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Allergy skin tests: an update on Skin Prick Test and Prick to Prick

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SUMMARY

Skin prick testing (SPT) is an essential tool in allergy diagnostics, allowing the identification of IgE-mediated hypersensitivity reactions to specific foods or environmental allergens. Among its variations, the prick by prick (PTP) test plays a crucial role in food allergy diagnosis, particularly when commercial allergen extracts fail to capture heat-sensitive or enzymatically labile proteins. PTP testing involves pricking a fresh food sample before introducing the allergen into the skin, thus ensuring exposure to the full allergenic profile. This method enhances diagnostic sensitivity and specificity, reducing the likelihood of false-negative results. The choice of SPT devices, whether single-prick or multiple-prick, significantly impacts test accuracy, reproducibility, and patient comfort. While single-prick devices offer precise allergen application, multiple-prick devices improve efficiency in clinical settings. Despite its advantages, PTP testing lacks standardization, with results influenced by food properties, regional variations, and test administration techniques. Additionally, PTP is a cost-effective alternative in areas where commercial extracts are unavailable. When combined with serum-specific IgE testing and oral food challenges, PTP enhances clinical decision-making, minimizing unnecessary dietary restrictions. This review provides an update on SPT and PTP methodologies, highlighting their strengths, limitations, and future perspectives in allergy diagnostics. Standardization and improved training protocols remain key to optimizing the reliability of these essential tests.

KEYWORDS: Skin prick test, Prick by prick test, Prick to prick test, Allergy diagnosis, IgE-mediated hypersensitivity, Food allergy testing, Aeroallergens and skin testing, Allergen extracts and standardization, Diagnostic accuracy in allergy testing, Automated Skin Prick Test

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1. SKIN PRICK TEST (SPT)

The skin prick test (SPT) is widely used to demonstrate immediate IgE-mediated allergic reactions and is a reliable major diagnostic tool in the allergy field. SPT is one of the most commonly used screening and diagnostic tools in modern allergy practice and is considered the 'gold standard' for epicutaneous allergy testing [1]. It is widely accepted as a safe, reproducible, convenient, and cost-effective procedure. In the 1860s, Charles H. Blackley conducted what many consider to be the first skin test. He scratched a small area of his own skin, applied grass

pollen grains, and observed significant swelling and erythema. Later, the scratch test was introduced by Schloss, while the intracutaneous test was independently developed by Schick and Cooke. SPT was standardized in the 1920s by Lewis and Grant and remains the primary technique used by allergy specialists today with some modifications [2]. The skin prick test (SPT) works by activating IgE antibodies on mast cells in the skin. It detects tissue-bound IgE and indicates an atopic state in patients with type 1 allergies. The test involves pricking the stratum corneum with a specialized device, allowing the epidermis to come into contact with an allergen solution. Liquid allergen droplets are placed on the skin and then pierced with a sterile needle or lancet, delivering the allergen into the dermis. SPT devices vary in materials (such as plastic or metal), design (including lancets and needles), and configuration (single-use or multipuncture systems) (Fig. 1). A new lancet is used for each allergen to prevent contamination [1,3]. When a specific allergen is introduced into the skin of allergic individuals via a lancet, dermal mast cells begin to degranulate mainly due to the crosslinking of allergen-specific IgE bound to their membrane receptors. This degranulation triggers the immediate release of histamine and other mediators, which induce a cutaneous response, clinically characterized by a wheal (sometimes with pseudopods) and surrounding erythema (flare) that can be measured to assess the degree of cutaneous sensitivity [2]. Both methods require positive (histamine) and negative (saline) controls. Skin reactions are evaluated after 15 to 20 minutes, characterized by wheal formation and surrounding erythema [1,2,4]. The wheal diameter, measured in millimeters, determines the reaction's severity, with a diameter of 3 mm or greater considered positive (Fig. 2). Larger wheals indicate greater sensitivity, though not necessarily more severe symptoms. The absence of a wheal indicates no allergy to that specific allergen, while the positive control should produce a wheal and the negative control no reaction [2,4,5]. The sensitivity and specificity of SPT for aeroallergens range, respectively, from 70-95% and 80-97%, whereas they are lower for food allergens, ranging from 30-90% and 20-60%, respectively [5].

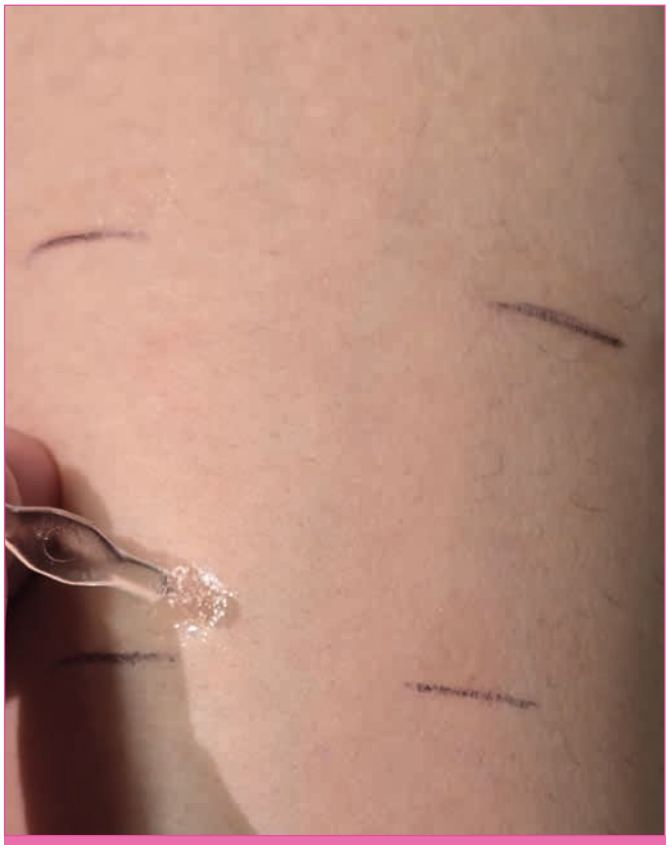

FIGURE 1. Skin prick test: technique.

