



Immunology team - 437

1- Immunology of Bronchial Asthma

Objectives :

1. To know the difference between extrinsic and intrinsic asthma.
2. To be familiar with the types of allergens and their role in allergic sensitization.
3. To understand the inflammatory processes operating in allergic asthma.
4. To know about airway remodeling.



Asthma

Characterized by:

- Episodes of **reversible** airway obstruction
- Increased **bronchial reactivity**
- Airway **inflammation**

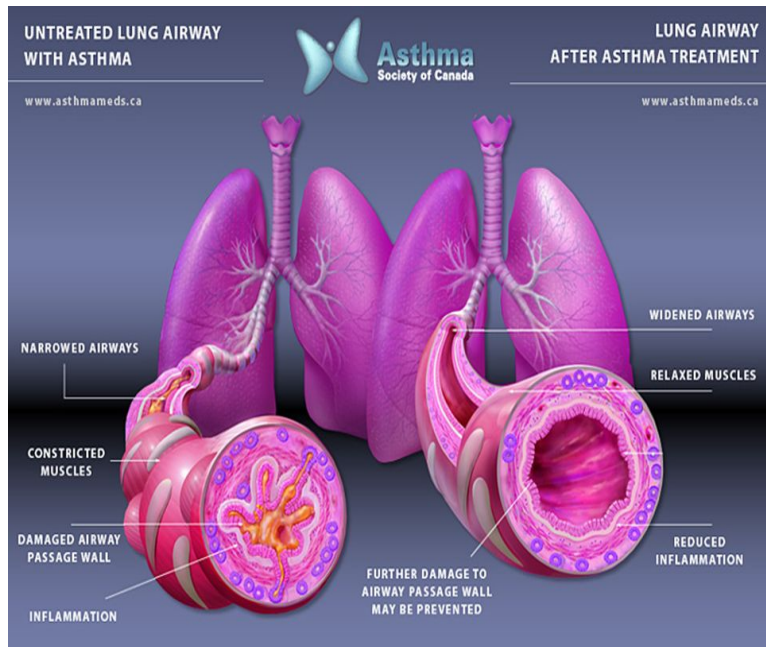
Asthma symptoms:

1. Breathlessness (difficulty breathing)
2. Wheezing
3. Persistent cough
4. Chest tightness

Classification of asthma:

1. Intrinsic (**non-atopic**)
2. Extrinsic (**atopic**)

Atopy: genetic tendency to develop allergy



Classification of asthma:

Intrinsic (non-atopic)	Extrinsic (atopic)(genetic)
(10-33% of asthmatics)	Allergies trigger asthma attacks in: (60-90% of Children and 50% of adults)
<ul style="list-style-type: none"> • Negative skin test (used in hypersensitivity I) • No clinical/family history • Serum IgE level are usually normal • Older patients • More severe 	<ul style="list-style-type: none"> • Approximately 75-85% of patients with asthma have positive (immediate) skin test reactions to various allergens • Serum IgE level elevated • Immune response



Role of antigens:

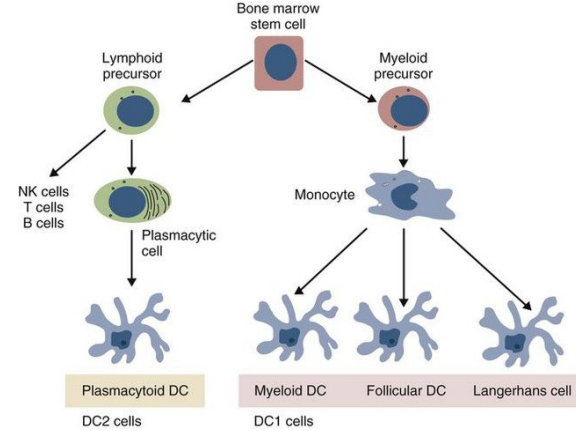
- Allergen sensitization is linked to the risk of developing asthma
- Allergen is an antigen that triggers an allergic reaction.
- The main cause of hypersensitivity type I

Indoor allergens	Outdoor allergens
<ul style="list-style-type: none"> - House dust mites - Domestic pets (cat fur & dander) - Cockroaches (insects) - Molds (fungal spores) 	<ul style="list-style-type: none"> - Fungal spores (e.g. Alternaria) - Grass, tree, & weed pollen

