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Allergy Skin Testing Methods Immunological Comparison

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ABSTRACT

This literature review discusses how immunological reactions develop and evaluates which skin testing method for allergies is preferred in clinical settings. This paper explains the different types of allergic reactions and their classification, as well as how the body responds to allergies and why they form. Through discussing the four main comparison criteria, accuracy, safety, comfort, and efficiency, this paper discusses the difference between skin prick testing and intradermal testing, and finds that skin prick testing is more clinically preferred. Following an inclusive comparison between the two most common skin testing methods for allergic reactions, this review then examines papers which contradict the argument of skin prick testing being clinically favoured. Overall, this review concludes that skin prick testing is generally preferred as the first-line method because of its cost efficiency, less technically demanding skills, higher specificity with fewer false-positive results, more comfort for the patient, and efficiency of being able to test multiple substances at once, while intradermal remains a second-line approach and is used in specific cases where greater sensitivity is required. Finally, this paper emphasizes the importance of skin testing and highlights future clinical development.

SKIN TESTING METHOD FOR ALLERGY TESTING INTRODUCTION

When people eat certain foods and develop sneezing, skin issues, nasal congestion, asthma, and in some cases even die without knowing why, they are experiencing an allergic reaction (Undem & Taylor-Clark, 2014). Since the acknowledgement of hay fever in 1870, allergic reactions have increased to now being called an allergic epidemic (Krempski et al., 2020). Some common allergic reactions are eczema (dry and itchy skin) and hay fever, which have shown an increase in the 19th century (Jarvis & Burney, 1998). The most serious allergic reaction is asthma, where 1 in 15 people have trouble breathing, causing 100, 000 hospital admissions each year in England and Wales alone (Jarvis & Burney, 1998). Because of the increased rates and the commonality of it, it is clear that allergic reactions are extremely serious.

In order to understand why these allergic reactions occur and how they can be so dangerous, it is important to understand what causes the body to react internally. This stems from the immune system, where immunoglobulin E is found to play an important role in regulating a wide range of allergic reactions: asthma, skin issues, and food allergy (Krempski et al., 2020). To know which substances can trigger an individual to develop allergies, safe testing must be used (Nevis et al., 2016).

Skin testing is often used to test different substances on patients because of its accuracy (Nevis et al., 2016). The most commonly known forms of skin testing are skin-prick and intradermal testing (Nevis et al., 2016). Skin-prick testing is seen to be more common since it only involves the pricking of skin, allows a huge variety of substances to be tested on a small surface area, and shows quick results (Nevis et al., 2016). On the other hand, intradermal testing involves injecting the patient, which needs more patience and care since substances are being injected into deeper layers of the skin (Nevis et al., 2016). Previous studies demonstrate that skin prick testing is a common way to test for allergies, although contraindications do arise. Even though skin prick testing only has 49% sensitivity[1], and intradermal testing has 73% sensitivity, and even with higher sensitivity, intradermal testing still shows higher rates of false-positives[2] (Gupta & Anand, 2023). With these in mind, it raises some questions. What makes one method better than the other? Do efficiency, sensitivity, and previously discussed factors play a role in determining a better method? What does skin testing look like for the future? How does skin testing relate to the immune system? Through the review of skin testing methods, this paper investigates how the immune system reacts to allergens and argues that skin prick testing is noted as the preferred method for accurately determining allergy severities over intradermal testing because skin prick testing provides a better balance of accuracy, safety, patient comfort, and clinical efficiency.

2. ALLERGIC REACTIONS

This section will explain the four different types of allergic reactions and how they are classified, with a table summarizing their key characteristics. This section will also discuss common allergens that cause allergic reactions, such as food, seasonal, and materials. Finally, it will also explain the role of the immune system in each type of reaction and explore how these mechanisms are related to skin allergic reactions.

2.1 Categorization of Allergies

There are four main allergic reaction types: Type I, Type II, Type III, Type IV (Buelow & Kaliner, 2024), as shown in Figure 1 below. These reactions are classified based on their underlying mechanisms and the time it takes for symptoms to appear. Type I reactions occur immediately after exposure to an allergen, Type II reactions develop within minutes to hours, Type III reactions occur several hours to at most, 48 hours, and Type IV reactions appear 48 hours or more after exposure (Rajan, 2023). The type and intensity of treatments depend on the patient's immune response and the type of allergen involved (Krempski et al., 2020).