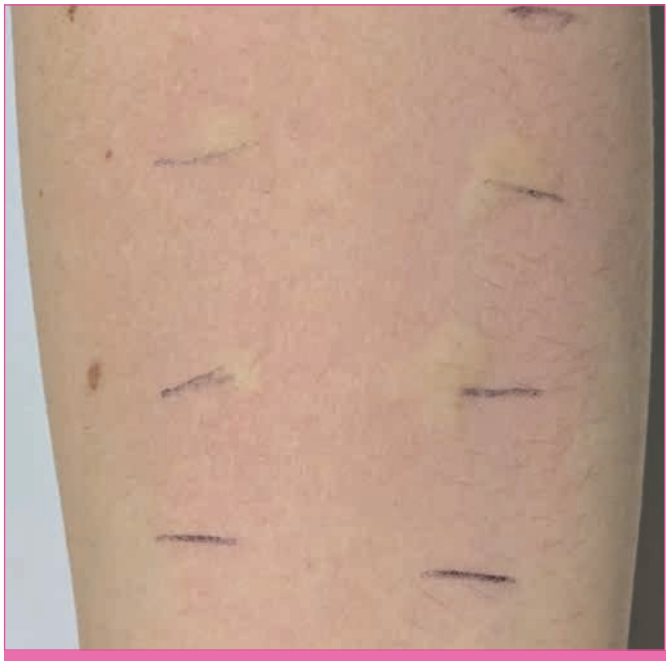

FIGURE 2. Wheal' and 'Flare' reactions after SPT to different allergens.

1.1. ALLERGEN EXTRACTS FOR SPT

The selection of allergens for SPT is a critical step in ensuring accurate and clinically relevant diagnostic results. The choice of allergens should be guided by the patient's clinical history, geographic exposure, and local epidemiology of allergic diseases. Standardized extracts are preferred whenever available, since they improve test reproducibility and allow for better comparison of results across different centers [5]. However, while it is often proposed that the panel of allergens tested should be tailored to local allergen exposure, this approach has limitations [1,5]. Allergic patients travel across different regions and countries, and new sensitizations are emerging due to climate change [6]. Additionally, cross-reactivities between allergens may be unsuspected, making it essential to include a standardized set of allergens in SPT panels to ensure comparable and reliable diagnostics [1].

To address this need, the Global Allergy and Asthma European

Network (GA^{2}LEN) has recommended a standardized allergen battery for clinical practice and research across Europe, ensuring that all adolescents and adults be tested with a consistent panel. The GA^{2}LEN-suggested panel includes [7]:

- **Pollens**: Birch (*Betula verrucosa*), Cypress (*Cupressus sempervirens*), Grass pollens (single or mixed species), Mugwort (*Artemisia vulgaris*), Olive (*Olea europaea*) or Ash (*Fraxinus excelsior*), Parietaria (*Parietaria officinalis*), Plane (*Platanus occidentalis*), Ragweed (*Ambrosia elatior*);
- **Mites**: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*;
- **Animals**: Cat (*Felis domesticus*), Dog (*Canis familiaris*);
- **Molds**: *Alternaria alternata*, *Cladosporium album*;
- **Insects**: Cockroach (*Blattella sp.*).

For food allergy diagnosis, extracts for milk, egg, peanut, tree nuts, soy, wheat, fish, and shellfish are commonly used. However, as heat-sensitive proteins in some foods degrade during the extract preparation process, prick-to-prick testing with fresh foods may be necessary to improve diagnostic accuracy [8]. Additionally, allergens relevant to occupational exposure (e.g., latex, flour, animal proteins), insect venoms (bee, wasp), and drugs (penicillin, local anesthetics) may be included based on clinical suspicion [9]. Ultimately, SPT panels should be tailored to each patient, ensuring a balance between comprehensive assessment and clinical relevance [2,4].

