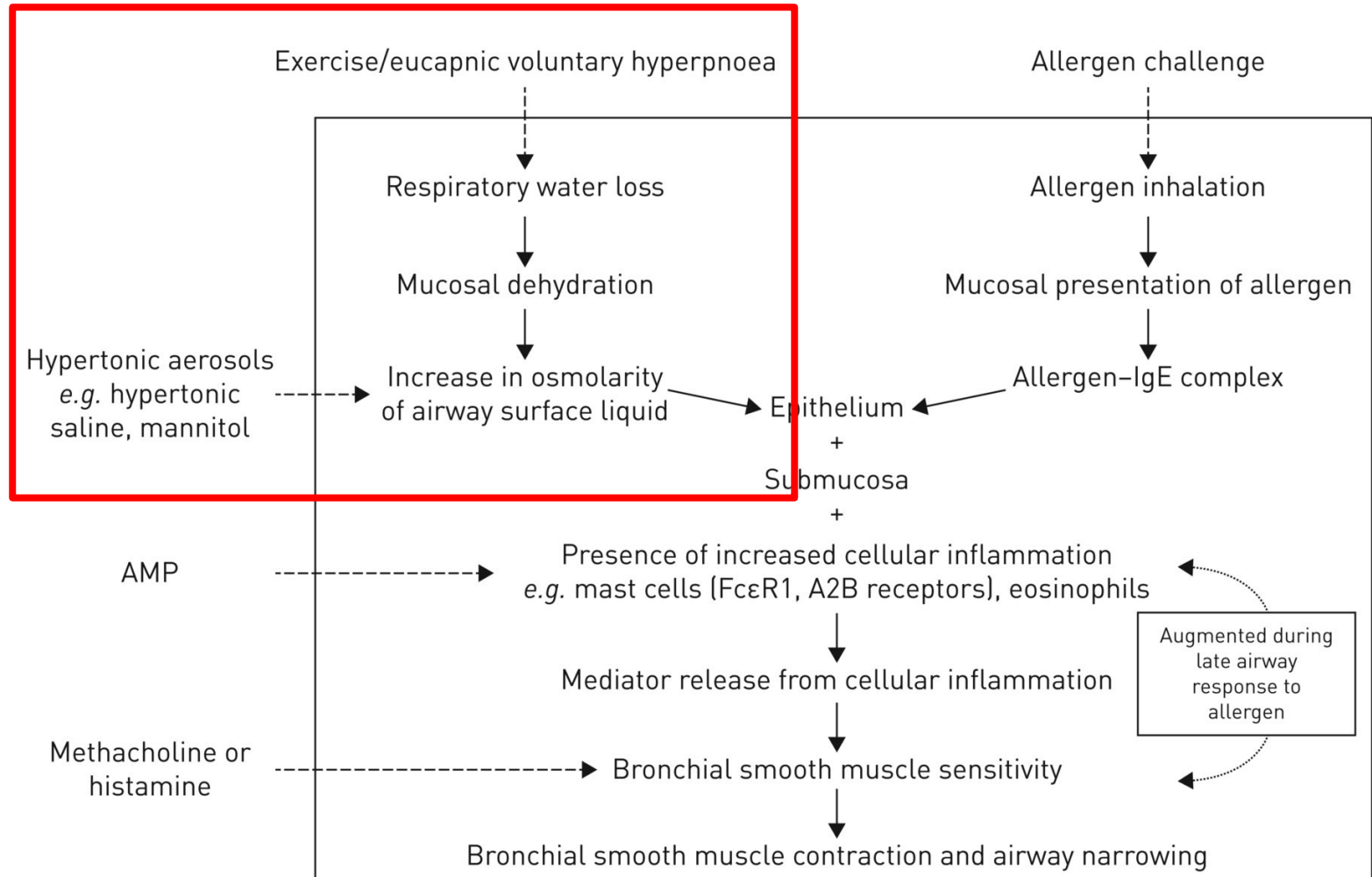


## INDIRETTI

- **Single Strong Stimulus Test**
  - Test da Sforzo
  - Test di iperpnea eucapnica
  - Test con aria fredda
- **Incremental Challenge Test**
  - Aerosol con soluzione ipertonica
  - Test al Mannitolo
  - Test all'Adenosina

# ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing

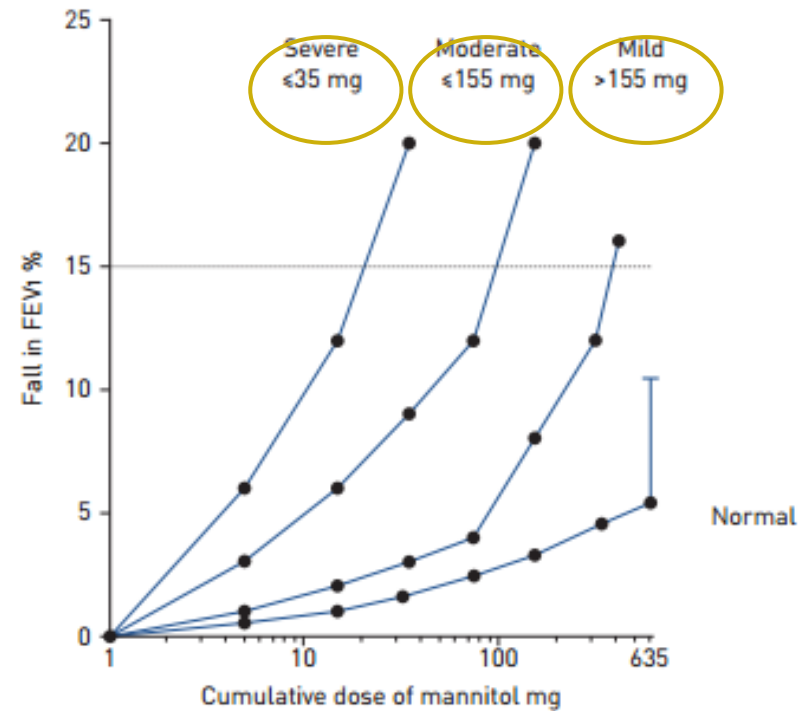
Hallstrand TS *Eur Respir J* 2018



# ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing

Hallstrand TS Eur Respir J 2018

- Following spirometry, increasing doses of mannitol (5, 10, 20, 40, 2×40, 4×40, 4×40 and 4×40 mg) are administered using the same cycle of the inhaled dose from the dry powder inhaler, followed by two acceptable spirometry manoeuvres conducted 1min after administration of the dose.
- A mannitol challenge test is considered positive if there is a **15% decrease from baseline FEV1** in response to the cumulative total dose, or a **10% decrease in FEV1 between two consecutive mannitol doses**.



- The **PD15** mannitol can be used to classify the severity of indirect AHR as mild (>155 mg), moderate (>35 and ≤155 mg) or severe (≤35 mg)

# The safety and feasibility of the inhaled mannitol challenge test in young children

*Eur Respir J 2013*

- Mannitol challenge tests are used clinically to diagnose asthma and, in particular, exercise-induced bronchoconstriction (EIB) in adults and children above 6 years of age
- 20 children aged 3-7 years were recruited; 10 of these children were healthy and 10 children had a history of parentally reported exercise-induced symptoms (EIS) in the past year.
- FOT was performed 1 min after each stage and 15 min after salbutamol inhalation at the end of the challenge.
- A positive response to the challenge was recorded if there was one of the following: 1) an increase in Rrs8 by 50% from the control inhalations; 2) persistent cough after mannitol inhalation; 3) wheeze on auscultation and 4) a drop in SpO<sub>2</sub> to ,90%.



# The safety and feasibility of the inhaled mannitol challenge test in young children

*Eur Respir J 2013*

Subject	Age years	Success <sup>#</sup>	Duration min <sup>†</sup>	Response type <sup>+</sup>	Response dose mg	Inhalation per capsule <sup>§</sup>	Increase in RrsB <sup>†</sup> %
<b>EIS group</b>							
1	6	Yes	48			2.3	17.6
2	6	Yes	37			1.3	5.4
4	6	Yes	40	Persistent cough	475	1.9	28.9
5	5	Yes	46			2.1	5.2
6	5	Yes	54	Wheeze	635	1.9	13.2
8	6	Yes	21	FOT	155	1.7	54.4
9	7	Yes	24	FOT	315	1.2	60.2
10	7	Yes	40			2.1	5.8
13	5	Yes	8	FOT	15	1.5	52.4
14	4	Yes	41	Wheeze SpO <sub>2</sub> 87%	635	1.3	38.2
Mean ± SD	6 ± 0.95		35.9 ± 14.06			1.73 ± 0.39	28.13 ± 21.82
<b>Healthy group</b>							
3	6	Yes	44			1.8	19.7
7	4	Yes	52			2.1	20.9
11	3	No	5			1.0	-8.8
12	5	Yes	48			1.9	15.3
15	3	No	27			2.2	46.5
16	5	Yes	51			2.3	40.3
17	4	Yes	53			1.9	5.4
18	5	Yes	38			1.4	37.1
19	3	No	0			0.0	17.6
20	6	Yes	41			1.7	9.2
Mean ± SD	4 ± 1.17		36 ± 19.30			1.63 ± 0.69	20.64 ± 17.97

