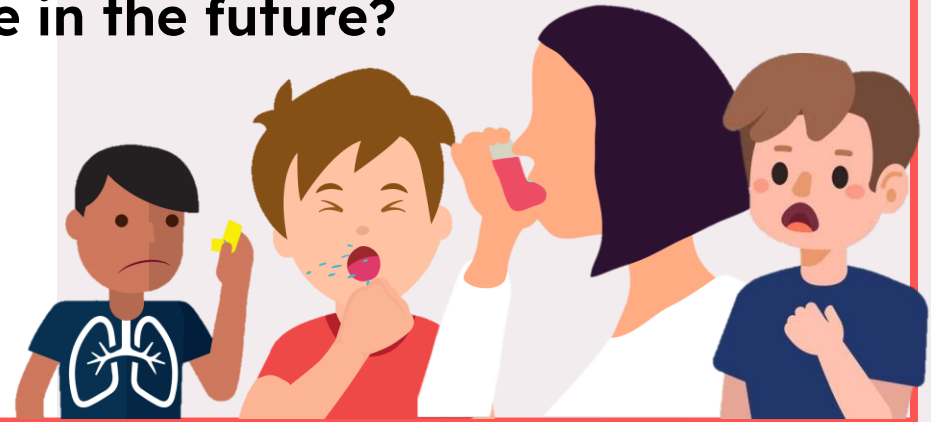




Asthma Prevention

Will it be possible in the future?



By: Dr. Mozhgan Moghtaderi

Asthma is a complex syndrome:

Genomic and environmental factors as well as aberrant immune maturation early in life can contribute to the onset of disease.

Gene- environmental interaction





Primary prevention targets reductions in asthma incidence

Secondary prevention is the mitigation of established disease and involves disease detection, management, and control

Tertiary prevention is the reduction of complications caused by severe disease

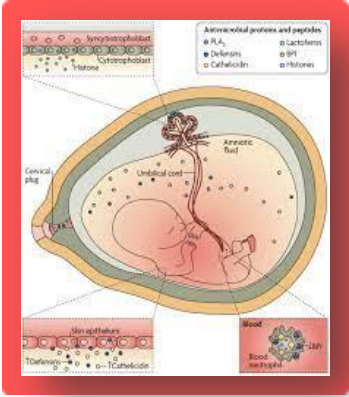
A magnifying glass with a red handle and a yellow frame. Inside the lens is a blue circle containing a white and red DNA double helix structure.

Asthma is a polygenetic disease with over 400 single nucleotide polymorphism-trait associations identified in genome wide association studies (mostly 17q21)

A family history of asthma clearly increase the risk of developing asthma in the child. In a child, the chance of developing allergy is 50% when one parent has allergy and it is 66% when both parents are allergic.

Genetic predisposition is non- modifiable

Mechanisms of protection Neonatal immune system



At birth, the adaptive immune system is still immature and needs to develop. Neonates must rely on their innate immunity, as well as maternal antibodies and protective factors in breast milk, to protect themselves against pathogens.

The neonatal immune system is still skewed towards type 2 responses (as imposed in utero), which are necessary to condition the maternal immune system and protect the fetus from rejection.

Microbial exposure is the most important trigger for induce adaptive immunity.