1.2. REGULATORY BARRIERS IN SPT AVAILABILITY

The availability of diagnostic allergens for SPT in Europe has significantly declined in recent years due to the withdrawal of marketing authorizations by pharmaceutical companies and the increasing regulatory and economic burdens associated with maintaining these products on the market [10]. This reduction is particularly critical for less common allergen sources, many of which are essential for diagnosing occupational allergies and other rare allergic conditions [11]. The resulting diagnostic gap poses a significant challenge for allergists and clinicians who rely on SPT as a primary tool for diagnosing IgE-mediated hypersensitivities. The absence of certain test allergens may force physicians to rely solely on standard commercial panels, which do not always include regionally relevant or occupational allergens, potentially leading to misdiagnosis or underdiagnosis of allergic conditions [10,12]. In this context, prick-to-prick testing has emerged as a valuable alternative for assessing allergens that are no longer available as commercial extracts, particularly for food allergy diagnosis [3]. Recent studies have explored alternatives to mitigate this issue. A study by Terlouw et al. examined the feasibility of using homemade food allergen extracts for prick-to-prick as a substitute for commercial extracts that are no longer available [13]. Their findings demonstrated that homemade extracts for certain allergens, such as hazelnut and walnut, showed strong correlation with commercial extracts, while other allergens exhibited more variability [13]. As an alternative approach, some European countries, such as Germany, have explored the possibility of producing diagnostic allergens in public pharmacies under specific legal provisions, including the German Medicinal Products Act (AMG) and the European Pharmacopoeia. Pharmacy-based production could help bridge the diagnostic gap by ensuring the availability of allergen extracts tailored to specific patient needs. However, this solution comes with significant challenges, including the need for rigorous quality control, standardized production methods, and harmonization with existing pharmaceutical regulations to guarantee safety, efficacy, and reproducibility [14,15]. In the absence of readily-available diagnostic allergens for in vivo testing, there is a growing reliance on serological tests, such as specific IgE measurements in blood. While these tests can provide valuable information, they do not assess clinical reactivity, which is crucial for determining the true relevance of a sensitization. Additionally, increased reliance on serological testing may lead to higher healthcare costs and delayed diagnoses, ultimately impacting patient care [11]. To address these issues, an urgent revision of the European regulatory framework is needed to facilitate the approval and distribution of diagnostic allergens. Simplified authorization pathways, reduced regulatory fees, and financial incentives for manufacturers could all help maintain a broad portfolio of test allergens. A coordinated effort among allergists, regulatory authorities, and pharmaceutical companies is essential to ensure that allergy diagnostics remain comprehensive, accessible, and clinically effective across Europe. Moreover, given the increasing reliance on prick-to-prick to compensate for the unavailability of certain diagnostic extracts, the development of standardized protocols under the guidance of organizations such as European Academy of Allergy & Clinical Immunology (EAACI) and World Allergy Organization (WAO) could help ensure greater consistency in test execution and interpretation. These guidelines could include recommendations on food preparation methods, lancet techniques, test interpretation, and quality control measures to enhance prick-to-prick reliability and facilitate its broader adoption in clinical practice [10].

2. AVAILABLE DEVICES FOR SKIN PRICK TESTING

The accuracy and reproducibility of SPT results depend not only on the quality of allergen extracts, but also on the type of device used to introduce allergens into the epidermis. Various devices are available for performing SPTs, and can be broadly categorized into single-prick devices and multiple-prick devices. Each category has distinct advantages and limitations in terms of precision, efficiency, and patient comfort [3].

2.1 SINGLE-PRICK DEVICES

Single-prick devices include sterile disposable lancets and needles that are used to introduce allergens into the skin by puncturing the

stratum corneum. These devices are specifically designed for allergy testing, ensuring controlled penetration depth and minimizing inter-test variability. Each allergen extract is applied separately using a dedicated lancet to prevent cross-contamination [4,16].

Single-prick devices have several advantages. They are widely regarded as the gold standard for SPT because they allow precise allergen delivery and produce consistent wheal-and-flare reactions. Additionally, the risk of cross-contamination between allergens is virtually eliminated when a fresh lancet is used for each test site. However, single-prick methods can be time-consuming, particularly when testing multiple allergens. Each allergen must be applied and pricked individually, which increases the overall duration of the procedure and may lead to patient discomfort, especially in pediatric populations or in individuals undergoing extensive allergy panels [1,17].

2.2 MULTIPLE-PRICK DEVICES

To improve efficiency, multiple-prick devices have been developed, allowing the simultaneous application of multiple allergens [18]. These devices typically consist of multi-head applicators with several prongs that deliver allergens uniformly across multiple test sites in a single application. Multi-prick devices are designed to standardize the amount of pressure applied during the test, which helps reduce variability in wheal size caused by inconsistent application techniques [2,3,18].

Multiple-prick devices offer several benefits, particularly in high-volume allergy clinics where large numbers of patients need to be tested efficiently. They significantly reduce testing time and improve patient throughput while maintaining an acceptable level of accuracy. However, despite their efficiency, multi-prick devices pose potential challenges. There is a risk of cross-contamination if proper precautions are not taken, as allergens are applied simultaneously in close proximity. Additionally, some studies suggest that multi-prick devices may produce smaller wheals compared to single-lancet methods, potentially leading to reduced sensitivity in borderline cases. The reproducibility of results may also vary depending on the specific design of the device, pressure applied, and skill of the operator [2,3,18].

2.3 COMPARISON OF SINGLE- AND MULTIPLE-PRICK DEVICES

Several comparative studies have evaluated the performance of single- and multiple-prick devices in terms of sensitivity, specificity, reproducibility, and patient comfort [19–21]. Generally, both methods yield comparable diagnostic accuracy when standardized protocols are followed. Single-prick devices remain the gold standard and the preferred choice when precise wheal measurement is required, particularly in research settings or for patients undergoing confirmatory allergy testing [19]. In contrast, multiple-prick devices are advantageous for initial screenings or when a large panel of allergens needs to be tested rapidly [19]. Regardless of the device used, adherence to best practices in SPT technique is essential to ensure reliable results. Standardized allergen extracts, appropriate test site preparation, and consistent interpretation of wheal diameters are crucial for maximizing diagnostic accuracy. The choice between single- and multiple-prick devices ultimately depends on the clinical setting, patient population, and specific testing requirements [19,22].

