*REVIEW ARTICLE*

# EXERCISE-INDUCED ASTHMA: AN UPDATE

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**Exercise-induced asthma (E.I.A) affects 12-16% of the general population and most of the patients affected by extrinsic or intrinsic asthma. Surprisingly, also a high percentage of professional and Olympic athletes are affected, showing that E.I.A. does not impair physical activity, whereas endurance sports bear a higher risk than the others. The mast cell role, late asthmatic responses, diagnosis, therapy, theories and data about immunological parameters in sports are taken into consideration in this review.**

Exercise-Induced Asthma (E.I.A.) is characterized by a temporary increase of the airways resistance and reactivity after a period of hard physical exercise from 3 to 8 minutes. From a clinical point of view it shows itself with air deficiency, coughing and whistling breath (1-2).

Between 12 and 16% of the population suffers from E.I.A. (2-3). Children and adolescents are more frequently affected than adults (3). According to different studies, most of the symptoms induced by physical exercise go from 36 to 92% in patients with asthma (4-6). So high a variability is probably related to exogenous factors such as the different intensity of the exercise, lack of uniformity in the study methods aimed at identifying the answer and the lack of standardization of the environmental variables, which can affect the seriousness of the bronchial obstruction induced by its immediate cause.

Questionnaires and/or studies of bronchial provocation estimate that asthma in professional athletes varies from 4.3% to 22.8% (7). At the same time, a variable percentage, of patients between 13.6 (8) and 40% (9) affected by rhinitis and atopy manifests itself with exercise causing bronchial obstruction, data not confirmed by any other author (10). A recent study (11), which covered a large, apparently healthy academic community, indicates that the resistance of bronchial hyper-reactivity to exercise challenge has a low positive predictive value for the development of additional asthma symptoms. It is well known that the percentage of asthmatic subjects is very high (compared with normal population) in élite athletes, particularly between swimmers, skiers and cyclists.

Some data (Tab. I) show a high percentage of atopy also in élite athletes during summer and winter Olympic Games.

From the pathogenetic point of view, although E.I.A. has been known for 300 years (12-13), two theories, the vascular and the osmolar one, are probably to be taken into account together and have had a large consensus (2, 14-20).

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*The mast cell and the eosiniphil role*

Mast cell activation, as a consequence of the phenomena described above, might be the final common cause of bronchial constriction in E.I.A. Despite its ambiguous pathologic role, until recently, this was inferred from pharmacological data, such as the inhibition of the response to physical exercise made by a mast cell "stabilizer", such as the cromolyn sodium.

There is no doubt that, when in E.I.A. the phenomena due to vascular and osmolar factors occur, also an aspecific activation of immunological inflammation may undergo through the intervention of various factors.

A study has shown a significant and simultaneous increase of LTB4, PGD2 and histamine in the asthma sufferer bronchial alveolar washing after an isocapnic hyperventilation at 22°C. This theory seems to be supported by a recent study observing in urine an increase of prostaglandin F2, principal PGD2 metabolite, produced by the cyclo-oxygenase from the mast cells, in children and adults affected by E.I.A. There are different studies about urinary excretion of LTE4, the final product of leukotrienes, but the simultaneous urinary levels reduction of that metabolite and of the exercise-induced bronchoconstriction induced by the Montelukast, points towards the leukotrienes' emergent role in the pathogenesis of such clinical damage.

The role of inflammatory mediators in E.I.A. is questionable. Physical exercise would release the bronchial obstruction inhibitory prostaglandin, in particular those of the PGE2 type (21). This protection might be important to explain the refractory period in E.I.A., which is reinforced because the inhaled PGE2 alleviates the bronchial constriction caused by physical exercise (22) and premedication with indomethacin, a powerful prostaglandin inhibitor (23), and flurbiprofen (cyclo-oxygenase inhibitor) (21) reduces or eliminates the refractory period in E.I.A.