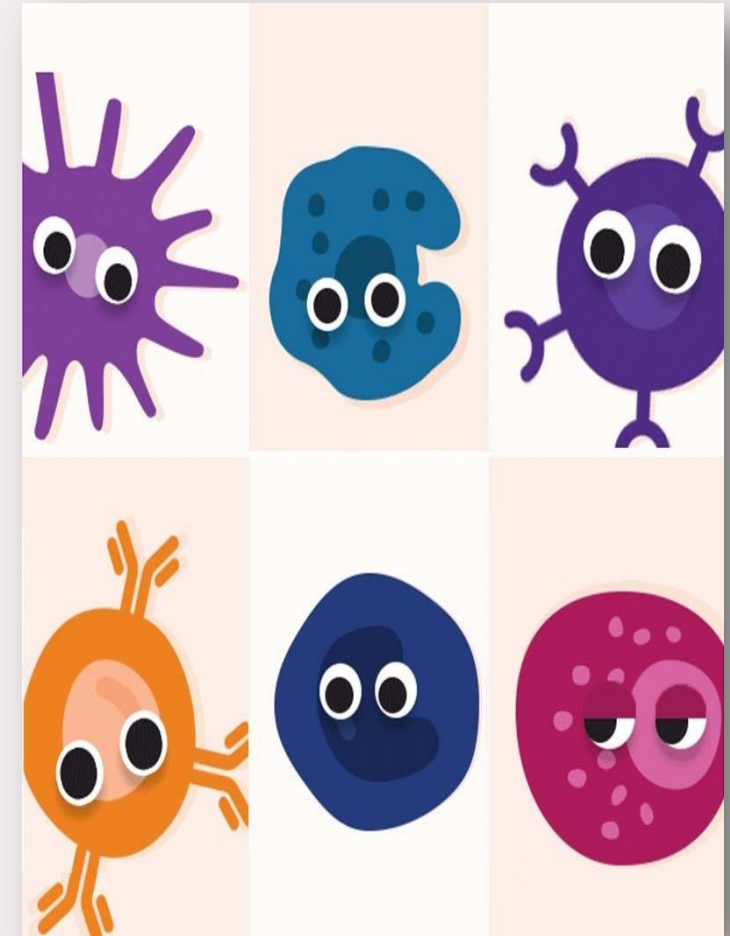
Immune homoeostasis and immune maturation

If no sufficient learning activities (such as microbes) are provided, the time of maturation is extended, leading to extended shifts around the set-point with higher chances of extended tissue damage due to uncontrolled inflammation.

Use of antimicrobial agents will strongly disturb this balance and extend the time necessary to calibrate the immune system.

Living conditions associated with **lower prevalence of childhood asthma**, such as farming and traditional lifestyles, are associated with higher diversity of the gut microbiota, which could relate to closer contact with **animals, soil, dietary fiber, and intake of fermented foods**.

These conditions have a profound impact on the activity of the immune system, showing both increased innate and regulatory (adaptive) responses in children and adults of these rural communities.



**Breast feeding no conclusive evidence
exists for a protective effect**



Vitamin D and Fish oil

In Denmark, a double-blind randomized controlled trial of vitamin D3 supplementation during pregnancy to a daily dose of 2800 IU versus 400 IU from pregnancy week 24 to 1 week postpartum.

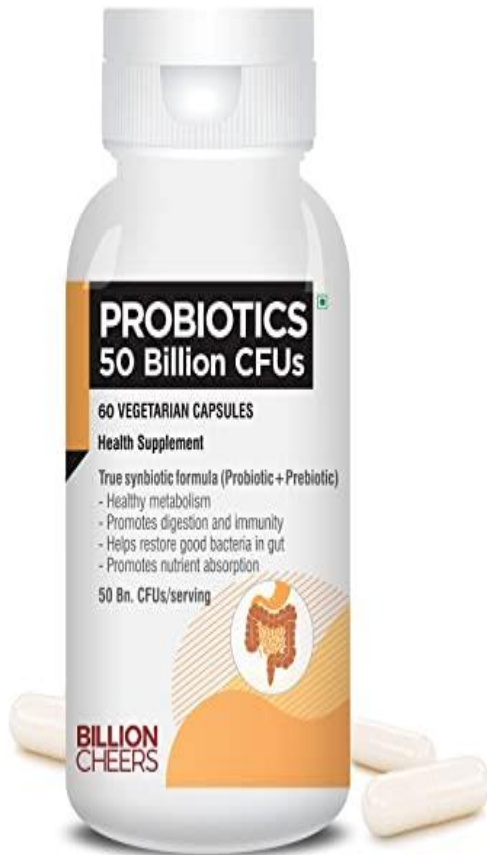
A non-significant difference in the incidence of persistent pre-school wheeze but the effect was not sustained into school age.