Furthermore, different allergens are associated with different types of allergic reactions. Type I immediate reactions are most commonly triggered by food and pollen; Food allergic reactions can be particularly

[1] Proportion of true positive tests out of all patients with the condition

[2] This is because skin prick testing inserts substances near the surface of the skin while intradermal inserts the substances deeper, which causes the immune system to respond more to intradermal testing causing higher sensitivity; But because intradermal testing involves inserting the needle deeper into the skin, it can also cause irritations and swelling which contributes to more false-positives than skin prick testing (Longo et al., 1986).

dangerous because they are being inserted into the body and can block airways, which then become life threatening (Valenta et al., 2015). Type II and Type III are very similar, as both mainly consist of drugs or medicines, as well as infections and bites (Valenta et al., 2015). In contrast, allergens found in cosmetic products and materials used in our daily life are associated with delayed reactions, particularly Type IV; few cases of cosmetic and material allergies have been seen as deadly because most cosmetic products and materials are only used on the surface of the skin, unlike food, which does not block airways so it is easier to treat (Valenta et al., 2015). Although skin allergies are not usually life-threatening, chronic conditions, such as dermatitis and eczema, were the most commonly found skin issues, and in long term cases, they can significantly affect patients (Fonacier et al., 2010).

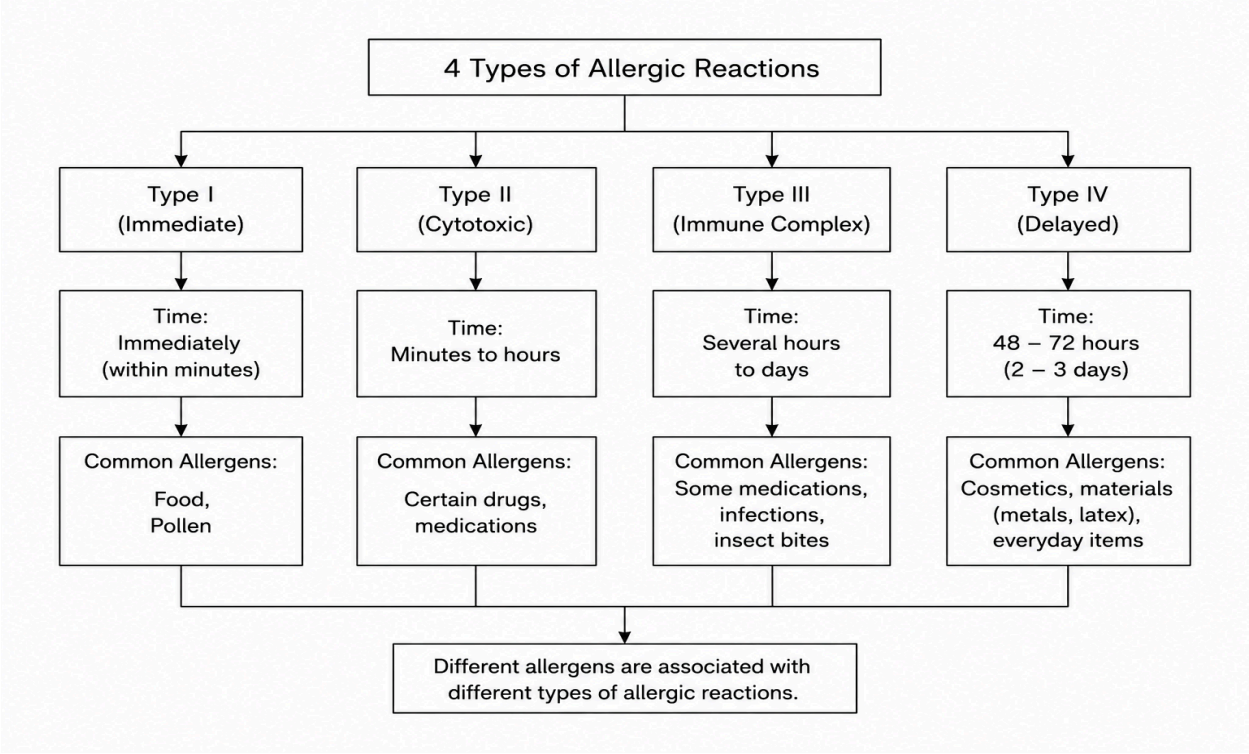

Figure 1.

The Figure 1 above presents the different types of classified allergic reactions and their connections to skin responses. As the types of allergic reaction appear on the skin, various skin conditions can be associated with each of the four types of hypersensitivity reactions. By examining the time required for each reaction to occur and the differences among the four types, Figure 1 provides a broad perspective on the relationship between allergy classification, skin responses, and common allergens.

3. HOW DOES THE IMMUNE SYSTEM WORK

The immune system is the central focus in the field of Immunology, where doctors look at the immune system's defense and strength (Zach & Greslehner, 2023). This section provides a basic background understanding of allergic reactions that occur through a series of immune responses designed to protect the body from perceived threats. By understanding how the immune system functions and how these defense mechanisms fail, healthcare specialists are able to find antibiotics and effective treatment to help the patient's immune system be able to fight against certain bacteria, allergies, and viruses. While evaluating the immune responses, specialists consider several factors, including the intensity of the response, particular substances involved, whether the location of the reaction (whether external or internal) and the length of time the response persists (Zach & Greslehner, 2023). Allergic reactions are one example of an abnormal immune response. They help understand how the immune system functions and develop diagnostic methods.