Antigen presenting cells (APCs) in the lung:

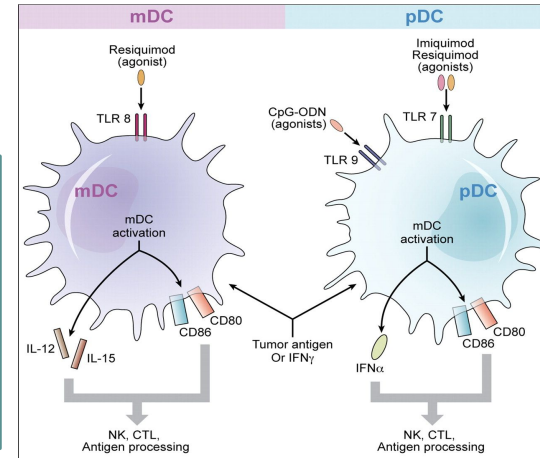
Two subsets of dendritic cells (DCs) in the lungs:

- **Myeloid DCs (mDCs):** help in the development of asthma symptoms
- **Plasmacytoid DCs (pDCs):** aid in respiratory tolerance to allergens

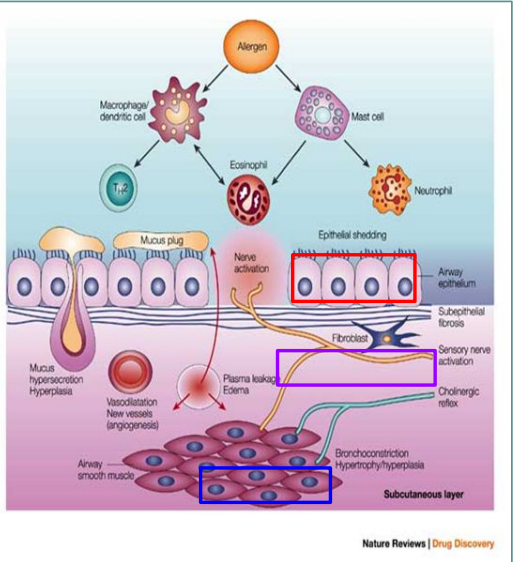


In susceptible individuals (people who are prone to develop asthma):

- First encounter with allergens activate B-cells to produce IgE
- Subsequently, Inhaled allergens activate submucosal mast cells in the lower airways
- ❖ **Mediators** are released within seconds causing:
 1. Bronchoconstriction.
 2. Influx of eosinophils & other inflammatory cells.



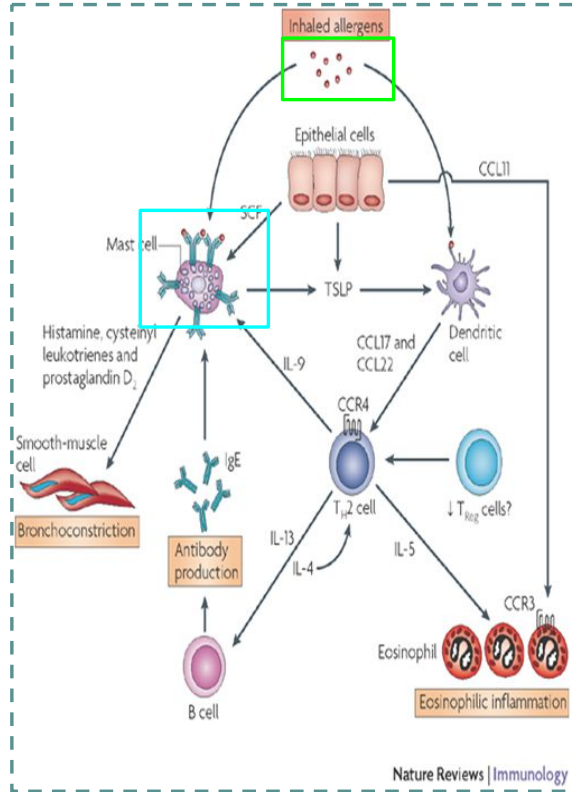
Asthma results from complex interactions among the inflammatory cells that involve:



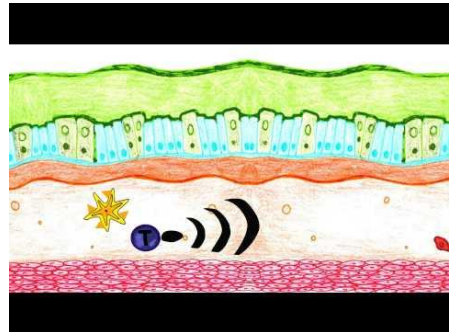
1- Airway epithelium

2- Nervous system

3- Bronchial smooth muscles



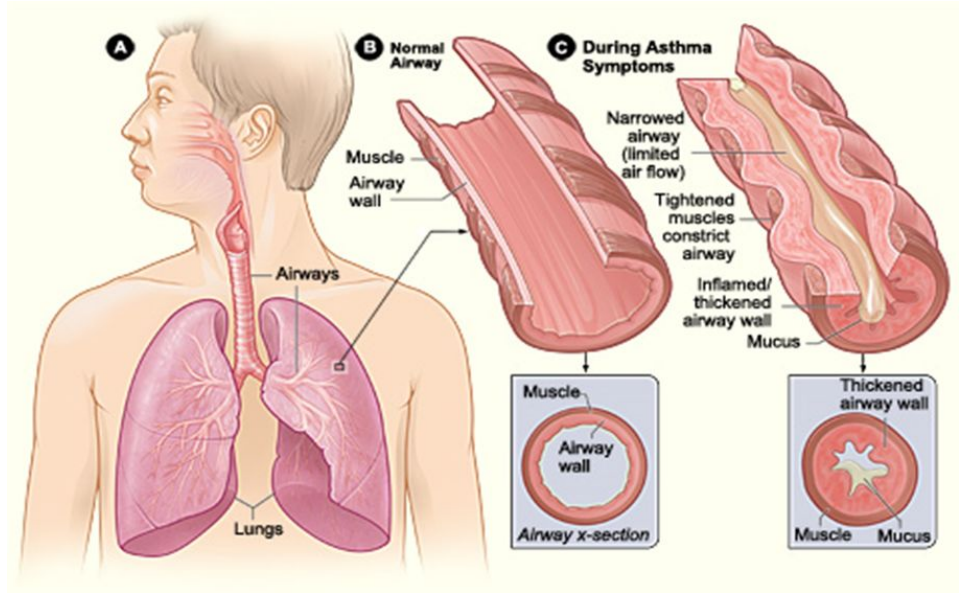
- 1- Inhaled allergen
- 2- Submucosal mast cells in lower airways



Nice video explaining the pathophysiology of asthma

Factors contributing to airflow obstruction leading to difficulty in breathing include:

- 1- Narrowed airway
- 2- Contracted (constricted) muscles
- 3- Inflamed/thickened airway wall
- 4- Excessive mucus production



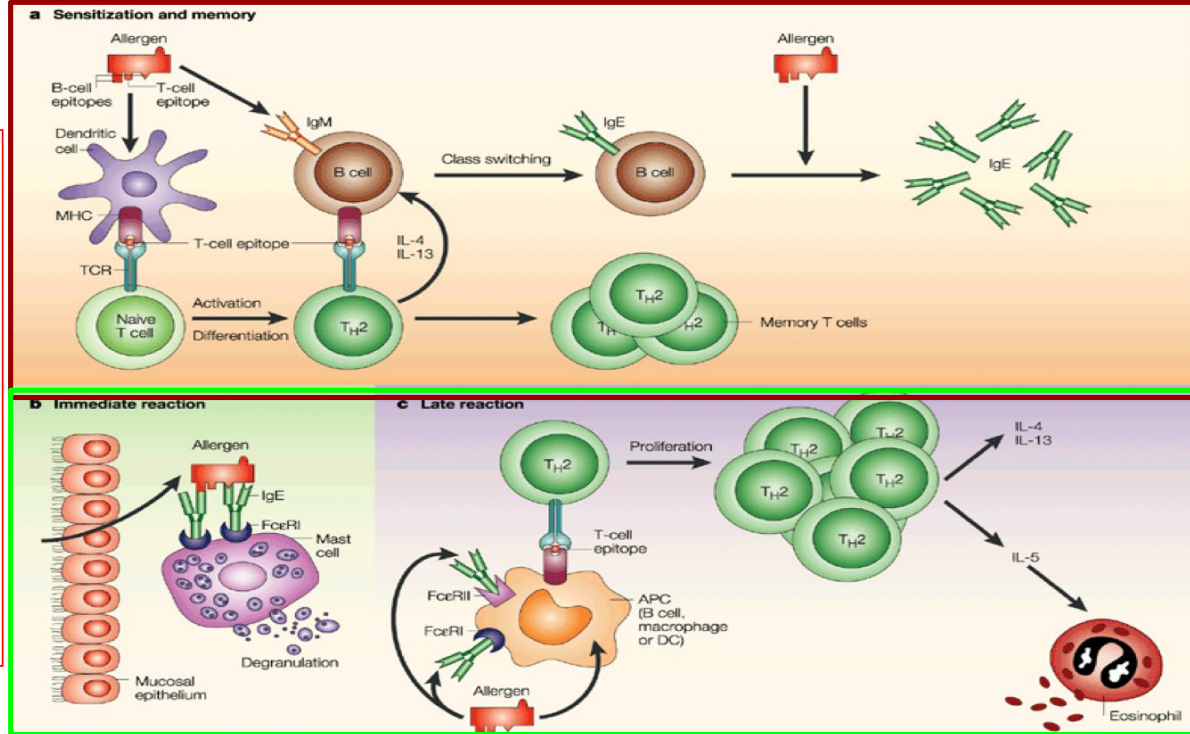
Response to allergens occur in two phases

