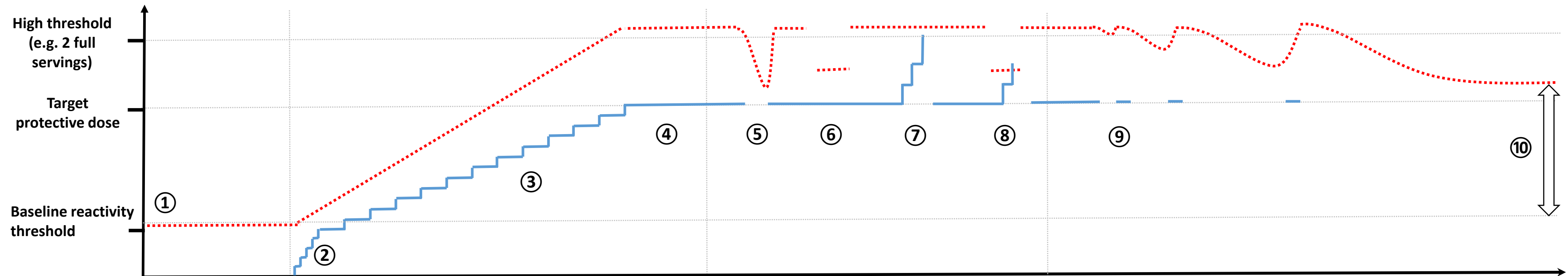
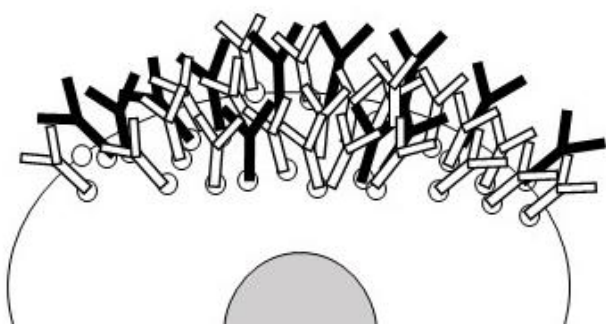


- ① Reactivity threshold (**dotted red line**), corresponds to the amount of food that will trigger a reaction. It varies between patients and can also vary over time.
- ② During the **initial food escalation**, the food allergen (**full blue line**) is introduced in clinic for the first time to identify a dose below the reactivity threshold to begin daily home dosing.
- ③ The amount of the daily home dose is then increased periodically under medical supervision during **up-dosing visits**.
- ④ Once the target maintenance dose is achieved, the patient is protected against accidental exposure to at least that amount (**protective or partial desensitization**) as long as the food is eaten regularly.
- ⑤ Regular ingestion of the food is paramount. If food dosing is stopped, the reactivity threshold will decrease progressively patient could react upon reintroduction.

- ⑥ In presence of external **co-factors**, which contribute to additional mast cell activation or disturb gastro-intestinal barrier function resulting in spikes of allergen absorption, the reactivity threshold can decrease even below the daily food dose. Patient training and action plan is thus required to recognize and adapt treatment in presence of co-factors.
- ⑦ A **high threshold challenge** can be performed to a higher amount (e.g. 2 full servings of the food) to determine the full extent of protection while on maintenance (**complete desensitization**).
- ⑧ To assess the risk posed by co-factors, a challenge with the allergen can be performed after administering aspirin and alcohol or with concomitant exercise.
- ⑨ **Sustained tolerance testing** can be performed by progressively increasing the dosing interval and monitoring for return of reactivity.
- ⑩ When stopping food doses after prolonged treatment, some patients will have achieved sustained unresponsiveness to their allergens. Most will find their reactivity threshold to have increased compared to baseline level before treatment.