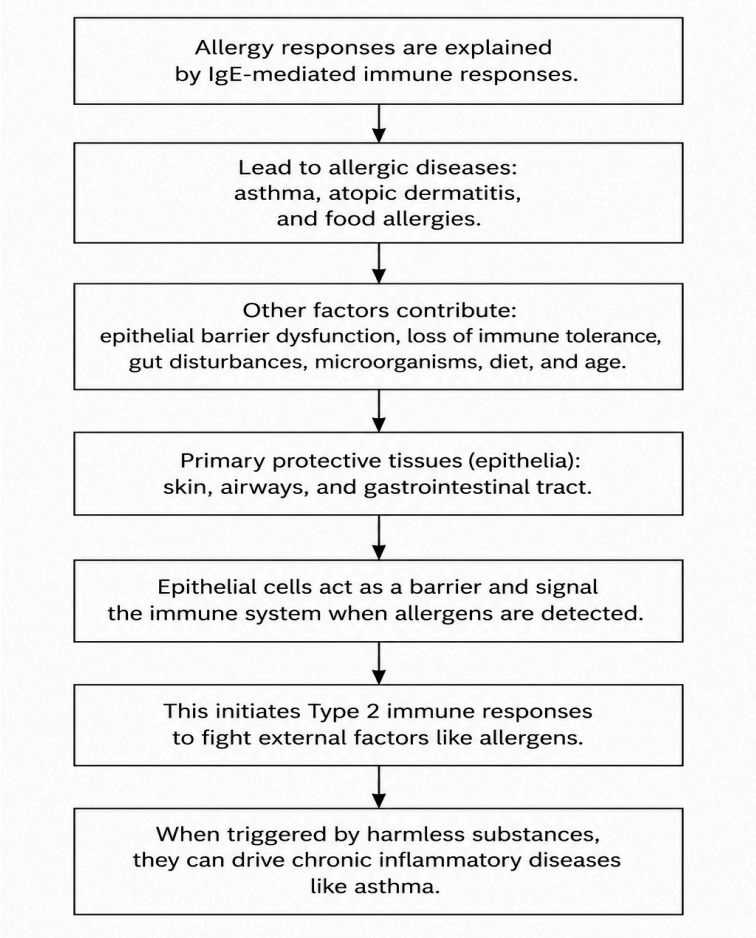

Figure 2. (Krempski et al., 2020)

After discussing the background of how the immune system responds to stimuli, it is important to relate it to allergen factors and the process of the immune response when exposed to allergens. Allergy responses described above are illustrated above. Figure 2 illustrates IgE-mediated immune responses for asthma, atopic dermatitis, and food allergies (Krempski et al., 2020). Previous research suggests there are other factors that contribute to allergic diseases: inherent epithelial barrier dysfunction (defect in cellular barriers that line body surfaces), loss of immune tolerance, disturbances in the gut, microorganisms, diet, and age (Krempski et al., 2020). The primary tissues protecting patients from external insults are the epithelia of skin, airways, and the muscular tube running from mouth to anus (Krempski et al., 2020). The epithelium of the skin (outermost layer) not only acts as a physical barrier but also actively responds to stimuli from allergens by signalling proteins from the barrier cell to alert the immune system of external threats. This then initiates Type 2 immune responses[3], which are defence mechanisms evolved to fight external factors such as allergens (Krempski et al., 2020). When they are triggered by harmless substances, they can drive chronic inflammatory diseases like asthma (Krempski et al., 2020).

4. SKIN TESTING

Because of ease of administration and being less invasive, skin-prick testing, pricking skin with substances, is recommended for determining allergic rhinitis, the collection of symptoms that develop when the immune system becomes sensitized and overreacts to allergens, followed by intradermal testing, the injection of a substance under the skin (Nevis et al., 2016). Nasal provocation, substances injected into the nose, can also be used as a reference for allergic rhinitis, also known as hay fever (Nevis et al., 2016). Some symptoms caused by allergic reactions include: nasal congestion, itchy eyes, sneezing, asthma, and itchy, swollen skin (Undem & Taylor-Clark, 2014). These symptoms can occur due to mediators being released during allergic reactions that interact with sensory nerves that alter the transmission in the nervous system's fight-or-flight response (Undem & Taylor-Clark, 2014).

Skin prick testing and intradermal testing are two commonly used methods of skin testing. Although the choice between these methods may depend on the patient's comfort levels and the practicality of the situation, skin prick testing is generally used and highly preferred because it is less invasive and easier to administer.