3. MEASUREMENT AND INTERPRETATION OF SKIN PRICK TEST

Inhalant allergen sensitivity is frequently observed from early childhood, and SPTs can be safely conducted and interpreted even in infants [23]. However, in very young children, the limited surface area of the forearm may restrict the number of allergens that can be tested, making the back a suitable alternative when necessary. In preschool-aged children, establishing a clear connection between a positive SPT result and clinical symptoms can be challenging, since conditions like asthma and allergic rhinitis may be difficult to diagnose at this stage [24]. Accurate measurement and interpretation of SPTs are vital for the reliable diagnosis of IgE-mediated allergies. One critical technical factor is the distance between individual pricks. Standard guidelines recommend that each allergen test site be spaced at least 2 cm apart. This separation is essential to prevent overlapping of wheal and flare responses, which could lead to misinterpretation due to merging reactions from adjacent allergens [4]. In interpreting SPT results, a reaction is generally considered positive when the wheal diameter is 3 mm or greater than that of the negative control. The measurement is obtained by averaging the longest diameter of the wheal and its perpendicular counterpart. Positive (histamine) and negative (saline) controls are indispensable: the histamine control confirms that the patient's skin is reactive, while the saline control ensures that any reaction observed is specific to the allergen and not due to non-specific skin reactivity [2]. Despite these guidelines, false-positive and false-negative results can occur. False positives may result from non-specific skin reactivity, such as dermographism, or from cross-reactivity among allergens, leading to wheal formation even in the absence of a true sensitization [2]. On the other hand, false negatives can be caused by various factors, including recent intake of antihistamines or other medications that suppress skin responses (Tab. I), improper test technique (e.g., inadequate skin penetration), or inherently low skin reactivity, which is often seen in the elderly or in patients with extensive eczema [2].

4. AUTOMATED SKIN PRICK TEST

Automated Skin Prick Testing (ASPT) represents a significant technological advancement aimed at overcoming the limitations of conventional manual SPT. While SPT remains the gold standard

TABLE I. Pharmacokinetics of First- and Second-Generation H1 Antihistamines and Inhibitory Effects on Skin Prick Tests [1,2,4,25,26].

Treatment	Recommended Discontinuation Before the Skin Test*
First-Generation H1 Antihistamines	
Diphenhydramine	At least 2–5 days
Hydroxyzine	At least 5–8 days
Chlorpheniramine	At least 2–6 days
Second-Generation H1 Antihistamines	
Cetirizine	At least 2–10 days
Levocetirizine	At least 2–10 days
Loratadine	At least 7-10 days
Bilastine	At least 4–5 days
Ebastine	At least 3–10 days
Corticosteroids	
Systemic corticosteroids (short term)	None
Systemic corticosteroids (long term)	Possible suppression of immediate skin test reactions
Inhaled corticosteroids	None
Topical corticosteroids (skin)	At least 7 days
Other Medications Affecting SPT	
Intranasal H1-antihistamines	None
Imipramines	At least 21 days
Phenothiazines	At least 10 days
Montelukast	None
Specific immunotherapy	None
UV light therapy (PUVA)	At least 4 weeks
Omalizumab	At least 6 weeks, but false negative results may still occur for up to one year.

* Despite the intervals indicated, the higher limit of the interval is recommended

for diagnosing IgE-mediated allergic diseases, its manual execution is inherently limited by operator-dependent variability, subjective interpretation of wheal measurements, and inconsistencies in allergen application [27]. ASPT addresses these challenges by integrating computer-controlled allergen deposition, standardized lancet pressure, and automated wheal measurement into a single streamlined process [28].

4.1 STANDARDIZATION AND REPRODUCIBILITY

ASPT systems have been developed to standardize the entire testing process, thereby enhancing reproducibility and accuracy. A study comparing ASPT with conventional manual testing (SPMT) found that ASPT significantly reduces intra-subject variability. Intra-subject coefficients of variation were lower for ASPT compared to SPMT when measuring wheals from house dust mite, timothy grass, and birch pollen. These findings suggest that ASPT minimizes the inconsistencies associated with human-dependent factors, such as differences in pressure applied during allergen introduction [29]. Additionally, ASPT provides more precise wheal measurements, as automated imaging and analysis remove the subjectivity of manual tracing. Unlike conventional methods, which rely on visual assessment, ASPT employs high-resolution imaging combined with software-driven measurement algorithms, ensuring higher accuracy in wheal size detection [28,30].

4.2 EFFICIENCY, PATIENT COMFORT, AND RESOURCE UTILIZATION

ASPT enhances both testing efficiency and patient experience, making it particularly valuable in high-throughput clinical settings. Studies have shown that ASPT significantly reduces testing time (20 seconds per participant vs. 144 seconds for manual SPT), allowing for faster patient turnover in busy allergy clinics and large-scale research studies. Additionally, ASPT improves patient comfort, with lower discomfort scores (median VAS 2 cm vs. 2-4 cm for manual testing), an important factor in pediatric patients [29]. Beyond efficiency, ASPT also helps minimize human error and optimize resource utilization. The technology reduces prick failures ($p < 0.0001$) and lowers allergen consumption, requiring 2.7 times less histamine solution (4.5 mL vs. 12.0 mL) compared to manual methods. Given the economic and regulatory constraints on allergen extract production, this improves cost-effectiveness further supports ASPT as a viable alternative in allergy diagnostics [29].