A second intervention trial was into the cohort, in which pregnant women at 24 weeks of gestation were assigned to fish oil or placebo (olive oil) per day. The intervention resulted in a significantly **reduced risk of wheeze in preschool children and infections of the lower respiratory tract, but not asthma exacerbations, eczema, or allergic sensitization.**

Vitamin D or fish oil in the mother can prevent wheeze in pre-school children but no asthma in school-age children.



Prebiotics and Probiotics



**Probiotics, prebiotics and synbiotics seem to be attractive choices for:
the ability to change the T helper balance (Th1/Th2) from Th2 to Th1,
induction of regulatory T cell and immune tolerance.**

Result of meta-analysis: food supplementation with probiotics given to atopic mothers in pregnancy and during lactation can prevent the development allergies in the offspring. There is no role of probiotics in prevention, though they may have role in treatment of asthma.



Smoking and Air pollution

Maternal smoking and passive child can increase asthma.

A meta-analysis study showed air pollution can increased the risk of wheeze 70% by 2 years.

Second- hand smoke exposure has been shown to increase developing asthma.

??? Modifiable factor





- Type of delivery
- Maternal and child's use of paracetamol
- Prematurity and low birth weight

- Day care assistance during the first 6 months of life **decreased** the risk of asthma in school age.



C Section
Vs
Normal Delivery



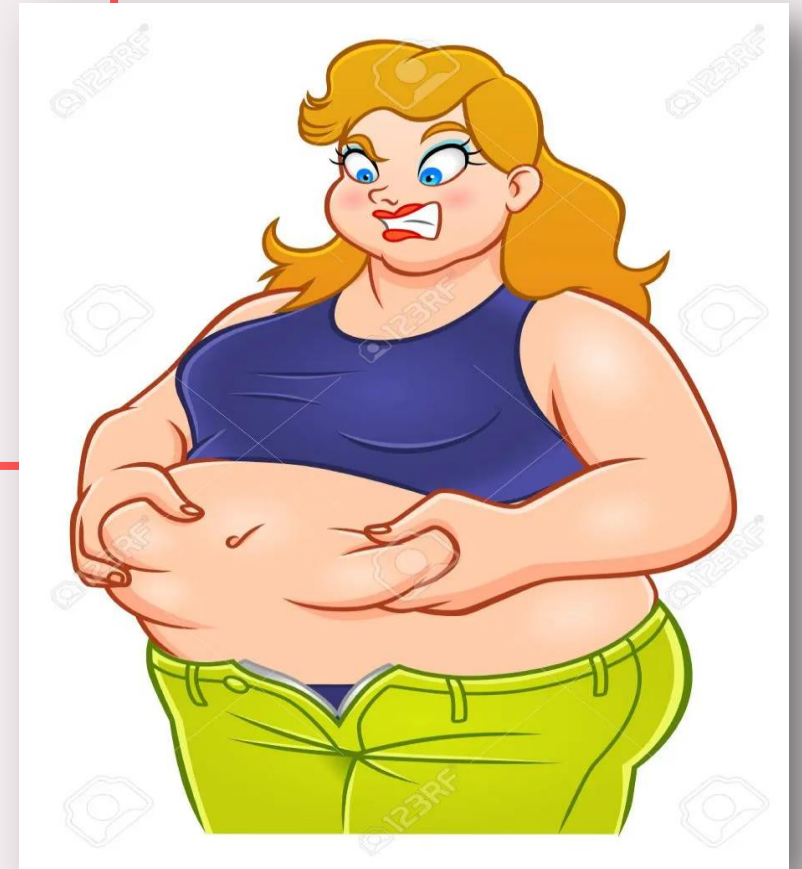


Maternal overweight and Child obesity are traits associated with asthma