5. METHOD

The present study aims to explore and discuss the two skin testing methods, skin prick testing and intradermal testing. This study used secondary research data. This research method consisted of three steps. First, to find these articles, keywords were searched on two academic databases: Google Scholar and PubMed. The list of keywords is given below. “Skin testing methods and comparison”, “Skin prick testing”, “Intradermal testing”, “Allergic reaction immune response”, “Accuracy of skin testing methods”, “ Comfort and safety of skin testing methods”, “Efficiency of skin testing methods”, “Types of allergic reactions and classification”. Then, official academic peer-reviewed journals were collected through these databases. Following this, the abstract, introduction, results, and discussion sections were carefully

[3] Defense mechanism primarily designed to fight parasitic infections and repair tissue

evaluated to ensure that the collected journals were related to the present study. Finally, the articles found were categorized into three sections: background of allergic reactions, the two skin testing methods, and contradictions against the two skin testing methods.

In total, 40 articles were found for the initial overview, but were narrowed down to 25 in the end. 12 articles consisted of the background information or definitions, (Buelow & Kaliner, 2024; Fonacier et al., 2010; Jarvis & Burney, 1998; Knol & Gilles, 2022; Krempski et al., 2020; Rajan, 2023; Ross & Montoya, 2015; Schmid-Grendelmeier & Crameri, 2001; Shreffler & Huecker, 2023; Undem & Taylor-Clark, 2014; Valenta et al., 2015; Zach & Greslehner, 2023). 11 articles consisted of the two skin testing methods, (Ansotegui et al., 2020; Dreborg, 1993; Gupta & Anand, 2023; Heinzerling et al., 2013; Longo et al., 1986; Nevis et al., 2016; Patel & Saltoun, 2019; Peltier & Ryan, 2007; Reid et al., 1993; Singh et al., 2021). Finally, 2 articles were used for contradictions (Hurst et al., 2002; Harries et al., 1984).

No restrictions were placed on publication dates to examine changes in the development of allergy testing over time. This paper includes peer-reviewed literature reviews and experimental studies. The inclusion criteria were peer-reviewed journal articles addressing at least one of the following topics: the background of allergic reactions, two skin testing methods, or contradictions between the testing methods. The exclusion criteria included online sources, articles unrelated or short academic papers containing insufficient or incomplete information. Reports and posters were also excluded because they were not peer-reviewed and officially published in credible academic journals.

6. ARGUMENT: WHICH SKIN TESTING IS COMMONLY USED BY DOCTORS

By synthesizing and discussing numerous studies in skin testing, this section examines skin prick testing and intradermal testing according to the four main criteria: accuracy, safety, patient comfort, and efficiency. Findings from both experimental and review papers were considered to provide a comprehensive evaluation of the two testing methods. Although some studies report contradictory findings, these contradictions are discussed at the end of the section to provide a balanced evaluation of both testing methods.

6.1 Accuracy

In order to examine the accuracy of both methods, it is important to understand that “sensitivity and specificity are essential indicators of test accuracy and help healthcare providers assess the appropriateness of the diagnostic tool” (Shreffler & Huecker, 2023). Specificity is the percentage of true negatives out of all subjects who do not have an allergy (Shreffler & Huecker, 2023). Sensitivity, on the other hand, is the percentage of true positives out of all the patients who have the allergy (Shreffler & Huecker, 2023). Specificity and sensitivity are inversely related, which means when a skin testing method has a higher specificity, it has a lower sensitivity and vice versa (Shreffler & Huecker, 2023). An important aspect to note is that experimental studies do not measure accuracy directly; Instead, accuracy

is often evaluated using measures such as specificity and sensitivity, depending on the aspect of the testing method being investigated.

Numerous experimental studies support the use of skin prick testing. One of the earliest studies was conducted by Longo et al. (1986), who compared skin prick testing and intradermal testing in patients with suspected inhalant allergies. An important factor to note in this experiment is that the researchers also tested on children at least 4 years of age as well, making the patients more diverse and creating stronger results. By comparing blood test results with both skin tests, Longo et al. found that intradermal testing had higher sensitivity levels but also produced a higher false-positive reaction, which can be due to inflammation. Skin prick testing, on the other hand, has lower sensitivity levels and generally causes less inflammation, and therefore may produce fewer false-positive results. After comparing the two methods, Longo et al. concluded that skin prick testing is simpler, quicker, cheaper, and results in fewer false positives than intradermal testing. Although this study was published decades ago without mentioning the sample size, it remains important because it was among the first to compare the two testing methods across different age groups.