4.3 CLINICAL IMPLICATIONS AND FUTURE PERSPECTIVES OF ASPT

ASPT has the potential to improve accuracy, reproducibility, and efficiency in allergy diagnostics by minimizing operator variability and ensuring standardized allergen application [30]. Its ability to produce more consistent results across different centers makes it particularly valuable for multicenter trials and epidemiological studies. Additionally, ASPT enhances patient comfort and workflow efficiency, reducing both testing time and allergen waste [28]. However, several challenges limit its widespread adoption. The high cost of ASPT devices, along with maintenance and calibration requirements, makes it less accessible for smaller

clinics compared to manual SPT, which remains more affordable and widely available [27,30]. Additionally, ASPT lacks the flexibility of manual methods, as most automated devices rely on predefined allergen panels, making them less suitable for fresh food testing or customized allergen selection. Anatomical constraints in young children or patients with limited skin surface area may also pose difficulties, since ASPT is primarily studied in adult populations [27,30]. ASPT may still be prone to false positives and false negatives. Factors such as individual skin reactivity, allergen deposition, and lancet pressure can affect wheal formation. False positives may arise from standardized allergen deposition techniques that fail to account for individual variations in skin barrier function, while false negatives can result from inadequate allergen penetration due to controlled lancet pressure, potentially diminishing sensitivity in some cases. Comparative studies evaluating ASPT and manual SPT across different patient populations are needed to better understand these diagnostic differences [27]. Moreover, while digital image analysis improves objectivity, the lack of universal standardization may introduce variability in clinical interpretation across centers [28]. Future developments, including AI-driven wheal analysis, hold promise for enhancing diagnostic accuracy and automation.

5. PRICK-TO-PRICK TEST

The prick-to-prick (PTP) test is a specialized variation of the conventional SPT, primarily used for diagnosing food allergies. Unlike standard SPTs, which utilize commercially available allergen extracts, the PTP test involves pricking a fresh food sample such as fruit, vegetables, nuts, or seafood and then immediately using the same lancet to prick the patient's skin. This method is particularly useful when testing for allergens that may degrade in commercial extracts or when fresh food allergens contain labile proteins that are difficult to standardize in commercially prepared solutions [5].

5.1 MECHANISM AND RATIONALE

The PTP test follows the same immunological principles as the traditional SPT. By introducing an allergen into the epidermis, it triggers a localized IgE-mediated reaction in sensitized individuals. The test elicits mast cell degranulation, leading to the release of histamine and other mediators, which cause a characteristic wheal and flare reaction that is measured after 15-20 minutes. However, PTP reactions tend to produce larger wheals than standard SPT due to the higher concentration of allergenic proteins in fresh foods compared to commercial extracts [1].

The PTP test is essential in food allergy diagnostics, particularly when commercial allergen extracts fail to represent the full allergenic profile of fresh foods. Many allergenic proteins, such as profilins and pathogenesis-related (PR-10) proteins, are heat-sensitive or enzymatically labile; they degrade during extract processing, potentially leading to false-negative results with standard SPTs [3,8]. By using the actual food in its natural state, PTP testing ensures exposure to all relevant allergenic epitopes, thereby improving diagnostic sensitivity for fresh fruits, vegetables, nuts, and seafood a feature particularly valuable in conditions like pollen-food syndrome and seafood allergies [2,8]. Moreover, PTP testing is also highly useful in assessing milk and egg allergies. Clinicians can perform tests with fresh cow's milk or raw egg, or even target specific fractions such as the egg white or yolk. Additionally, conducting PTP tests using baked forms of egg or milk can provide a predictive response regarding the tolerance or threshold provocation outcome, further enhancing the overall diagnostic accuracy [31]. PTP is especially useful when commercial extracts are unavailable, allowing clinicians to test regional or uncommon food allergens. Additionally, PTP testing is more cost-effective and readily available in geographic areas where certain commercial extracts are inaccessible, making it a practical alternative in resource-limited settings [32,33].

5.2 ADVANTAGES AND LIMITATIONS

Compared to standard SPT, PTP offers improved sensitivity for certain food allergens, particularly those with unstable proteins, but lacks standardization due to variability in food preparation and allergen content. Additionally, PTP allows clinicians to test for allergies using the exact food that the patient consumes, enhancing the clinical relevance of the results. While SPT remains the gold standard for aeroallergens and well-characterized food allergens, with commercially available standardized extracts, its cost can vary depending on the number of allergens tested. In contrast, PTP can be a cost-effective alternative in settings where commercial extracts are unavailable, providing a practical solution for assessing regional or less common food allergens (Tab. II). Recent studies have highlighted the growing clinical relevance of PTP testing for emerging allergens, including plant-based proteins. A systematic review and meta-analysis by Terlouw et al. compared the diagnostic accuracy of SPT and PTP for fruits and vegetables, demonstrating that PTP remains a valuable tool for detecting sensitization to fresh food allergens [34]. The study found a strong correlation between SPT with frozen fruit juice and PTP with fresh fruits and vegetables, suggesting that PTP testing maintains its relevance in assessing heat-labile allergens. These findings further support the role of PTP in diagnosing food allergies, particularly when commercial extracts have reduced allergenic activity due to processing [34]. However, several limitations should be considered. Unlike commercial extracts, fresh foods vary in allergen content based on ripeness, storage conditions, and geographic origin. This variability can affect test reproducibility. Additionally, when using fresh foods, certain limitations must be considered. Harder foods, such as tree nuts, have a harder consistency, making the procedure more challenging. The distribution of allergenic proteins within the food may be uneven. For example, in peaches, the concentration of nsLTP proteins differs between the peel and the pulp, potentially affecting test

TABLE II. Comparison between Skin Prick Test (SPT) and Prick-to-Prick Test (PTP).