# The safety and feasibility of the inhaled mannitol challenge test in young children

*Eur Respir J 2013*

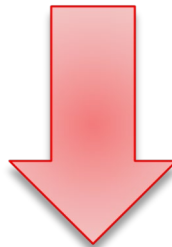
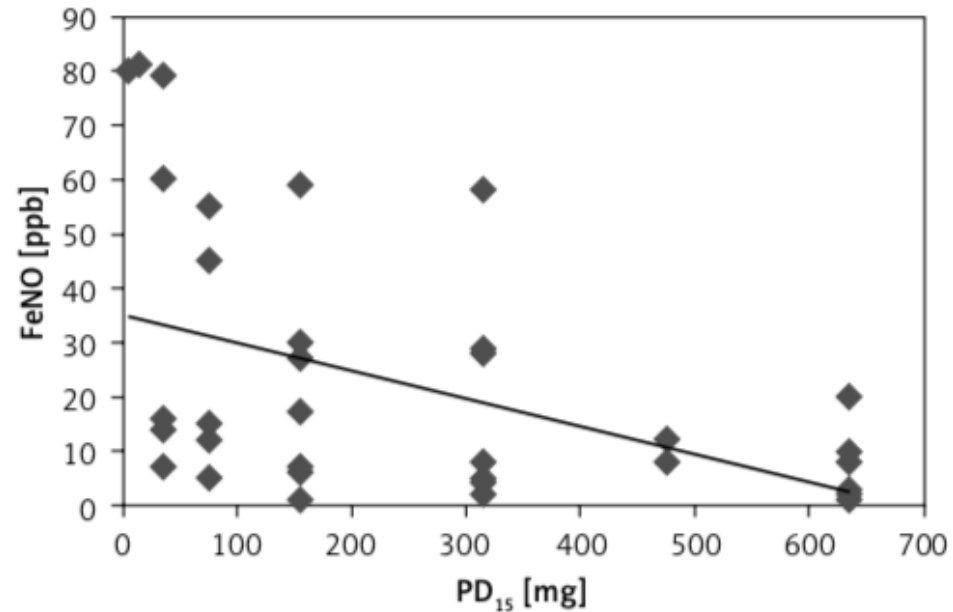
Subject	Age	Success	Response	Increase in Rrs8 <sup>1</sup> %
EIS group				
1				
2				
4				
15				
1				21.82
He				
3				19.7
7				20.9
11				-8.8
12				15.3
15				2.2
16	5			2.3
17	4	Yes		1.9
18	5	Yes	36	1.4
19	3	No	0	0.0
20	6	Yes	41	1.7
Mean ± SD	4 ± 1.17		36 ± 19.30	1.63 ± 0.69
				20.64 ± 17.97

- All 10 children with EIS and seven healthy children completed the challenge
- Six of the 10 children with EIS responded to the mannitol challenge, while none of the healthy children had a positive response
- Three of the six children that responded to the mannitol challenge did so by an increase in Rrs8, suggesting that FOT can be used with mannitol challenge to facilitate the diagnosis of EIS in young children.

# Bronchial hyperresponsiveness to mannitol, airway inflammation and Asthma Control Test in atopic asthmatic children

Marina Attanasi Arch Med Sci 2016

- All the subjects showed positive AHR to mannitol.
- Pearson's correlation test revealed a significant **inverse correlation between AHR (mannitol PD15) and FeNO** ( $p = 0.020$ ).
- Significant **positive correlation between ACT and PD15** ( $p = 0.020$ ) and a significant negative correlation between ACT and FeNO levels ( $p = 0.003$ ).
- The study population was divided into **two groups according to FeNO levels (group A  $\geq 16$  ppb vs. group B  $< 16$  ppb)**.