1st phase sensitization phase:

- First encounter with allergen
- Activation of B lymphocytes into plasma cells
- Secretion of IgE
- Binding of IgE to mast cells

- 2nd phase challenge phase

- Recurrent encounter with same allergen
- Antigens Bind to IgE
- Degranulation of mast cells
- Release of histamine
- Physiological actions



The types of allergic responses

Early allergic response	Late allergic response
Occurs within minutes	Appears 4 to 10 hours later
Manifests clinically as: <ul style="list-style-type: none"><li data-bbox="280 470 738 505">● Bronchial constriction<li data-bbox="280 522 611 557">● Airway edema<li data-bbox="280 573 635 609">● Mucus plugging	<ul style="list-style-type: none"><li data-bbox="979 422 1525 509">● Results from infiltration by inflammatory cells.<li data-bbox="979 522 1554 609">● Activation of lymphocytes & eosinophils
Is reversible and responds to bronchodilators (treatment)	Responds to steroids (Anti-inflammatory drugs)

Th2 cells and role of cytokines in allergic asthma

Allergens drive T-cells towards Th2 type:

Th2 secrete the cytokines:

IL-4, IL-5, IL-9 & IL-13

which promote :

1. Production of IgE by B cells
2. Eosinophil attraction and infiltration
3. Airway inflammation
4. Increased bronchial reactivity

Role of IL-4 in allergic asthma

The main role of IL-4 is carried out during the initial priming of Th2 cells :

1. Regulates **isotype switching** in B cells to **IgE**. (naive B cells usually

contain IgM & IgD antibodies but with the help of IL-4 it switches(isotype switching) to IgE which plays a role in allergic reactions)

2. **Induces MHC II** on antigen-presenting cells.

3. **Induces adhesion molecule** expression.

(important in chemo-attraction)

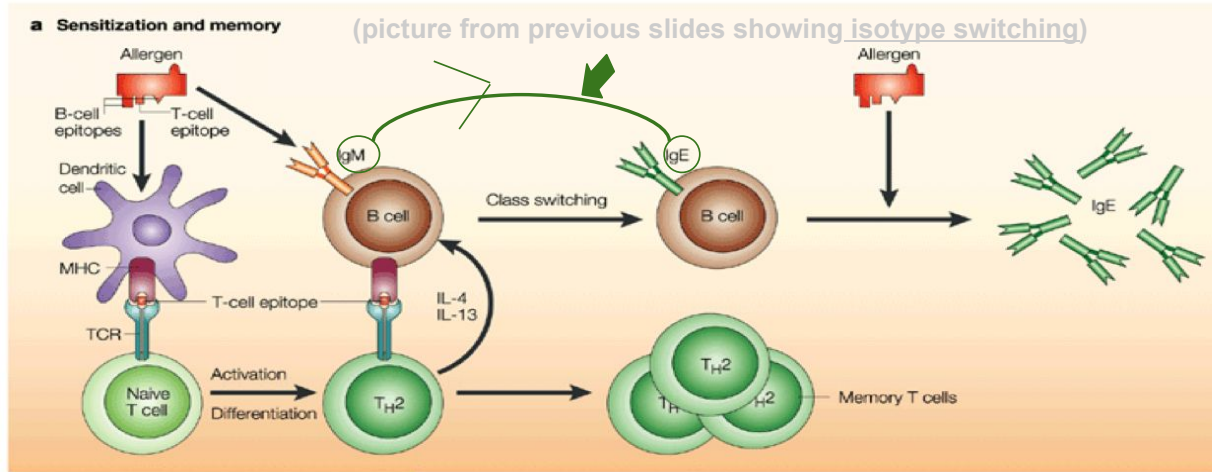
4. **Activate mast cells and eosinophils.**