Feature	Skin Prick Test (SPT)	Prick-to-Prick Test (PTP)
Sensitivity[5]	70-95% for aeroallergens, 30-90% for food allergens	Higher for fresh food allergens, but variable
Specificity[5]	80-97% for aeroallergens, 20-60% for food allergens	Variable; influenced by cross-reactivity and irritant components
Cost	Standardized extracts are commercially available, but their cost and availability vary depending on the region and the number of allergens tested	Can be a cost-effective alternative when commercial extracts are unavailable
Standardization	High; well-standardized extracts and devices available	Low; results influenced by food properties and preparation method

accuracy [35]. Furthermore, some foods contain histamine or other vasoactive substances that may cause nonspecific skin reactions. For example, tomatoes and citrus fruits can induce irritation-related wheals independent of IgE-mediated mechanisms. In these cases, specialized personnel are required to ensure proper execution of the test [1,2,34].

5.3 COMPARISON WITH OTHER ALLERGY TESTS

SPTs testing is often used in conjunction with other diagnostic methods to improve the overall accuracy of food allergy assessment [1]. When comparing skin tests to serum-specific IgE (sIgE) assays, several key differences emerge. SPTs provide an immediate, in vivo assessment of mast cell degranulation, reflecting both the presence of allergen-specific IgE and the skin's reactivity [2]. They are generally more sensitive and cost-effective, making them the preferred initial screening tool. In contrast, sIgE tests, which are performed in vitro, offer a quantitative measure of circulating IgE antibodies [36]. Although these assays are less susceptible to local skin factors, they may lack the direct clinical correlation provided by SPTs and can be affected by high total IgE levels or cross-reactivity [2]. Consequently, both testing methods are often used in a complementary manner to enhance diagnostic accuracy and guide effective allergy management. Oral food challenges (OFCs) remain the gold standard for diagnosing food allergies, but are time-consuming and carry the risk of severe allergic reactions. When combined with history, standard SPT, and sIgE testing, PTP testing serves as a valuable tool in refining diagnostic precision while reducing the need for unnecessary OFCs [1].

6. PRECAUTIONS AND CONTRAINDICATIONS FOR THE PRICK TEST

SPT is widely recognized for its safety and minimal discomfort; nevertheless, even though adverse reactions are infrequent, they must be carefully considered to ensure patient safety and reliable test interpretation. While the majority of patients tolerate the procedure without significant issues, there are instances where unintended reactions both allergic and non-allergic may occur [37]. Locally, highly sensitive individuals might develop a late-phase response characterized by tender, painful swelling at the test site; although such reactions are generally self-limiting and rarely persist beyond 36 hours, they can cause considerable discomfort. Systemic reactions, though very rare, have been documented to arise within 15 to 30 minutes after SPT administration [37–39]. These systemic responses, which can manifest as generalized urticaria or respiratory distress, underscore the importance of identifying patients who are at increased risk such as infants, individuals with a history of anaphylaxis, those undergoing testing with multiple allergens or fresh food extracts, and patients with uncontrolled asthma or extensive eczema [37-40]. Additionally, non-allergic reactions like vasovagal syncope and headache have been observed, typically occurring shortly after the test [37-39]. Although the overall incidence of systemic reactions remains low reported at less than 0.055%, with even lower rates necessitating epinephrine [41]. It is therefore essential that SPT be performed in settings equipped with immediate emergency support, by trained personnel, and with careful pre-test evaluation to identify contraindications such as the absence of normal skin reactivity, recent use of interfering medications, or unstable medical conditions [37].

7. CONCLUSION

SPT and PTP testing remain cornerstone diagnostic tools in allergy practice, providing rapid, reliable, and cost-effective assessments of IgE-mediated hypersensitivity. The continued refinement of SPT techniques, including the selection of standardized allergen extracts and optimized testing devices, has improved diagnostic accuracy and reproducibility. PTP testing, in particular, has emerged as an essential complementary tool, especially for diagnosing food allergies where commercial extracts may not fully capture labile allergenic proteins. Despite their clinical utility, several challenges persist. The lack of standardization in PTP testing, variability in fresh food allergens, and regional disparities in allergen availability pose ongoing hurdles. Additionally, regulatory restrictions in Europe have limited access to certain test allergens, necessitating alternative approaches or reliance on serological testing. Furthermore, factors such as medication interference, dermatological conditions, and patient variability must be carefully managed to ensure accurate interpretation of results. Looking ahead, greater efforts are needed to harmonize allergy diagnostic protocols across regions, enhance allergen standardization, and improve clinician training in SPT and PTP methodologies. Future research should focus on refining predictive models for oral food challenges, expanding allergen panels, and integrating novel diagnostic techniques to complement traditional skin testing. By addressing these challenges, SPT and PTP testing will continue to play a pivotal role in personalized allergy diagnosis and patient management.