Both a risk factor and disease modifier

Maternal obesity and high weight gain associated with 15-30% asthma

?Modifiable



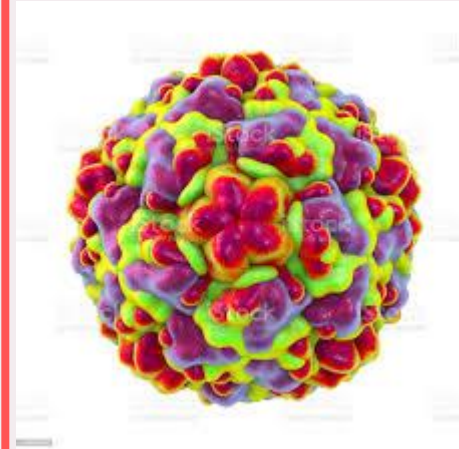
RSV bronchiolitis or other Infection with certain respiratory viruses (rhinovirus, metapneumovirus) in infancy has been recognized to be associated with later asthma in many studies up to 18 years .

RSV increase Th2 cytokines and enhanced airway sensitization to allergens , the mechanism is multifactorial.

Intervention:

Prophylactic administration of palivizumab, a monoclonal antibody for RSV, has been shown to reduce recurrent wheezing in high- risk children aged 1-3 years, but did not decrease the incidence of atopic asthma.

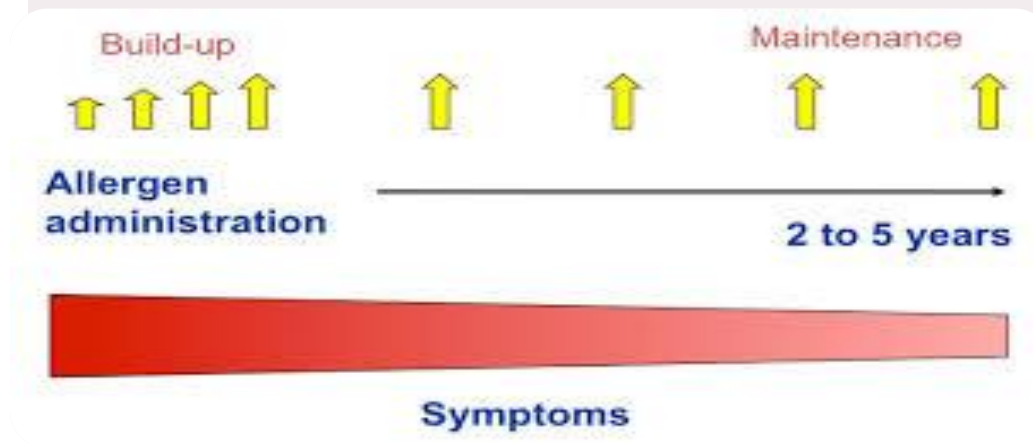
The use of early azithromycin at the beginning of LRT infection decrease severity. A large study for it is in progression.



Immunotherapy

Allergic sensitization is closely associated with some asthma phenotypes, and allergic rhinitis can precede new asthma onset. Immunotherapy could prevent asthma? but present evidence remains inconclusive.

The blinded Asthma Prevention Study 82 applied sublingual treatment with grass pollen in children with grass pollen-induced allergy. The study showed reduced asthma symptoms and decreased asthma medication use with sublingual grass pollen immunotherapy compared with placebo, but no effect on asthma incidence at the 2-year follow-up. targeted age group was 6–12 years



SUMMARY



Primary prevention aims to reduce the incidence of disease on a general population level or in individuals at risk of developing disease.(lancet)