Another recent experimental study, conducted by Singh et al. (2021), provides further support for the findings of Longo et al. Singh et al. offer a more detailed description of their participants. They interviewed 49 patients with a history of cutaneous drugs and each patient underwent skin prick testing and intradermal testing and found that the sensitivity level for skin prick testing was 49% while intradermal testing was 73%[4], indicating that intradermal testing was more effective at detecting patients with true allergic reactions. However, they concluded that skin prick testing is a safer option for patients exposed to cutaneous drugs because sensitivity is only one measure of accuracy. Intradermal testing may cause stronger inflammatory reactions with more false-positive results. Nevertheless, the sample size in this study is relatively small with a focus on patients with cutaneous drug reaction, which limits the reliability of its findings. Intradermal testing remains an effective second-line testing method.

In addition to experimental studies, secondary research provides support for the accuracy of skin prick testing and its clinical usefulness. Nevis et al. (2016) conducted a systematic review of studies from several databases, including EBM Reviews from 2005 to March 2015; Embase from 1980 to March 2015; and Ovid MEDLINE(R) from 1946 to March 2015. Their meta-analysis of seven studies including a total of 430 patients showed that intradermal testing had higher sensitivity, while skin prick testing demonstrated stronger specificity, with specificity rates ranging from 60% to 100%. Higher specificity means that if the patient tests positive, they are confirmed to be allergic, rather than resulting in a false-positive leading it to be accurate. Their findings suggest that skin prick testing provides more reliable results by reducing false-positive reactions. Nevis et al's study is highly convincing as they have reviewed a large number of papers from multiple databases.

[4] However, higher sensitivity does not directly indicate higher accuracy. Higher sensitivity means there are more true positives in patients with the allergy, but sensitivity is only one of the indicators of test accuracy because specificity should also be considered.

Similar to Nevis et al's study, Gupta and Anand (2023) conducted a more recent study where they collected data from studies published from 1880 to 2023 instead of 2005 to 2015, having a larger vast collection. After reviewing previous studies regarding the accuracy of skin testing, they concluded that skin prick testing contains 50% Glycerin that makes the reaction more stable, while intradermal testing does not contain Glycerin at all. Based on their review of multiple experimental studies, they suggested that skin prick testing can replace intradermal in many cases because intradermal testing is associated with higher rates of false-positive results. Nevertheless, intradermal testing is particularly useful for certain patients with drug allergies, especially beta-lactam allergies. However, the extensive publication raises questions about the reliability of the evidence because testing methods and clinical practices may have changed over time.

Overall, it is clear that accuracy is an important factor to consider. These studies highlight the importance of balancing diagnostic accuracy with clinical applicability. Although the skin prick testing method is used more often, clinics still use intradermal testing as a second-line approach, mainly for patients with specific drug allergies. From the two testing methods, it is important for patients to understand the difference between the two testing methods before their appointment so they understand which method is most suitable for themselves. It is also important for clinic professionals to be understanding about the method patients choose to use while still suggesting the most beneficial method for them.

6.2 Safety and Patient comfort

Another factor that is important to consider is the patient's safety and comfort when comparing the two skin testing methods. Skin prick testing is when the needle only pricks the surface of the skin, causing less bleeding when used compared to intradermal testing, which goes deeper into the arm, often causing more bleeding and tissue damage for the patient (Gupta & Anand, 2023). The less invasive nature of skin prick testing may also contribute to greater patient comfort because of less bleeding and tissue damage. In comparison, patients may experience greater sensitivity or discomfort during intradermal testing (Singh et al., 2021). What is important to note is that there are no experimental studies in this section. One possible explanation is that patient comfortability that ties into safety, is extremely opinion-based and biased; many articles do not specifically conduct experiments relating to patient comfort and safety.

Dreborg's (1993) review of previous research (Niemeijer et al's study) provides evidence to show that skin prick testing can still be seen as the preferred method over intradermal, demonstrating ongoing method favourability. Dreborg (1993) discussed skin testing methods and materials used in the past to assess the degree of sensitization and safety in patients with allergic diseases. This article examined skin testing methods in terms of safety performance, sensitivity, and clinical preference. Dreborg stated that, "In the last decade, routine skin testing has been more commonly performed by skin prick testing. At the same time, some investigators still use intradermal skin testing even when testing with new substances of unknown allergenic potency, ignoring the old experience that severe general reactions may occur"(Dreborg, 1993 p. 474). This provides evidence that intradermal testing may cause more severe systemic reactions, which is unsafe for the patient, making skin prick testing a safer alternative in routine allergy testing. This review provides a detailed discussion of the differences between the two testing

methods and uses previous research. On the other hand, this literature review focuses on specific previous research, making it a limitation, so its findings cannot be generalized to a broader debate between skin prick and intradermal testing. Furthermore, other factors, such as cost, testing different allergy types, and patient preference, are not considered. Overall, the detailed discussion of safety and clinical use makes Dreborg's review a valuable early source comparing the two testing methods.