Despite only a few studies implicate a role for eosinophils in the E.I.A. pathogenesis, it is clearly established their importance in the pathogenesis of the airways inflammation, the main physio-pathologic phenomenon of chronic asthma. Venge et al. (24) observed in individuals with E.I.A. an increase of the eosinophil cationic protein (ECP), immediately after physical exercise. Recent studies (25-26) have shown higher levels of eosinophils and cationic protein (ECP) in expectorations induced in E.I.A. (+) patients compared with E.I.A. (-) asthma sufferers and healthy individuals, suggesting that the eosinophil infiltration level contributes to the mechanism of bronchial obstruction provoked in asthmatic patients by the challenge of physical exercise and that this eosinophils infiltration has a direct influence on the bronchial reactivity to an indirect agent such as physical exercise. At the same time, there is a strong correlation between the degree of infiltration with eosinophils and the seriousness of asthma induced by physical exercise. The real implications of this study are unknown, but it is considered that the presence of leukotrienes D4, E4 and C4, in the liquid phase of the induced expectoration, might explain the eosinophils' influence typical in E.I.A. sufferers, increasing the bronchial constriction stimulated by different types of the mast cells mediators.

In the recent years an important role of some pro-inflammatory cytokines like IL-1, IL-6 and TNF-α has been envisaged for the pathogenesis of E.I.A. In fact, IL-1 and TNF-α produced during the exercise seem to induce muscular proteolysis and subsequent new production of pro-inflammatory factors. Moreover, IL-1 has been found increased in muscular tissue and, together with IL-6 and TNF-α, in blood after acute exercise (27-31). Also IL-8 as a chemotactic factor of neutrophils is now under consideration.

IL-4 seems to be reduced during an entire season of regular training in a professional team, suggesting that a correctly-performed exercise can even protect against exacerbations of allergic symptoms (30).

Physical exercise increases the humoral sympathetic activity protecting the individual against a bronchial spasm and causing a momentary bronchodilatation. The high density of beta-2 adrenergie receptors agonists in human airways suggests that the catecholamines are responsible for this first bronchial spasm protective effect (31).

*Late asthmatic responses*

It has been suggested that physical exercise, as an antigenic challenge to airways, can produce a dual model of response producing late changes in the pulmonary function.

The first description of LAR caused by physical exercise, goes back to 1980; but there are some conflicting studies about its real existence and about its possible physio-pathological and clinical implications in people suffering from E.I.A. (32-37).

A series of methodological circumstances and their interpretation can help to make this happen. First of all, there would be few doubts about the existence of a biphasic fluctuation of the pulmonary function after physical exercise, even if the importance of this phenomenon leads to discussions and its predominance is sensibly less than the one observed during the typical allergic reaction (35-37).

A universally accepted criterion on what LAR means in physical exercise doesn't exist. The approximate criteria adopted by different authors correspond to the fixed drop of FEV1 or of the peak flow in comparison to pre-exercise values or limited to the pulmonary mechanism changes in relation to a "control day" without any previous physical exercise.

There is a lack of consistency, with the analysis of the available data, which suggests that the connection between exercise and LAR cannot by its very nature be a causality; as a matter of fact, a great number of authors have not been able to reproduce it (33), showing a high variability in its expression. Moreover, study designs often turn out to be complex and the choice of the 'control day' can be difficult. In his first study (36), Boner observed the phenomenon in 26% of his patients; when the research was repeated after a day of control LAR was not identified (38). Some authors speculate on the fact that LAR associated with an extreme exercise can be more an epiphenomenon, and not related to E.I.A. physio-pathogenesis or physiopathology.

*Factors which affect the seriousness of exercise induced asthma*

Reaction to physical exercise can be influenced by a series of factors indicated in the following Tab. II.

