Allergy Skin Testing in Clinical Practice

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INTRODUCTION

Diagnosis of allergic disease can be made by comprehensive anamnesis and physical examination. However, skin testing as the supporting examination is very useful in making the diagnosis of allergic diseases and identifying the specific allergen. The ideal methods of skin testing can be done easily in short time and can be repeated. In clinical practice, we also know skin testing is called the patch test which is very useful in diagnosing contact dermatitis. Unfortunately, this particular test will not be discussed in this paper. The methods of skin testing will be discussed later and only will be done in making diagnosis of type 1 IgE mediated hypersensitivity reactions such as bronchial asthma, allergic rhinitis, and atopic dermatitis.

SKIN TESTING PATHOPHYSIOLOGY

In vivo skin test is very useful in identifying the specific allergen which is IgE specific by inserting the relevant allergen extract into the skin. The bind that occurs between specific surface IgE of sensitized skin mast cell will make the redness of the skin and wheal reaction. This reaction is the same as histaminic reaction which is the products of inflammatory reaction or cellular neurogenic interaction.

The rapid reaction is initiated by mast cell degranulation which releases preformed and newly synthesized mediators. One of these is histamine, the main mediator which causes erythema and wheal can be found in 5 minutes after exposure to allergen and the following peak reaction will occur in 15 minutes. The biological effects of histamine are vasodilatation, plasma fluid extravasation and nerve stimulation. The rapid reaction manifestations are local erythema, edema and flare redness of the skin.

Rapid reaction in the skin may be followed by delayed reaction manifestation such as diffuse edema, mild induration around the redness of skin area and wheal. Isolated rapid reaction accounts for about 6% – 14%. Approximately 85% of delayed reaction is initiated by rapid reaction. Delayed reaction intensity is associated with rapid reaction. It begins in about 1 – 2 hours after exposure to specific allergen and will reach the peak in 6 – 12 hours and then will disappear in 24 – 48 hours. Like the rapid reaction, delayed reaction also needs specific allergen and the IgE interaction although its pathophysiology is still unclear. It is presumed that mast cell mediators mobilize inflammatory cells such as CD4, neutrophils and eosinophils, which are not only initiating but also maintaining the delayed reaction. Various kinds of mediators such as histamine, kalikrein, thromboxan b2, interleukin-4, interleukin-5, RANTES, leucotrien C4, prostaglandin D2 and platelet activating factor have roles in occurrence of delayed reaction. The fact that not all rapid reaction is followed by delayed reaction remains unclear.

SKIN TESTING METHODS

In vivo allergy testing includes intracutaneous and epicutaneous skin testings. In epicutaneous, the allergen is applied on the skin before being introduced to the epidermal layer, while in intracutaneous method the allergen is inserted into the skin. The epicutaneous methods are scratch test, prick test. In the scratch test, skin surface is scratch by particular tool which is not sharp and then allergen is applied to skin area of 0.3 to 0.6 in diameters. This method is less meticulous, thus it is now rarely used in making diagnosis of allergic diseases. The most applied allergy skin testings are the scratch test and prick test. Intracutaneous test is used for less potential and less sensitized extract. The benefits of prick test are less painful method, less side effects and easy procedure.
Prick test
The skin reaction may vary because the amount of allergen introduced is not exactly the same and also the difference in endurance, length, depth or angles of insertion. Hence, now the uniform standard technique and diagnostic tools have been widely developed commercially.

SKIN TESTING PREPARATION
The first generation of antihistamine is generally must be stopped at least three days before doing the examination, while the second and third generation of antihistamin must be stopped for at least 7 days. The use of inhaled steroids does not influence the skin testing result, but long term oral steroid will. It is recommended to stop the steroid drugs for at least 3 to 5 days before examination.