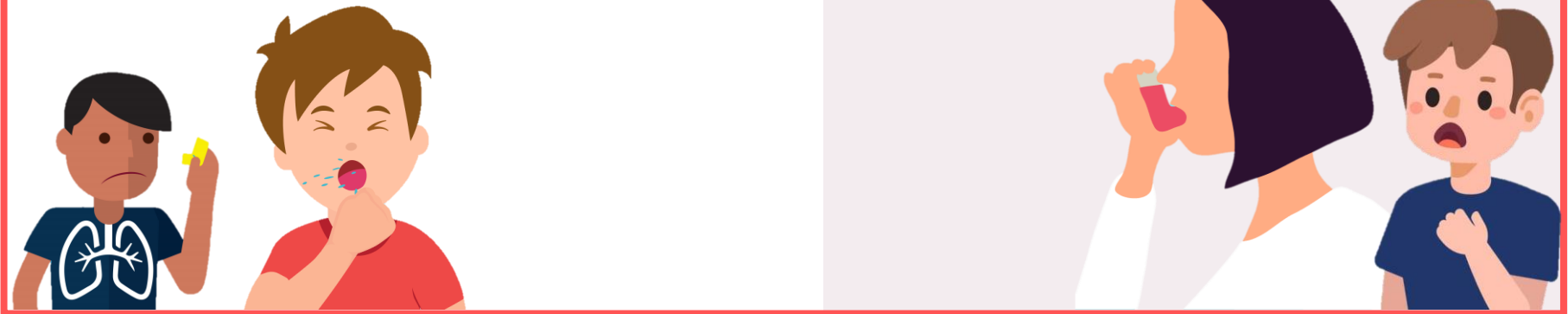
-Re-introduce protective factors that were once part of traditional lifestyles (eg, farming, fermentation of foods, intake of unprocessed cow's milk, fruits, and vegetables, contact with farm animals and pets).

-The ban of smoking in public places significantly reduced hospital admission rates for asthma. For example, in Scotland in 2006 , a reduction in the overall exposure of children to second-hand smoke

-Obesity



Secondary prevention



Is it possible?



**Secondary prevention of asthma:
infants and children who are at high risk for the development of asthma
but who have not yet developed asthma symptoms or signs.**

**Have a family history of allergic disease and 1 or more of the following:
atopic dermatitis or eczema, allergic rhinitis, food allergy, bronchial
hyperreactivity, blood eosinophilia, elevated total IgE levels, elevated
allergen-specific IgE, or skin-test reactivity to specific allergens.**

**From three angles:
pharmacologic treatment
control of environmental allergens and environmental tobacco smoke
allergen-specific immunotherapy**





Pharmacotherapy for secondary prevention of asthma

Certain antihistamines have minor benefits in the secondary prevention of asthma in certain subgroups of children.

The Early Treatment of the **Atopic Child** Study investigated 817 children aged 12–24 months, Cetirizine were administered for 18 months. The overall result of the entire study group showed **no difference** in asthma onset.

In the subgroup of children sensitized to **mite**, cetirizine **delayed asthma** onset at the end of the treatment period, and this effect was sustained **for three years** post treatment. Similarly, in the **grass-sensitized** subgroup there was also a sustained reduction in asthma onset.

ketotifen twice daily for a year showed a significant reduction in asthma at the end of the year's treatment however, the benefits of ketotifen were observed only in those children with a raised total **IgE at study** entry.

The use of **levocetirizine** in this study did not lead to a significant reduction in asthma development.





There is no evidence of a secondary preventive effect in those at risk of asthma with **ICS and montelukst**

A small Italian study published in 2010 showed that **the early diagnosis and management of AD led to a reduction in the evolution to asthma from 15% to 29%**. There is some evidence that early and effective eczema treatment can reduce the progression to aeroallergen sensitization and asthma.