Most patients develop E.I.A. only after relatively hard exercise of 6-8 minutes; whereas, when the "time" is longer, the bronchial spasm can possibly not occur or achieve its "plateau" (2). The studies carried out show clearly that the seriousness of E.I.A. reaches effort levels corresponding to 2/3 of the highest predictive oxygen consumption for patients; furthermore, the seriousness of E.I.A. is not intensified by any increase in the intensity of effort (24).

Physical exercise is the only asthma precipitant which causes tachyphylaxis (2). The bronchial obstruction decreases gradually when facing one-hour effort challenges. This phenomenon has been called the "refractory period" (39). At present, the debate indicates the responsibility for its production to the inhibiting prostaglandin mediators (21), to the fluctuations of the intra-bronchial capillary vessels dilatation or constriction, with the consequent destruction of the airway thermic gradient and the loss of a greater amount of water from the airway caused by the initial exercise (16). The induction of this refractory period is very useful as non-pharmacological measure for E.I.A. prevention, in particular for athletes, in view of the fact that effective warm-up exercises can reduce and attenuate the effect of the obstructive phenomenon.

The individual's bronchial reactivity degree is an important factor that can influence the seriousness of the bronchial response to physical exercise. Some studies show that an allergenic challenge after physical exercise produces, in its turn, a significant increase in physical exercise reactivity one week after the specific antigenic provocation (40). This shows that even if under the same weather conditions and intensity to the stimulus, atopic patients will vary their response to the exercise depending on their current exposure to significant allergens. Environmental pollution, especially that produced by sulphur dioxide, increases E.I.A. significantly. Active or passive smoking of tobacco and recent viral infections can increase bronchial reactivity, but there are no studies that show that these factors can increase the E.I.A. impact and seriousness (2).

The way in which E.I.A. is influenced by drugs will be discussed in the paragraph regarding treatment.

The explicit symptoms (see Tab.III) are not different from those brought about by other causes or stimuli. Coughing, dyspnoea and whistling breath represent the typical symptomatology, which occur a few minutes after the physical effort, while laughing and crying are auto-limited

to 20 and 40 minutes. Palpitations, thoracic compression, dizziness, nausea and epigastralgia (2) can follow them.

A distinction must be made between dyspnoea and normal hyperpnoea which can manifest itself in children and adults who are out of training, and disappears quickly after the exercise is over (2).

*Diagnosis*

E.I.A. diagnosis is clear and based on the typical clinical symptoms which the patient manifests in particular with exercise. If the inhalation of an agonist beta2 drug prevents the symptoms caused by exercise, there is a higher possibility of making a diagnosis.

The final diagnosis consists in a bronchial provocation test with exercises (41-45). There are different standardized studies which employ free running, the ergometric bicycle, the treadmill or the conveyor belt.

For any technique taken into consideration, the response evaluation is done by measuring the drop in FEV1 in relation to the pre-exercise basal value, with determinations at 1, 3, 5, 10, 20 and 30 minutes after the physical stimulus (34). The international recommendations (45) consider a test positive when the function parameter falls by 15% in comparison to pre-exercise basal value, even if some authors (3, 12) consider that a fall of 10% is enough, according to a calculus based on the formula (basal FEV1 – post exercise FEV1) x 100/ basal FEV1.

After a potential asthmogenic exercise (basing this choice on intensity and characteristics), the maximum FEV1 drop happens between 5 and 10 minutes after the exercise (38-41), with a spontaneous recovery between 30 and 120 minutes. The recovery speed depends on the seriousness of the induced bronchial obstruction (41).

When the drugs' protective effect needs to be tested on E.I.A., there are two additional yardsticks that can be considered: recovery time which averages between the FEV1 maximum drop waiting for the pre-exercise basal value (with a difference of –5%) and the area above the curve calculated with serial measurements of that parameter one hour after the exercise (AUC 0-60 min), and represents the maximum drop fixed impact and FEV1 recovery, assessed with the trapezoidal method (46).