Secondary research supports skin pricking testing as a safe and practical approach to allergy diagnosis. Heinzerling et al. (2013) reviewed a large number of articles, rather than focusing on a single investigation. They provided a comprehensive summary of skin prick testing and compared it with intradermal testing. They reported that skin prick testing has a strong safety record, with no reported fatalities in a 5-year USA study that analyzed questionnaires from the American Academy of Allergy and Immunology regarding the fatality rates from skin testing (Reid et al., 1993). Furthermore, because skin testing methods deal with allergens, proper safety equipment should be on site regardless of the safety of a skin testing method. Other serious side effects are rare. This further highlights the use of skin prick testing as a safer first-line approach for allergy diagnosis, with intradermal testing often being reserved as a secondary method because of its higher sensitivity. Moreover, skin prick testing only penetrates the epithelial layer of the skin without causing bleeding, indicating this procedure can be less traumatic for patients who are sensitive with blood and needles. Heinzerling et al. (2013) provide strong evidence, especially because they reviewed and incorporated findings from multiple experimental studies, including (Reid et al., 1993; Nevis et al., 2016), which provides a more solid general conclusion than the previous literature review by Dreborg (1993), which only focused on one study and lacked a conclusive result.

Compared to Dreborg's (1993) and Heinzerling et al's (2013) studies, Patel & Saltoun's (2019) study provided a new perspective and reported that skin prick testing should be used before intradermal testing because of its advantages in patient comfort, safety and sensitivity for the patient. They provided an overview of several test reports comparing skin prick testing and intradermal testing based on procedure, safety, and diagnostic use. In their study, they stated, "the rate of reactions to the prick test and the intradermal test were found to be 0.04% versus 3.2%, respectively. Seven fatalities were attributed to skin testing. Five of these were attributed to intradermal testing." This shows that skin prick testing has less severe reactions than intradermal testing, highlighting how it is safer. Furthermore, patients who are uncomfortable in healthcare environments or procedures generally find skin prick testing to be a more tolerable method rather than intradermal testing. Although Patel & Saltoun's (2019) did not explicitly explain the references of the test reports collected in their study, compared to the two previous studies, Dreborg's (1993) and Heinzerling et al. (2013), Patel & Saltoun's (2019) generalized data charts (as given below) based on substances tested, which allows the reviewer to understand clearly the difference between skin prick testing and intradermal testing.

Following a paper that was previously mentioned in the last section about accuracy, among all the reviewed papers, this study by Gupta & Anand's (2023) examined the safety of two different skin testing methods, providing detailed information about the needles and process of inserting the needle into the skin. In skin prick testing, approximately 3 μL of the substance is introduced, and the needle penetrates approximately 1mm into the epidermis layer only. Because the procedure involves only superficial

penetration, it is considered a bloodless and minimally painful technique. In contrast, an intradermal needle injects 0.02-0.05 mL of tested substance into the body, which causes the needle to have to go deeper into the skin to inject all of the substance. As the needle for intradermal testing is removed, blood from under the skin is able to be released, causing more pain and discomfort for the patient. This paper is reliable because it is one of the few papers that has discussed the tools and the practical uses for skin prick testing and intradermal testing.

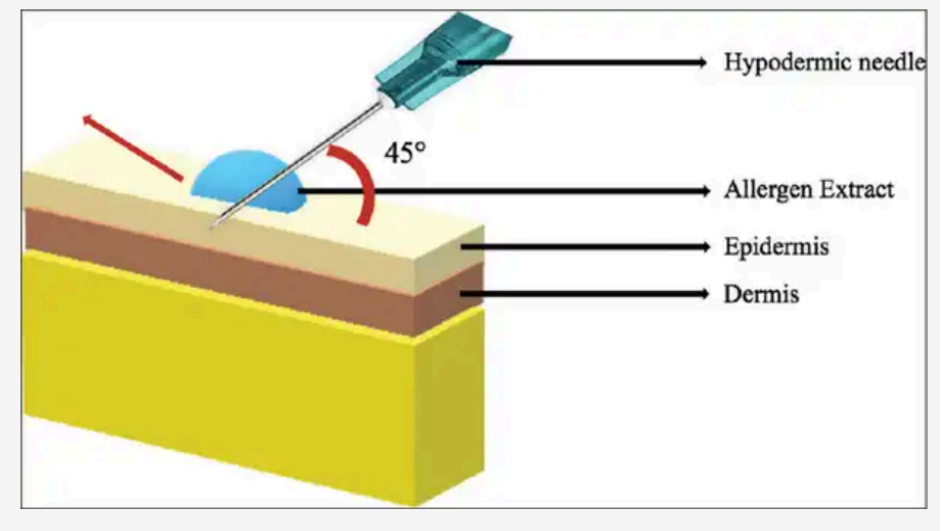

Figure 4 Technique of Skin Prick Testing (Gupta & Anand; 2023)

Figure 4 above is an example of skin prick testing where the hypodermic needle is being inserted into the epidermis layer of the skin. The needle is seen to be pointing at a 45 degree angle, where only 1 mm of the needle is pricked under the skin.