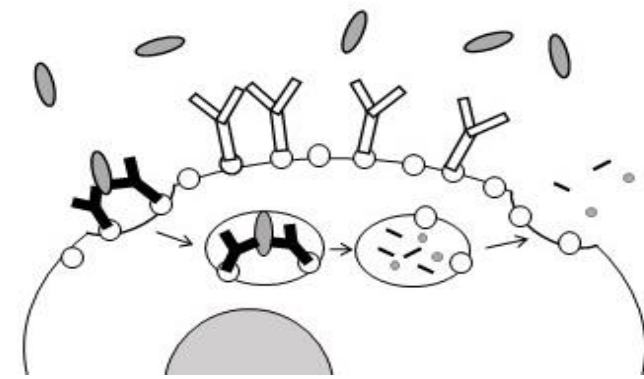


Avoidance



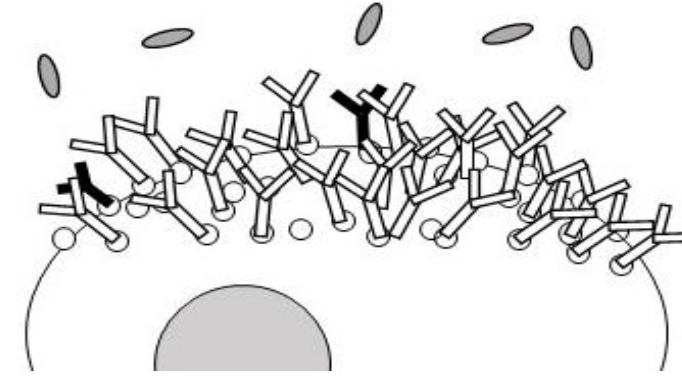
During avoidance, mast cells are armed with various IgE antibodies including those specific to the allergen (black). These act as detonators to activate the allergic cascade. The reactivity threshold is in great part determined by the extent of allergen-specific IgE on the mast cell surface.

Escalation phase



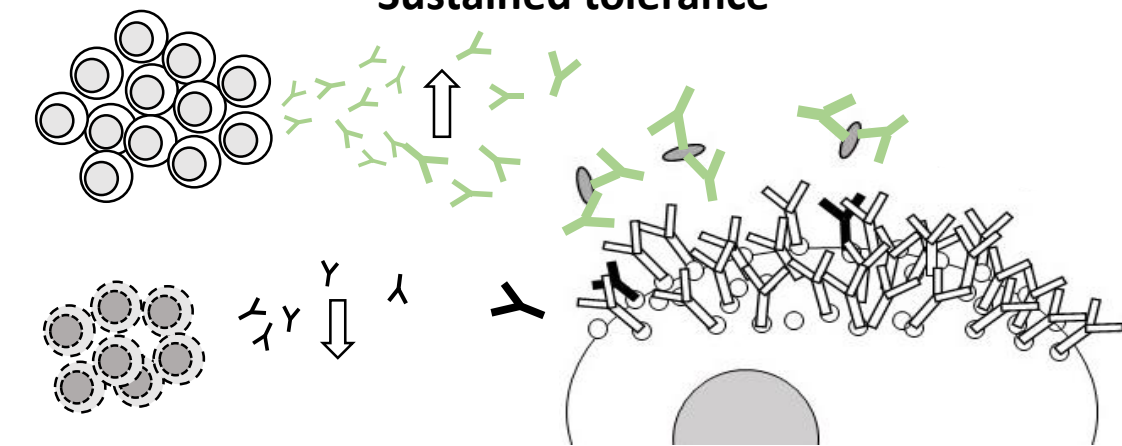
When IgE antibodies bind their allergens, the IgE-allergen complex is internalized and digested by the cell, with only the empty receptor recycled to the surface. The receptor will rearm with a new IgE, possibly non-specific to the allergen. OIT consists in ingesting the food allergen in amounts that are below the reactivity threshold in order to progressively disarm the mast cells and increase that threshold.

Maintenance



Newly bound specific IgE is cleared continuously as long as the food allergen is eaten regularly. If regular ingestion is stopped, mast cells will rearm more or less rapidly with IgE specific to the allergen.

Sustained tolerance



Over time, usually 3 to 5 years, continuous exposure to the allergen can exhaust and/or modulate the immune response against the allergen resulting in decreased production of IgE and new production of IgG4 neutralizing antibodies, which can contribute to sustained unresponsiveness to the allergen despite discontinuation of regular food dosing.