The exercise test can involve some potential risks. Coughing, dyspnoea or whistling breath in some occasions is alarming (41), and a serious reduction in the oxygen haematic saturation can occur, together with a drop in blood pressure and electrocardiographical abnormality. This is the reason why this test must be carried out carefully in a hospital environment by an expert physician equipped with resuscitation devices for extreme cases, as well as the possibility of measuring the oxygen saturation, to perform electrocardiograms and take blood pressure (45). Risks will be reduced by giving the patient adequate information about the treatment, starting the provocation test in a normal basal pulmonary function (basal FEV1 75% over the predictive normal value) (44) and having drugs and emergency teams ready for a potential intervention in unexpected clinical situations.

The refractory period dictates that a second challenge must not take place until 2 hours after the first, and even occasionally 4 hours. The patient must take other necessary *precautions* such as: neither drinking nor eating before the test, a period of at least 7 days after the last asthma crisis and no preventive medication, unless you want to study the protective effect of certain drugs (45).

Diseases that can lead to E.I.A. diagnostic mistakes have to be taken into consideration (table IV):

*Treatment*

Cough and rales associated with exercise interferes with sports and other physical activities in more than half of asthma patients. It is logical to suppose that asthma treatment, apart from its cause, will bring benefit to our patients' quality of life, including a better tolerance of physical efforts.

The delivery of certificates forbidding any physical activity in children is a negative course and not to be recommended, since we have non-pharmacological measures and pharmacological strategies able to prevent E.I.A. in most of the asthma sufferers. On the contrary, children with asthma should be induced to practise exercise and sports apt to give them less risk of E.I.A. This risk can be further minimized through non-pharmacological and pharmacological treatments.

So, many asthmatic elite athletes could win medals during World Championships and Olympic Games. For instance, as seen in Tab. I, whereas 28% of the athletes of the Italian Team at Sidney 2000 Olympic Games were positive to Skin Prick Tests to aeroallergens, many of them went back home with a medal.

*Non-pharmacological measures*

The control of the causes is the first step towards asthma treatment; even if for good reasons physical exercise must not be avoided in most situations, but, on the contrary, stimulated in our asthma patients (47).

The choice of sport depends on the facilities provided for the patient by his town local services. It has been proved that an effective aerobic training improves toleration of physical exercise (47). The ideal thing is to recommend people to take exercise in a warm and humid environment, after a correct warm-up period such as 10-15 minutes of stretching, running slowly for 5-10 minutes and running quickly in short spurts for 10-30 seconds, provoking the refractory period for a better tolerance after the chosen exercise (47). The use of a scarf or a facemask is recommended in winter or in cold environments. There are some physical activities that are better tolerated than others and which can be recommended. Swimming is perfect, because it is done in a temperate and humid environment which together with the horizontal position helps the mobilisation of excretions and tones the chest muscles. Other activities which involve short efforts such as sports of alternated participation (skating, golf, high jump, water polo, baseball etc.) (47) are the most acceptable. Sports such as bicycle racing, free running, hockey and athletics are the most asthmogenic. Albeit each patient is free to choose the sport he likes best. We don't have to forget that physical activity has a positive influence on the patient's emotional and social condition, and helps him/her to socialise and increases his self-confidence.

*Prevention and pharmacological treatment*

Pharmacological treatment consists in a premedication immediately before the physical exercise and the basic "controlling", anti-inflammatory treatment. The symptoms caused by the exercise must be treated with a " reliever" medication. In Tab. V is shown an overall view of the effects of the different drugs clinically used for E.I.A.

Treatment with anti-inflammatory drugs is the choice, because it keeps under control the disease activity including a control of the symptoms caused by the exercise. The first treatment starts with the inhaled steroids.