SKIN TESTING AND RISK OF COMPLICATION
Although it seems that the skin test is a simple procedure but it also has the risk of complication from mild to severe one like anaphylactic shock. Among things that must be given careful attention are:
• Skin testing will only be done in the presence of in charge doctor who will be ready to give proper treatment if the reaction occurs during the test
• The emergency drugs and equipment are well provided
• Must not be done in patients who have allergic symptoms such as wheezing, wheals, etc
• The potential and stability of extracts is used in the skin testing is well known
• Make sure the allergen concentration is accurate
• Use the negative and positive controls
• Do the test on the healthy skin surface
• Read the test in appropriate time

SKIN TESTING INTERPRETATION
The reaction to aeroallergen is considered positive if the wheal is 3 mm or more in diameter and there is no reaction on negative control. The positive result means the presence of allergen which is IgE specific on the surface of mast cell and induces the degranulation response. Positive result may be found in person who has no clinical symptoms. Interpretation of skin test depends on history and clinical symptoms as response to allergen exposure. These are not easy to be evaluated in patients who have chronic symptoms or are unaware to low exposure of specified allergen.

The peak response of rapid hypersensitivity skin testing may occur in 10 – 15 minutes after allergen insertion. In clinical practice, the test result can be observed in 15 minutes. The skin testing interpretation usually observes the size of wheal and not the redness. Skin testing interpretation is as follows:
0 same as negative reaction
1+ Erythema and wheal 2 mm in diameter
2+ Erythema and wheal 4 mm in diameter, no pseudopodia
3+ Erythema and wheal > 5 mm in diameter, with or without pseudopodia
4+ Erythema and wheal > 10 mm, with or without pseudopodia

The skin testing interpretation according to other references:
0 Same reaction as negative control/no response
1+ Only erythema
2+ Erythema with wheal < 3 mm in diameter
3+ Erythema with circular wheal 3mm indiameter
4+ Erythema with wheal 3mm in diameter and pseudopodia

Factors That May Influence The Skin Testing
a. Drugs
Histamin antagonist will prevent the skin reaction to allergen and histamine. The duration of this effect depends on generation classification of antihistamin (see the skin test preparation above)
Other drugs that could prevent the rapid reaction are antidepressant, phenotiazine, dopamine and clonidine. Theophyllin, b-agonist and cromolin can be consumed before the skin testing. ACE inhibitor and b-blocker may increase skin reactivity. In general, the positive control of histamine may be used as the appropriate basic interpretation.

b. Age
Babies until the age of one year show low histamine reactivity, redness predominant and small wheal. Skin reaction to histamine increases gradually in children under five until aged 15 – 20 years and maintained steady. It begins to decrease after the age of 50. Skin reaction to allergen also increases in accordance with increasing age. Thus, skin testing can be done in all of age but the interpretation of the result must be compared to reaction induced by allergen or histamine. After one year of ages, the skin testing is best done using special diagnostic tool called Multitest. By using this, 8 kinds of allergen can be inserted at the same time without causing much pain. The place of insertion in child is usually in thigh
because this skin area is wider than the volar arm.

c. Other variable

Skin reactivity is varied and it depends on area of prick test is done. The upper and middle back is more sensitive than the lower part. However, for practical reason, the optional area is the lower volar arm. The seasonal reaction may be found in pollen allergy. The reaction increases after pollen season, assumed due to priming effect to skin and it decreases after the season passes by.

Patients with atopic dermatitis may show decreased response. Spinal cord diseases, peripheral neuropathy, malignancy, renal failure can show decreased skin reaction as well.

ALLERGEN EXTRACT SELECTION

Hundreds of commercial allergens are available for skin testing. In the allergic examination, it is recommended to use high quality and standardized allergen extracts. The extract potential is usually labeled according to weight per volume or protein nitrogen unit (PNU). New standard in the US is BAU/ml (bioequivalency allergy units per ml). The allergen potency is determined based on in vitro reaction. Standard extracts containing allergen are consistent, safe and efficient. For making good and long lasting products, the extract is stabilized in 50% glycerin. Some products have also preservatives. The potency will decrease in time and need to be restored in cool place of 4 – 8 C.

REFERENCES