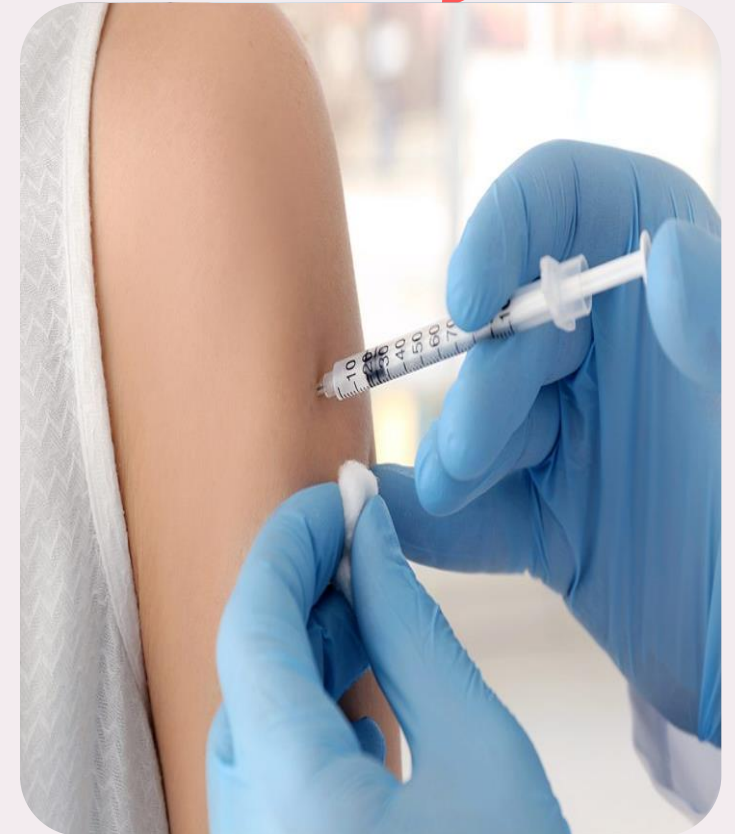


Allergen immunotherapy in healthy children at risk of asthma and allergic diseases

Two studies for allergen immunotherapy in children with eczema, allergen sensitization or family history **but without established AR.**

One of these studies used a HDM, Timothy grass- cat mix and the other only HDM. Neither study showed evidence of the reduction in the development of asthma

Recently published EAACI guideline suggests that sufficient evidence exists to recommend a **three-year** course of allergen immunotherapy for **children and adolescents with moderate-to-severe AR and grass or birch allergy**, in order to prevent asthma for **at least two years post allergen immunotherapy (? Cost)**



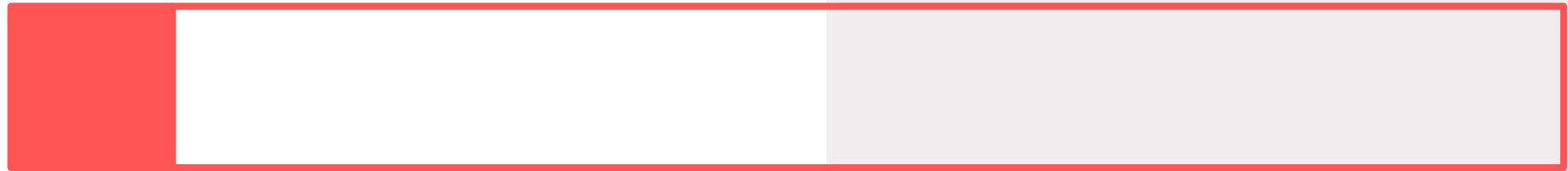
The association between passive smoking and asthma in children, including asthma development and asthma severity, is well-documented.

However, it should be noted that although avoidance of tobacco smoke exposure in at-risk infants and children is logical and universally recommended by physicians, there are no studies proving that avoidance of passive smoking is useful in the secondary prevention of asthma. Moreover, long-term changes in parental smoking habits are difficult to achieve.





Tertiary prevention





Tertiary prevention is reduce symptoms in children with an existing allergic asthma

Medical treatment

Avoidance of known respiratory allergens

Dust mites

Pets

Cockroaches

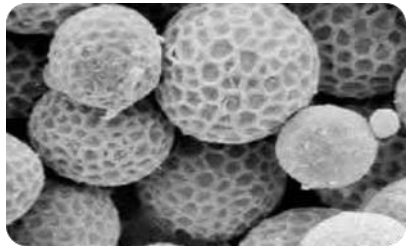
Indoor molds

Pollen

Control of air pollution

Influenza vaccine

Specific immunotherapy has a real place





- **Thanks for your attention**