Inhaled steroids have been shown to have a quicker effect on E.I.A. than on the non-specific bronchial hyper-reactivity after metacholine provocation (48). After a week of inhaled bronchial Budesonide in well-trained athletes, researchers have observed an important E.I.A. reduction due to a slight FEV1 drop with the challenge of physical exercise in the pulmonary function laboratory (44). Another study has shown an early E.I.A. recovery after a treatment with inhaled Budesonide from 2 to 3 months, while the recovery thanks to a cholinergic agent can be seen after 12-22 months.

The protective effect of Budesonide on children is in varying doses, reaching 80% with doses of 400 μg per day. But recent data show that this capacity can diminish in long treatments (49). Thio et Al. assure than a dose of 1 mg of inhaled Fluticasone has a strong protective action against the bronchial response to exercise in a high percentage of children suffering from asthma, adding this action to its vasoconstrictive and anti oedematous qualities (50).

Inhibition of the disodium cromoglicate (CGDS) on E.I.A. was proved in the early 1970s and described in various articles of medical literature and introduced us to a single dose of 20 mg administrated by spin-haler. Recently introduced in simple doses, nedocromile sodium reduces the seriousness and the length of the attack to a slightly greater extent (51).

Its mechanism of action is unknown, but seems to work as mast cell stabilizers, blocking the membrane chlorine canals and activating the airways sensorial nerves.

These drugs' most beneficial effect is reached when used immediately before the exercise with an inhibitory action of about 2 hours (29) and produces a more than 50% reduction of the bronchial obstruction induced by the exercise; they show very few side effects (41).

CGDS combined with Terbutaline gives a beneficial protection for 4 hours, but not more than 6 (52). Even if there have been only a few comparative studies between agonist beta2 and cromones in E.I.A. prevention, an old study suggests that Salbutamol gives a higher inhibition than cromolyn sodium. Moreover the use of cromons is not recommended when there is an acute bronchial obstruction caused by exercise, or to reverse the symptoms caused by that stimulus (2, 46).

Agonist beta2 drugs are normally the most effective both for E.I.A. prevention and for overcoming the bronchial obstruction after that stimulus, a characteristic that does not exist in cromones. Their combination increases the bronco-protective effect, reducing E.I.A. in 98% of patients (2, 52).

Those of short and rapid action, such as Salbutamol, Terbutaline and Fenoterol, are of best quality. Inhalation is quicker and more effective. Despite its immediacy of action, it is unable to provide a protective effect for more than 3-4 hours after its administration (2,53). Salmeterol and Formoterol, selective beta2 agonist of long action, have been recently introduced. Thanks to their hydro-lipofilic qualities, Formoterol has a quicker starting action, between 1 and 3 minutes, (like as to Salbutamol) but both of them give protection from 9 to 12 hours (54-55).

A recent study (56) defines the existence of an heterogeneity, with subjective differences of response, in the bronco-inhibiting effect against E.I.A. thanks to long length agonist beta2; it means that a large group of children does not show any protection after the challenge with exercise, 8-12 hours after a simple antagonist dose. Furthermore, the E.I.A. inhibition declines using Salmeterol regularly for a long time. Nelson et al. (57), using Salmeterol for adults in a period of 30 days, proved that it is possible to have E.I.A. protection with a continued administration, but the action is considerably reduced. The simultaneous use of Salmeterol, in one daily dose, with inhaled Beclometasone for children and adolescents between 12 and 18 years did not prevent tolerance after one month's administration (58). Anyway, this study's clinical importance is still under discussion (59).

Despite all these studies, long action beta2 agonist single morning dose, can protect against the symptoms induced by exercise or any other activity, improving the asthma sufferer's quality of life, as well as a better compliance to the treatment (46).

The use of *anti-leukotrienes* drugs is the main innovation in the asthma pharmacological treatment over the last 25 years. Regularly given, they can improve asthma symptoms and the pulmonary function both in children and adults, blocking the immediate and late reaction to the allergens challenge and reduces eosinophylia in the induced expectoration, proving its anti-inflammatory effect (60).