Overall, it is understandable that patient comfort and safety are interconnected as seen through these articles. In these papers, skin prick testing is said to cause less bleeding, tissue damage, and systemic reactions that can be harmful to the body than intradermal testing, further emphasizing why skin prick testing is a first-line approach. However, it does not mean that intradermal testing should be replaced: it is still considered an effective technique in important circumstances regarding certain drug allergic patients and the need for higher sensitivity.

Further, an important factor to bear in mind is that there are rarely any experimental papers regarding specifically patient safety and comfort, likely due to how patient comfort connects with safety and it can be biased depending on the patient's personal relationship to healthcare. From the articles reviewed in this section, more experimental research is needed to measure patient comfort and safety, emphasizing the importance of understanding patient comfortability and safety, issuing that more clinics should conduct surveys and interviews focusing on comfort and safety in order to provide more accurate data for further studies.

6.3 Efficiency

Efficiency, the number of allergies tested at the same time and the rate of how fast the results from the two skin testing methods, is also a very important criteria to compare. This section has the least number of papers conducted, likely due to how other components such as accuracy are more important than how fast clinic professionals get results, and studies do not focus particularly on efficiency. This section, though, does provide experimental studies because efficiency, unlike patient comfort and safety, can be measured.

In Peltier & Ryan's (2007) study, they conducted an experimental study. They had 134 participants aged from 18-64 from the University of Texas Medical Branch. Participants were tested using skin prick testing and intradermal testing, and all skin test results were read in 15 mins after application. Specifically, Peltier & Ryan's (2007) selected participants who had a positive histamine and negative glycerin test because histamine provides immune release responses and glycerin can cause false-positive responses if the patient reacts to Glycerin instead of the substance (Buelow & Kaliner, 2024; Peltier & Ryan, 2007). During their experiment, they found that skin prick testing allergy size could predict intradermal results for several allergens, questioning whether or not it is necessary to use intradermal testing. Their results indicate that skin prick testing is less time consuming and less technically demanding than intradermal testing by comparing the spread of the reaction after 15 minutes. In addition, they proposed a modified quantitative testing that introduces skin prick testing and intradermal testing together. Overall, this study is important because it directly compares the efficiency of skin prick testing with intradermal testing.

Compared to Peltier & Ryan's (2007) study, Ansotegui et al's (2020) conducted a World Allergy Organization study reviewing a vast range of papers from 1965 to the early 2000s. They reviewed a large number of research papers and created data information tables and sections that discussed different allergy diagnoses and compared skin prick testing to intradermal testing. They described skin prick testing as a better first-line approach because it is assessed 15-20 minutes after application, providing fast results. It is also relatively inexpensive compared to intradermal testing, which is more expensive because of different needles and materials needed for the procedure. Because of the depth of injection for both methods, skin prick testing allows more substances to be tested. Adding on, intradermal testing is described as more technically demanding, requiring individual injections. This review paper not only considers the time difference for both applications but also the pricing and how technically demanding the technique is for clinical professionals.

As the most recent study in this section, Gupta & Anand's (2023) review study provides a general overview comparing the two skin testing methods. They discussed that although both skin testing techniques can receive results in a short period of time, skin prick testing is slightly quicker by 15-20 minutes compared to intradermal testing, which can take 30-60 minutes, because skin prick testing is closer to the surface of the skin and does not need to build up under the skin, unlike intradermal testing. Further, skin prick testing can perform around 30 different substances at once, while intradermal testing can only perform around 15. By comparing the number of substances tested and the time in minutes the reactions take, this study makes a direct comparison of the two methods.

Overall, this section displays how important it is to consider efficiency. In Peltier & Ryan's (2007) study, they demonstrate a reliable experimental study with a large sample, and efficiency can be seen as a practical and valuable aspect when comparing skin prick testing to intradermal testing. Ansotegui et al's (2020) study provides strong support for the reliability of information, mainly focusing on allergy diagnoses while also including clinical applications such as pricing and the professional technique needed. On the other hand, Gupta & Anand's (2023) demonstrates a very detailed comparison of skin prick testing and intradermal testing based on reviewing previous studies. In the end, skin prick testing is seen to be the clinically favoured option because of its faster results, less technique demanding, more substances tested at the same time, and less expensive procedure. However, intradermal testing is still used in clinics because of its specific drug allergies and higher sensitivity, providing a valuable alternative method and second option for patients. Both methods provide strong clinical applications and should be used for patients depending on their specific situation and preference.