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Conflicts of interest statement

SA declares that she has participated as an advisory board member, and/or consultant, and/or speaker/chair at scientific meetings for Aimmune, DBV, Ferrero, Mabylon, Novartis, Stallergenes Greer, Thermofisher and Ulrich outside the submitted work.

Authors' contributions

Conceptualization: GD, FC. Methodology: LP, AG, CM. Formal Analysis: GD, FC. Investigation: GD, FC. Writing-Original Draft Preparation: GD, FC. Writing-Review & Editing: SA, DC, SG. Supervision: RB, MMG.

References

1 Bousquet J, Heinzerling L, Bachert C, et al. Practical guide to skin prick tests in allergy to aeroallergens. Allergy 2012;67:18-24. https://doi.org/10.1111/j.1398-9995.2011.02728.x.

2 Ansotegui IJ, Melioli G, Canonica GW, et al. IgE allergy diagnostics and other relevant tests in allergy. World Allergy Organ J 2020;13:100080. https://doi.org/10.1016/j.waojou.2019.100080.

3 Popov TA, Passalacqua G, González-Díaz SN, et al. Medical devices in allergy practice. World Allergy Organ J 2020;13:100466. https://doi.org/10.1016/j.waojou.2020.100466.

4 Gupta N, Agarwal P, Sachdev A, et al. Allergy Testing — An Overview. Indian Pediatr. 2019;56:951-957.

5 Heinzerling L, Mari A, Bergmann KC, et al. The skin prick test - European standards. Clin Transl Allergy 2013;3:1-10. https://doi.org/10.1186/2045-7022-3-3.

6 Zemmer F, Cenk E, Dahl Å, et al. A multidisciplinary approach of outdoor aeroallergen selection for Skin Prick Testing in the geographical area of Greater Istanbul. Eur Ann Allergy Clin Immunol 2022;54:34-42. https://doi.org/10.23822/EurAnnACI.1764-1489.188.

7 Heinzerling LM, Burbach GJ, Edenharter G, et al. GA(2)LEN skin test study I: GA(2)LEN harmonization of skin prick testing: novel sensitization patterns for inhalant allergens in Europe. Allergy 2009;64:1498-1506. https://doi.org/10.1111/j.1398-9995.2009.02093.x.

8 Riggioni C, Ricci C, Moya B, et al. Systematic review and meta-analyses on the accuracy of diagnostic tests for IgE-mediated food allergy. Allergy 2024;79:324-352. https://doi.org/10.1111/all.15939.

9 Stingeni L, Bianchi L, Tramontana M, et al. Skin tests in the diagnosis of adverse drug reactions. G Ital Dermatol Venereol 2020;155:602-621. https://doi.org/10.23736/S0392-0488.20.06698-5.

10 Klimek L, Hoffmann HJ, Kalpaklioglu AF, et al. In-vivo diagnostic test allergens in Europe: A call to action and proposal for recovery plan—An EAACI position paper. Allergy 2020;75:2161-2169. https://doi.org/10.1111/all.14329.

11 Cardona V, Demoly P, Dreborg S, et al. Current practice of allergy diagnosis and the potential impact of regulation in Europe. Allergy 2018;73:323-327. https://doi.org/10.1111/all.13306.

12 Klimek L, Hans Jürgen H, Kugler A, et al. Impact of changed legislation on skin tests: the present and future. Curr Opin Allergy Clin Immunol 2016;16:465-468. https://doi.org/10.1097/ACI.0000000000000312.

13 Terlouw S, van Boven FE, Borsboom-Van Zonneveld M, et al. Homemade Food Allergen Extracts for Use in Skin Prick Tests in the Diagnosis of IgE-Mediated Food Allergy: A Good Alternative in the Absence of Commercially Available Extracts? Nutr 2022;14:475. https://doi.org/10.3390/nu14030475

14 Jost R, Kespohl S, Paulus-Tremel KE, et al. Possible manufacture of test allergens in public pharmacies for the diagnosis of type I allergies: Legal aspects. Allergol Sel 2024;8:251-264. https://doi.org/10.5414/ALX02514E.

15 Kespohl S, Jost R, Maryska S, et al. Procedure for a standardized preparation of skin prick test solutions for the diagnosis of occupational type I allergies in the absence of commercial extracts. Allergol Sel 2024;8:238-250. https://doi.org/10.5414/ALX02506E.

16 Muthupalaniappen L, Jamil A. Prick, patch or blood test? A simple guide to allergy testing. Malaysian Fam physician Off J Acad Fam Physicians Malaysia 2021;16:19-26. https://doi.org/10.51866/rv1141.

17 Treudler R, Simon JC. Update on Type-1 Allergy Diagnostics. Handb Exp Pharmacol 2022;268:393-403. https://doi.org/10.1007/164_2021_487.

18 Fatteh S, Rekkerth DJ, Hadley JA. Skin prick/puncture testing in North America: a call for standards and consistency. Allergy, Asthma Clin Immunol 2014;10:1-9.

19 Yoon IK, Martin BL, Carr WW. A comparison of two single-headed and two multi-headed allergen skin test devices. Allergy asthma Proc 2006;27:473-478. https://doi.org/10.2500/aap.2006.27.2937.