Their value in E.I.A. prevention is encouraging and has been assessed by the challenge to exercise and by questionnaires about the quality of life (41). Kemp (61) assessed in children between 6 and 14, the effect of a 5 mg dose of Montelukast in one daily dose from 20 to 24 hours after the administration, in a randomised double-blind placebo, controlled study observing E.I.A. attenuation; this study suggests that a simple oral dose of 5 mg given late at night to children can give protection the day after.

The protective effect seems to be similar for Montelukast, Zafirlukast and Zileuton, though the latter has a considerably shorter action (62).

In studies carried out on adults, Montelukast was compared to Salmeterol because it was able to give a longer protection against E.I.A. (63). In both cases, the starting protection was similar, but after 4-8 weeks, the protection was assured only by Montelukast, while the long action beta2-agonist was tolerated and its protective effect decreased with time. The same effect was observed in a more recent study (64).

The effect of 20 and 80 mg Zafirlukast, twice a day, was compared with placebo for E.I.A. protection with challenges held 2 and 8 hours after the latest dose of a regular administration in adults. It was observed that this drug had effect 8 hours after the regular dose.

Oral anti-leukotrienes drug administration, can improve the therapeutical results in chronic diseases such as asthma and can protect up to 24 hours, a protection given by no other drug used for asthma (65).

**Tab. I.** *Asthma in olympic athletes.*

| |
|---|
| US Team at 1984 Los Angeles Olympic Games: 11% (Voy RO, 1984) |
| US Team at 1996 Atlanta Olympic Games: 16,7% (Weiler JM et al., 1998) |
| US Team at Nagano 1998 Winter Olympics: 22,4% (Weiler JM et al, 2000) |
| Italian Team at Sydney 2000 Olympic Games: 28% positive to SPT (AIDA Study Group, 2000) |
| Australian Team at Sydney 2000 Olympic Games: 41% positive to SPT (Katelaris CH et al, 2000) |

**Tab. II.** *Factors affecting the seriousness of asthma induced by physical exercise.*

a. Type of exercise used.
b. Intensity and length of the stimulus.
c. Existence of the refractory period.
d. Environmental temperature, humidity and osmolarity.
e. Contaminative allergens in the environment.
f. Clinical severity of the asthma.
g. Previous medication.

**Tab. III.** *EIA Symptoms.*

- Cough
- Dispnea
- Thoracic Constriction
- Wheezing

→ Few minutes after exercise

- Symptoms occur 2 and 10 minutes (peaking at around 10-15 min) after exercise
- Symptoms disappear spontaneously after 30-60 min

**Tab. IV.** *Diagnostic mistakes.*

a. Normal hyperpnea related to exercise.
b. Anaphylaxis and laryngospasm induced by exercise.
c. Anxiety and hysterics.
d. Hyperventilation syndrome.
e. Arytenoids and vocal cords dysfunction.
f. Neuromuscular diseases.
g. Pulmonary and spontaneous pneumothorax embolism.
h. Restrictive pulmonary diseases.
i. Heart diseases.

Theophylline, taken orally, is E.I.A. second choice drug on account of its potential toxicity. It requires frequent close-level monitoring and its serum peak coincides with the time spent for the exercise giving great benefit (66). Its preventive action is less effective than that of the agonist beta2. It can be considered as an additional medication for chronic asthma preventive check with a consequent "peripheral" benefit on E.I.A.

Anti-cholinergic drugs are not very effective in blocking the abnormal bronchial response to the physical exercise. *Ipratropium bromide* can be added to short or long antagonist beta2, but its use as single drug in E.I.A. prophylaxis is limited by its slow starting action and its weak effect.

*Other pharmacological alternatives*

The preventive action of other drugs has been studied in order to understand the mechanisms involved in E.I.A.