6.4. Summary

After reviewing many papers comparing the two different methods through reviews and experiments, it can be seen that skin prick testing is more favorable as a first-line approach because of accuracy, safety, comfort, and efficiency; Intradermal testing remains useful as a second-line approach when greater sensitivity is required, or the patient is allergic to Glycerin or other drugs that may result in inaccurate results if they are using skin prick testing.

Although many studies support the argument that skin prick testing is one of the most efficient and common ways to test for allergies, contraindications do arise. Although skin prick testing is a safe procedure, it can rarely work for life-threatening allergies, causing chances of false-negative reactions (Gupta & Anand, 2023). Furthermore, not only does the type of skin testing matter, but the materials and safety procedure during testing are also important; If the needle or testing devices and proper safety measures are not taken, it can cause dangers and inaccuracies regardless of the skin testing type used (Nevis et al., 2016). Skin issues and skin reaction amount can also impact how the reaction forms and looks like. Finally, clinical professionals need to have proper knowledge on testing and diagnosing patients in order to make proper determinations of which skin testing is accurate. Therefore, there are articles arguing against skin prick testing that will be discussed in the next section.

6.5. Contradictions

After discussing the four components that need to be taken into consideration for determining which skin testing method is preferred, contradictions do arise. This can be because of different methodological differences and biases can make it difficult to provide an accurate determination of which skin testing method should be used in clinics when both methods have their own strengths and weaknesses (Hurst et al., 2002). This section will provide some studies that argue against skin prick testing being the first-line method and instead argues intradermal being a preferred method.

Harries et al. (1984) argued that intradermal testing is better at detecting allergies than skin prick testing through an experimental study involving wasps and bees. They compared skin prick testing to intradermal testing for 102 participants along with 46 control participants. They concluded that intradermal testing identified 13 patients who tested negative for skin prick testing, but 7 of them were actually positive and allergic to wasp and bee venom. They suggested that intradermal testing can identify more allergies than skin prick testing and is therefore should be a preferred option than skin prick testing.

Needless to say, Harries et al. (1984) is a very early study and provides a very detailed experiment and argument, making their paper very convincing. However, this study cannot be an accurate determination of allergy testing to some extent because it focused on wasp and bee venom, which cannot apply to other forms of allergies such as food and materials; This weakens their argument as it does not counterargue the general debate of skin testing being better than intradermal. However, this study was published very early, implying that skin prick testing has also been questioned for a long period of time.

Another study questioning skin prick testing is Hurst et al's (2002) study, where they explained how intradermal testing can be judged unfairly and skin prick testing should not be considered the better option than intradermal testing because there should be more accurate research done on both skin testing methods. Hurst et al. (2002) conducted an experimental study to test the use of skin testing with different glycerin concentrations on 49 patients at a clinic. After testing intradermal testing using 0.5% and 5% glycerin and measuring the initial reaction at 0 minutes to the final reaction at 10-15 minutes, they found that glycerin, only in skin prick testing, can result in false-positive reactions; Glycerin can exaggerate the reactions and sometimes may exaggerate the reaction so that professionals can mistake it for positive reactions. Intradermal testing does not use Glycerin, so there are no excessive reactions that can lead to false positives. They criticized that previous studies only used one amount of Glycerin control and how intradermal testing has been falsely concluded as an inaccurate testing method.

Hurst et al's (2002) study demonstrates a detailed method and research objective. They provided a strongly developed experimental study and stated that intradermal testing has been judged unfairly and further research should be conducted for higher accuracy. However, Hurst et al's (2002) study only focused on the accuracy of Glycerin control rather than the accuracy of the two testing methods. Therefore, the results only highlight a possibility of false-positive reactions using Glycerin control, but there is no evidence that intradermal testing is a more accurate approach. In contrast, even with Glycerin, skin-prick testing is seen to have less false-positives than intradermal testing, reinforcing that Glycerin control is not the most important aspect of false-positives (Gupta and Anand, 2023). However, intradermal is still an important component, as many patients are allergic to glycerin and should not use skin prick testing. This concludes that this paper shows valuable information about an opposite method that was not discussed.

7. CONCLUSION

Skin testing remains as one of the most important tools to diagnose allergies in clinics today. Intradermal testing can detect smaller reactions, professionals and researchers worldwide have stated that skin prick

testing is seen to be more accepted in clinics because of its efficiency, accuracy, safety, and patient comfort. Studies done comparing the two skin testing methods show intradermal as a strong second-line approach or first line approach for drug allergy patients, and skin prick testing as a first line approach that is used in general practices. Furthermore, future improvements can be made. Both testing show sensitivity levels, discomfort, and possibilities for false-positive reactions. Increased technology and developments of new testing methods should be introduced to minimize small inaccuracies. Ultimately, clinics should develop a more personalized approach where genetics, allergen exposure, and medical history can contribute to the determination of allergies rather than relying on a single skin testing approach.

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