Role of IL-13 in allergic asthma

1. IL-13 induces inflammation.
2. Stimulates mucus hypersecretion.
3. Induces subepithelial fibrosis.

Role of IL-5 in allergic asthma

1. IL-5 induces an increase in eosinophil production in the bone marrow.
2. Release of eosinophils from the bone marrow into circulation.



Role of:

eosinophils in allergic asthma	regulatory T-cells
Eosinophils initiate asthmatic symptoms by causing tissue damage in the airways of the lungs.	suppress the effector mechanisms that induce asthmatic symptoms.
Production of eosinophils is inhibited by IL-10.	Asthmatics may lack functional regulatory T cells that can inhibit an asthmatic response.

*Activation of inflammatory cells (mast cells, eosinophils etc,) is a major inducer of airway inflammation.

*Airway inflammation is the hallmark in the asthmatic lung.

Products of the inflammatory cells act on :

- 1. Airway smooth muscle cells**
- 2. Lung fibroblasts**
- 3. Mucous glands**

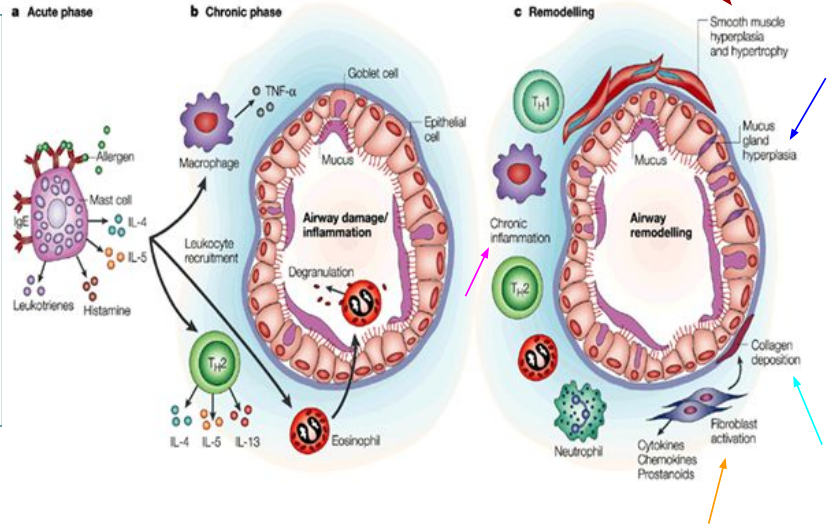
and cause :
Airway Remodeling

Which will lead to

Increased bronchial reactivity

Airway remodeling refers to:

1. Smooth muscle hyperplasia and hypertrophy
2. Mucous gland hyperplasia
3. Collagen deposition
4. Fibroblast activation
5. Chronic inflammation



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Inflammatory cells & their mediators \longrightarrow Airway inflammation $\begin{cases} \longrightarrow \text{Increased bronchial reactivity} \\ \longrightarrow \text{Airway remodelling} \end{cases}$

Outcome of increased airway reactivity:

Predisposes patients to develop asthma attacks on exposure to non-specific irritants:

1. Chemical irritants
2. Smoke & strong perfumes
3. Sulphur dioxide & air pollutants
4. Viral and bacterial respiratory infections أكثر من الشخص الطبيعي

Team 436: (Those are non-specific irritants which means they don't cause asthma they are **NOT allergens**, but they are considered as triggers of asthma attacks in people with asthma)

Outcome of airway remodeling

Can ultimately lead to fibrosis and irreversible airway obstruction in some patients.