# Bronchial hyperresponsiveness to mannitol, airway inflammation and Asthma Control Test in atopic asthmatic children

Marina Attanasi Arch Med Sci 2016

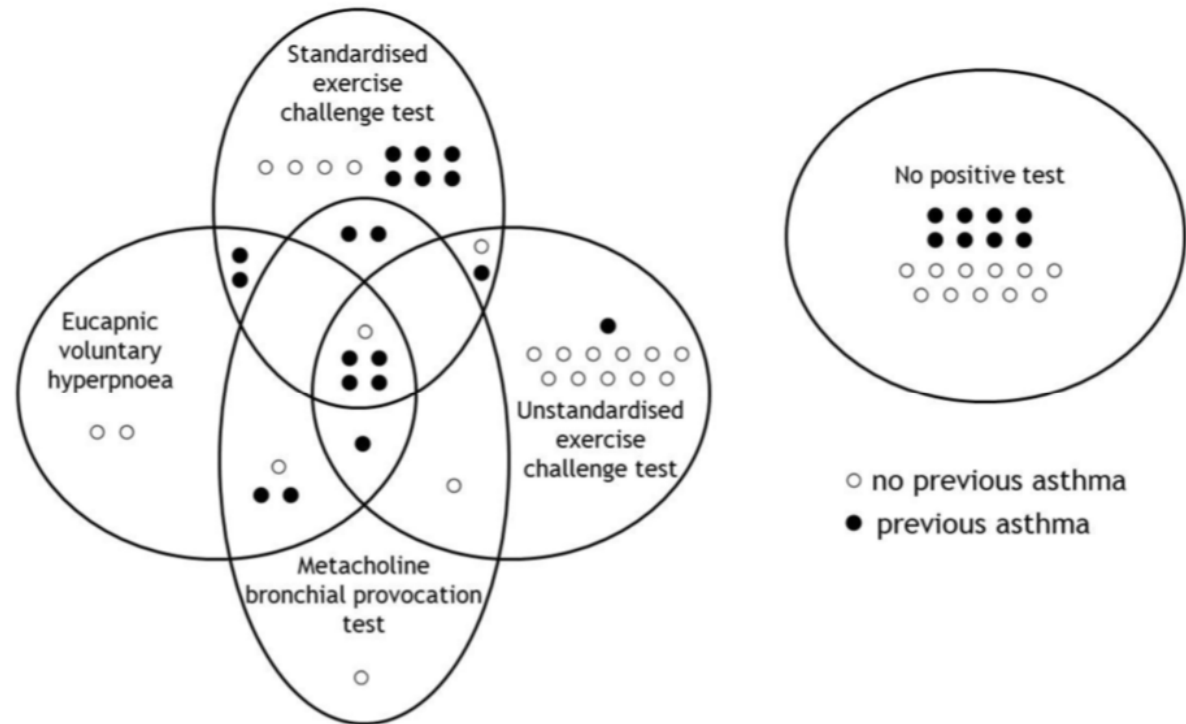
Parameter	Group A (n = 15)	Group B (n = 25)	Value of p <sup>a</sup>
Age [years]	10.3 ±2.3	8.7 ±2.6	0.099
Weight [kg]	42.7 ±14.3	35.6 ±11.5	0.089
Height [cm]	144.9 ±18.9	134.5 ±14.3	0.060
Gender (M/F)	8/7	16/9	0.739 <sup>b</sup>
Total serum IgE [kU <sub>A</sub> /l]	350.3 ±331.8	321.4 ±345.6	0.698
FeNO [ppb]	42.8 ±20.1	7.2 ±4.3	< 0.001
FEV <sub>1</sub> baseline (%-predicted)	103.4 ±10.5	111.7 ±16.5	0.096
Bronchial hyperresponsiveness and asthma control:			
AHR to mannitol (PD <sub>15</sub> ) [mg]	154.7 ±97.5	262.8 ±186.5	0.040
ACT score	22.1 ±2.4	24.4 ±1.1	0.001



# Unsupervised field-based exercise challenge tests to support the detection of exercise-induced lower airway dysfunction in athletes

Reier-Nilsen T, *BMJ Open Sport & Exercise Medicine* 2023

- 60 athletes (median age 17.5)
- 67% winter- sports
- 43% reported asthma
  
- **At least one positive BPT was observed in 68% (n=41/60)**
- **51% (n=21/41) for standardised ECT,**
- **49% (n=20/41) for unstandardised ECT**



# Test di provocazione bronchiale: a che punto siamo?



# Test di provocazione bronchiale: a che punto siamo?



Lele.....ci ho messo solo 1 mese, sono un fenomenoooo

Spirometria

ità

Fattori di rischio



# Test di provocazione bronchiale: a che punto siamo?



Lele.....ci ho messo solo 1 mese, sono un fenomenoooo



**GRAZIE**