The process begins with the allergen presenting on IgE bound to IgE receptor on mast cells and basophils. This leads to a cascade of events involving other immune cells and resulting in the release of numerous inflammatory mediators into the interstitial space, where they influence the growth and function of cell types within the airway wall. The drugs available for the treatment of asthma are targeted at inhibiting the inflammatory responses (of which steroids are the most important) and/or relaxing the bronchial smooth muscle (beta2 agonists).

**Beta2 Agonists**

- **Short acting (salbutamol):** for treatment of acute symptoms of bronchoconstriction
- **Long acting (salmeterol) for long term control of bronchoconstriction.**

**Antileukotrienes**

- **Cysteinyl leukotrienes (CysLTs):** include leukotriene D4 (LTD4) and leukotriene C4 (LTE4). All the leukotrienes are potent constrictors of bronchial smooth muscle, cause microvascular leakage and eosinophilic and mast cell mediated inflammation. Montelukast is a high affinity competitive antagonist of LTD4 and LTE4.

**Theophylline (Methylxanthines)**

- Methylxanthines are purine derivatives found in beverages, theophylline (theo), caffeine and theobromine (cocoa).
- The mechanism of action is inhibition of Phosphodiesterases (PDEs) which results in increased CAMP and therefore bronchodilation. The other mechanism is competitive antagonism at adenosine receptors which has a myriad of effects (possibly reducing bronchoconstriction and inflammation).

**Omalizumab**

- Omalizumab is a recombinant humanised monoclonal antibody of the IgG1 subtype. It is targeted against IgE bound to omalizumab cannot bind to IgE receptors on mast cells and basophils, thereby preventing the allergic reaction at a very early step in the process.

**Beta2 Adrenergic receptors are found throughout the airways and are involved in both smooth muscle relaxation and reducing release of inflammatory cytokines. Beta2 Agonists activate the G-Protein – Adenyly cyclase – cAMP pathway to cause reduced smooth muscle tone. Unlike the smooth muscle effects, anti-inflammatory response is quickly desensitised and therefore not useful to control inflammation long term.**

**Methacholine**

- Methacholine is a cholinergic agonist which produces bronchoconstriction by stimulating muscarinic receptors.

**Theophylline**

- Theophylline is delivered orally and is absorbed rapidly and completely. It distributes poorly into body fat and has a small volume of distribution.

**Corticosteroids**

- Along with Beta2 agonists these are the mainstay of treatment and are used to suppress the inflammatory response long-term in patients with moderate to severe asthma. They do not directly relax smooth muscle and therefore have little effect in direct bronchoconstriction.

**Antileukotrienes**

- Leukotriene receptor antagonists (Montelukast)
- S-lipoxygenase (leukotriene precursor) inhibitors (Zafirlukast)

**Cough**

- Cough is a common side effect of inhaled corticosteroids and can be managed with a stepwise approach involving education, expectorant medications and, in some cases, systemic treatment with oral antihistamines.

**Beta2 Agonist**

- Beta2 agonists are generally well tolerated, but side effects may include an increased incidence of various types of malignancies during a long study into the drug 5 in 2326 versus 4 in 2127 which requires further study.

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**Phosphodiesterase type 5 inhibitors (sildenafil) and Prostacyclin derivatives (iloprost and epoprostenol).**

- These provide the therapeutic targets. In addition to Ca Channel blockers, the main therapies are Endothelin receptor antagonists (Bosentan), Phosphodiesterase type 5 inhibitor (sildenafil) and Prostacyclin derivatives (iloprost and epoprostenol).