Take home messages

1. Asthma is characterized by episodic reversible airway obstruction.
2. Classified in 2 types: intrinsic & extrinsic.
3. In the extrinsic type allergens drive T-cells into Th2 pattern.
4. Airway inflammation is a hallmark finding in the asthmatic lung.
5. Inflammatory cells lead to increased bronchial reactions & airway remodeling which is not revisable.

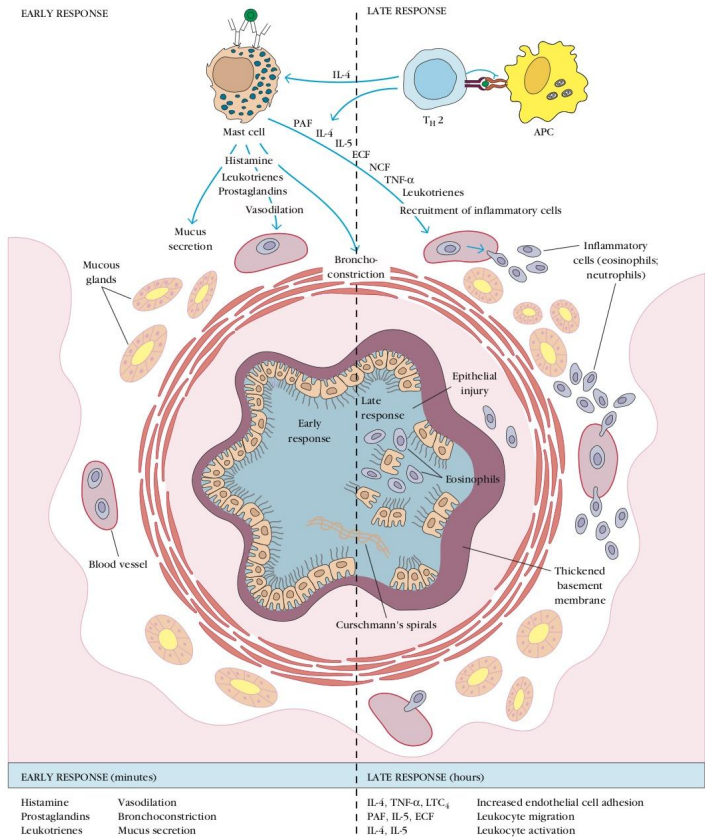


FIGURE 15-6 The early and late inflammatory responses in asthma. The immune cells involved in the early and late responses are represented at the top. The effects of various mediators on an airway, represented in cross-section, are illustrated in the center and also described in the text.

Quiz: Test Yourself!

1- Non-atopic asthma can be detected by skin test.

A) True B) False

2- Which of the following will aid in respiratory tolerance to allergens?

A) Macrophages B) Eosinophils
C) Myeloid dendritic cells D) Plasmacytoid dendritic cells

3- First encounter with allergens activate B-cells to produce:

A) IgM B) IgA C) IgE D) IgA

4- Which of the following induces MHC II on antigen-presenting cells?

A) IL-4 B) IL-5 C) IL-9 D) IL-13

5- Which of the following stimulates mucus hypersecretion?

A) IL-4 B) IL-5 C) IL-9 D) IL-13

6- Which of the following induces an increase in eosinophil production in the bone marrow?

A) IL-4 B) IL-5 C) IL-9 D) IL-13

7- The cell which suppresses the effector mechanisms that induce asthmatic symptoms is:

A) Self reacting T cell B) T helper cell
C) Mast cells D) Regulatory T cells

8- In extrinsic type asthma, allergens drive T-cells into?

A) Th1 pattern B) Th2 pattern
C) Tc pattern D) Self reacting T cell pattern

9- The hallmark in an asthmatic lung is:

A) Increased mucus secretion B) Decreased bronchial reactivity
C) Airway inflammation D) Edema

10- Which one of the following is an indoor allergen?

A) Grass B) Cockroaches
C) Pollens D) Alternaria

1:B
2:D
3:C
4:A
5:C
6:B
7:D
8:B
9:C
10:B

Team members :

- ١ - العنود المنصور
- ٢ - غادة الحيدري
- ٣ - شيرين حمادي
- ٤ - العنود المعيثم
- ٥ - غادة الحناكي

- ١- زياد الخنيزان
- ٢- عبدالإله الدوسري
- ٣- عبدالله العمر
- ٤- عبدالعزيز الدخيل
- ٥- عبدالرحمن الداود
- ٦- فيصل السيف
- ٧- حسين علامي
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