20 Dykewicz MS, Dooms KT, Chassaing DL. Comparison of the Multi-Test II and ComforTen allergy skin test devices. Allergy asthma Proc 2011;32:198-202. https://doi.org/10.2500/aap.2011.32.3441.

21 Carr WW, Martin B, Howard RS, et al. Comparison of test devices for skin prick testing. J Allergy Clin Immunol 2005;116:341-346. https://doi.org/10.1016/j.jaci.2005.03.035.

22 Ateş A, Kınıklı G, Turgay M, et al. The results of skin prick testing in patients with allergic rhinitis: a comparison between a multiple lancet device and a single lancet. Asian Pacific J Allergy Immunol 2004;22:109-114.

23 Ménardo JL, Bousquet J, Rodière M, et al. Skin test reactivity in infancy. J Allergy Clin Immunol 1985;75:646-651. https://doi.org/10.1016/0091-6749(85)90088-0.

24 Martinez FD. The connection between early life wheezing and subsequent asthma: The viral march. Allergol Immunopathol (Madr) 2009;37:249-251. https://doi.org/10.1016/j.aller.2009.06.008.

25 Frati F, Incorvaia C, Cavaliere C, et al. The skin prick test. J Biol Regul Homeost Agents 2018;32(1 Suppl 1):19-24.

26 Patel G, Saltoun C. Skin testing in allergy. Allergy asthma Proc 2019;406:366-368. https://doi.org/10.2500/aap.2019.40.4248.

27 Seys SF, Roux K, Claes C, et al. Skin Prick Automated Test device offers more reliable allergy test results compared to a manual skin prick test. Rhinology 2024;62:216-222. https://doi.org/10.4193/Rhin23.330.

28 Justo X, Díaz I, Gil JJ, et al. Prick test: evolution towards automated reading. Allergy 2016;71:1095-1102. https://doi.org/10.1111/all.12921.

29 Gorris S, Uyttebroek S, Backaert W, et al. Reduced intra-subject variability of an automated skin prick test device compared to a manual test. Allergy. 2023;78:1366-1368. https://doi.org/10.1111/all.15619.

30 Seys SF, Gorris S, Uyttebroek S, et al. Evaluation of skin prick location on the forearm using a novel skin prick automated test device. Front allergy 2023;4:1289031. https://doi.org/10.3389/falgy.2023.1289031.

31 Sirin Kose S, Asilsoy S, Uzuner N, et al. Outcomes of Baked Milk and Egg Challenge in Cow's Milk and Hen's Egg Allergy: Can Tolerance Be Predicted with Allergen-Specific IgE and Prick-to-Prick Test? Int Arch Allergy Immunol 2019;180:264-273. https://doi.org/10.1159/000502957.

32 Patti ML, De Rose C, Brancato F, et al. Sensitivity of prick test with walnut commercial extracts and of prick by prick with raw walnut compared with open food challenge in walnut allergy. Acta Biomed 2021;92(S1):e2021067. https://doi.org/10.23750/abm.v92iS1.10043.

33 Adomaite I, Stirbiene N, Marciukaitiene V, et al. Prick-by-Prick Test with Pasteurised Cow's Milk: A Valuable Tool in Paediatric Practice. Biomed Res Int 2022;2022:9738654. https://doi.org/10.1155/2022/9738654.

34 Terlouw S, van Boven FE, Borsboom-van Zonneveld M, et al. Comparison of skin prick test and prick-to-prick test with fruits and vegetables in the diagnosis of food allergy. Clin Transl Allergy 2024;14:e12375. https://doi.org/10.1002/clt2.12375.

35 Vlieg-Boerstra BJ, Van De Weg WE, Van Der Heide S, et al. Where to prick the apple for skin testing? Allergy 2013;68:1196-1198. https://doi.org/10.1111/all.12201.

36 SIAIP Allergy Diagnostic Commission, edited by. Bernardini R, Arasi S, Barni S, et al. Multiparametric or multiplex systems in allergy diagnostics. Italian Journal of Pediatric Allergy and Immunology 2024;38:17-21. https://doi.org/10.53151/2531-3916/2024-436.

37 Kowalski ML, Ansotegui I, Aberer W, et al. Risk and safety requirements for diagnostic and therapeutic procedures in allergology: World Allergy Organization Statement. World Allergy Organ J 2016;9:33. https://doi.org/10.1186/s40413-016-0122-3.

38 Liccardi G, D'amato G, Canonica GW, et al. Systemic reactions from skin testing: literature review. J Investig Allergol Clin Immunol 2006;16:75-78.

39 Norrman G, Fälth-Magnusson K. Adverse reactions to skin prick testing in children – Prevalence and possible risk factors. Pediatr Allergy Immunol 2009;20:273–278. https://doi.org/10.1111/j.1399-3038.2008.00761.x.

40 Lockey RF, Benedict LM, Turkeltaub PC, et al. Fatalities from immunotherapy (IT) and skin testing (ST). J Allergy Clin Immunol 1987;79:660-677. https://doi.org/10.1016/s0091-6749(87)80164-1.

41 Swender DA, Chernin LR, Mitchell C, et al. The rate of epinephrine administration associated with allergy skin testing in a suburban allergy practice from 1997 to 2010. Allergy Rhinol (Providence) 2012;3:ar.2012.3.0034. https://doi.org/10.2500/ar.2012.3.0034.