The prophylactic action of inhaled Furosemide (30mg) was, in a comparative study (67), similar to that of nedocromile sodium (4mg), the effect increasing by administering the two drugs. Bronco-protection given by Furosemide under the "indirect" stimulus such as physical exercise, seems to be independent from its diuretic action and it has no bronco-dilating effect.

Calcium channel antagonists could be useful because some studies have shown that many physiopathogenic events are calcium dependent, including the smooth muscle contraction and the cell mediators release. Sublingual nifedipine (20mg), 30 minutes before the exercise prevented E.I.A. in 10 patients suffering from asthma (68), even if the current studies do not clarify their precise mechanism of action.

Anti H1 antihistaminics so far didn't give any consistent result in the prevention of E.I.A., including the most recent ones (cetirizine, fexofenadine, loratadine and desloratadine).

Terfenadine gives a partial protection against E.I.A. and provokes isocapnic hyperventilation, but in strong doses (120-180 mg given orally before the exercise) (69). The effect seems to be dose-dependent and that is why the other antihistamines studied for E.I.A. could be not effective (70).

Aerosol heparin given in strong doses (1000 unites/kg up to 80000 unites) partially prevents E.I.A. without inhibiting the broncho-constriction induced by histamine (71). The drug was as effective as CGDS when both of them were given 15 minutes before physical exercise and more effective when given 1 or 3 hours before.

Immunotherapy (IT) in allergic patients

**Tab. V.** *Effect of the different anti-asthma drugs in the prevention of asthma induced by physical exercise.*

| Drug | Time before the exercise (minutes) | Effect | Length of protection (hours) |
|---|---|---|---|
| **Inhaled agonist Beta2 T** | | | |
| **Salmeterol** | 20-30 | +++ | 8-12 |
| **Formoterol** | 10-15 | +++ | 8-12 |
| **Salbutamol** | 10-15 | +++ | 2.0-2.5 |
| **Terbutaline** | 10-15 | +++ | 2.0-2.5 |
| **Cromolyn Sodium** | 10-15 | ++ | 1.5-2 |
| **Nedocromile Sodium** | 10-15 | ++ | 1.5-2 |
| **Leukotrienes antagonists** | ? | ++ | 4-24 |
| **Lethylxantine** | 30-60 | +/- | 6 |
| **Anticholinergic** | 30-60 | +/- | ? |

(+++) Maximum effect; (-) No effect

practising sports, when correctly prescribed and accurately administered, can be a useful way to reduce the reactivity of subjects mainly when they perform activity during the pollen season or indoors (mites).

## CONCLUSION

E.I.A. is highly common. The symptoms, are generally auto-limited, but can become so serious to influence negatively the quality of life of patients with asthma.

Despite the existence of an incalculable number of published researches, its precise physio-pathogenesis mechanisms are still unknown, even if the osmolar hypothesis is the most plausible. A better clinical characterization of the late asthmatic response proved by some authors, with cells and pro-inflammatory mediators (kinins, prostaglandins, leukotrienes, cytokines and chemokines) participation, is necessary.

The physician must recognize E.I.A. in children and adults suffering from asthma, since its appearance can be due to an inadequate control of the disease. A routine check of the activity level permits correct therapeutic treatment. A provocation test by physical exercise, carried out by experts, is a great help for the final diagnosis.

Physical activity is part of people's life styles and must not be prohibited. Non-pharmacological measures, such as suitable warm-up exercises and physical conditioning can inhibit the asthmatic response to the physical exercise. When necessary, agonist beta2 administration of short or long action, or cromolyn sodium administration 15 minutes before physical exercise prevents the asthma symptoms, which can occur, and also a treatment with anti-leukotrienes drugs can be suggested, mainly in children.

Nowadays, there is no reason why asthma sufferers should not practice any sport normally; they must stop when an asthmatic crisis occurs, of course, but it is an important task of the Physician to give precise information for a complete social and sporting participation, the most suitable answer to the limitations possibly caused by the disease, in order to give to people practising sport the best chances to perform at their best in their activities.

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