THE MOST COMMON ALLERGIC SKIN DISEASES AND RESPIRATORY SYSTEM DISORDERS IN LIGHT OF CURRENT DIAGNOSTIC AND THERAPEUTIC RECOMMENDATIONS

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Contrach dermatitis

Contact dermatitis (CD) is a common inflammatory skin condition, which include all adverse skin reactions that result from direct exposure of the skin or mucous membranes to external agents. The cutaneous response to such substances may be either immunologic or non-immunologic origin. It represents an inflammatory process of the skin that is triggered by:

- irritant agents (**acute or chronic irritant contact dermatitis, ICD**)
- sensitizing agents (**acute or chronic allergic contact dermatitis, ACD**).

Allergic contact dermatitis

It is estimated that at least 20% of the general population is allergic to commonly occurring haptens, such as metals, fragrance substances, and preservatives. Women are affected twice as often as men, with prevalence rates of around 11% in women and 5% in men in industrialized countries.

Mechanism of allergic contact dermatitis

ACD is an acquired eczematous inflammation of the skin triggered by exogenous chemical haptens , usually of low molecular weight(below 1000 daltons), that induce a type IV (cell-mediated, delayed) immune response.
This process occurs in two stages:

Stage 1: Induction (Sensitization)

- Hapten penetration: Small molecules (haptens) penetrate the skin and bind to proteins, forming hapten-protein complexes.

- Antigen capture and migration: Dendritic cells (DCs) in the skin capture and process these complexes and subsequently migrate to regional lymph nodes.
- T cell activation: DCs present antigens to naïve T lymphocytes, leading to the activation and differentiation of hapten-specific T cells.
- Systemic circulation: Sensitized T lymphocytes circulate throughout the body, establishing immune memory.

Stage 2: Effector Phase (Elicitation)

- Re-exposure to hapten: Upon contact with the same hapten, sensitized T lymphocytes recognize the antigen in the skin.
- T cell migration: Activated T cells migrate to the site of exposure in the epidermis/epithelium.
- Inflammatory response: T cells release cytokines and recruit other immune cells, causing local inflammation.
- Clinical manifestation: itchy eczematous eruption.
- Systemic memory: Although the reaction is localized, effector and memory T lymphocytes are distributed systemically, enabling rapid response upon future exposures.

Diagnosis

The diagnosis of contact dermatitis (CD) is based on:

a) clinical evaluation
b) detailed assessment of potential exposures
c) **patch testing** - which remains the **gold standard for identifying contact allergens**.

Recommendations before patch testing:

- Limit oral prednisolone to less than 10 mg per day.
- Avoid immunosuppressive agents that may reduce the test reaction.
- Do not apply potent topical steroids to the test site for at least few days before testing.
- Antihistamines can be taken as usual, as they do not interfere with the type IV hypersensitivity reaction.
- Avoid suntanning and UV therapy at least 2 months before testing.

Patch Test Application Procedure

1. Preparation
   - Ensure the patient's back is clean, dry, and free from creams, ointments, or topical medications.
   - Prepare test sets (chambers, haptens, adhesive strips, documentation form).

2. Allergen Loading
   - Using a micropipette or dropper, apply a small amount (≈20–30 µL) of each allergen into the center of the designated test chamber.
   - Avoid air bubbles and overfilling.
   - Load the chambers before application to avoid drying of test substances.

3. Application to the Skin
   - Ask the patient to stand or sit upright with relaxed shoulders.
   - Gently apply the loaded test strip to the patient's back.
   - Smoothly press along the strip to ensure full contact between chambers and skin.
   - Secure the strip with additional hypoallergenic tape if necessary.

4. Labelling and Documentation
   - Mark each edge of the strips on the patient's back to assist with repositioning during reading..
   - Label the strip on a diagram (test map) with the exact position and allergen name or number.
   - Record the date and time of application.

5. Patient Instructions
   - Keep the test area dry (no showering or rubbing).
   - Avoid physical exercise and tight clothing.
   - Return for the first reading at 48 hours (Day 2), followed by readings at 72, 96 hours and after 7 days.

6. Patch Removal and Reading
   - Remove the patches carefully at 48 hours.
   - Assess and document skin reactions according to criteria (-/+, +, ++, +++, irritant).
   - Perform second reading at 72,96 hours and 7 days.

Interpreting the test

Contact allergy is confirmed by a **positive patch test reaction.** Below is interpretation of patch test results according to the International Contact Dermatitis Research Group (ICDRG) scoring system.

Grade	**Description**	**Interpretation / Clinical Meaning**
– (Negative)	No visible change compared to surrounding skin.	No reaction to the tested allergen.
? / ± (Doubtful)	Slight, faint erythema only, without infiltration or papules.	Reaction uncertain; may not be clinically significant.

+ (Weak Positive)	Erythema, possibly with slight infiltration and/or fine papules.	Mild allergic reaction; may be clinically relevant if consistent with history.
++ (Strong Positive)	Erythema with infiltration, papules, and vesicles (small blisters).	Clear allergic reaction; usually clinically relevant.
+++ (Extreme Positive)	Intense erythema with coalescing vesicles, bullous	Severe allergic reaction; clinically significant and may
	formation, or spreading reaction.	be uncomfortable.
IR (Irritant Reaction)	Non-specific reaction caused by irritation (e.g., erythema without infiltration/vesicles, shiny or abrupt borders).	Not allergic; usually irrelevant to clinical diagnosis.

Very important aspect is the assessment of so called „clinical relevance", as it determines whether a positive reaction truly contributes to the patient's dermatitis.

Distinguishing between allergic contact dermatitis and contact allergy includes:

1. Allergic Contact Dermatitis

- The clinical manifestation of contact allergy.
- Occurs when a sensitized individual is exposed to the allergen, triggering an inflammatory skin reaction.

2. Contact Allergy

Refers to immune sensitization to a specific hapten (positive patch test result) with clinical manifestations.

Baseline series

The set of the series changes over time and across countries, reflecting variations in the relevance of different allergens.

The main criteria for including allergens in the baseline series are:

- The allergen is common in the environment, and the prevalence in the general population is over 1%.
- Testing results are reliable, with established concentration and vehicle.
- Results are easy to interpret, without marginal irritant effects that could obscure the distinction between allergic and irritant reactions.
- Adverse effects are minimal, with few severe (+++) reactions and no jatrogenic sensitization.

It has been suggested that for practical reasons the number of substances in a baseline set should be between 20 and 30 . The Polish Standard Series I and II include, among others, allergens such as metals (e.g., nickel, cobalt, chromium, palladium), preservatives (e.g., isothiazolines, parabens, formaldehyde releasers), fragrances, textile dyes, rubber components (e.g., thiurams, mercaptobenzothiazole), ingredients of personal care products, hair and nail cosmetics, and occupational or airborne agents such as adhesives, plants, and resins.

Clinical manifestation:

The skin reaction typically begins at sites of contact with the allergen, but over time it may spread to a generalized distribution.

Depending on the predominant morphology of skin lesions and their duration, ACD can be classified into:

1. **Acute ACD**: characterized by oedema, erythema and vesicles

2. **Chronic ACD**: Chronic ACD is characterized by xerosis (dry skin), scaling, hyperkeratosis, and fissures, with lesions persisting for more than three months.

Both subtypes can usually be distinguished clinically, although overlap between them is quite common.

Systemic allergic contact dermatitis. Systemic ACD is a rare form and, in some cases, a subject of debate. It is characterized by eczematous lesions that often appear in flexural areas following systemic exposure to an allergen via oral or parenteral routes. Reactions can be triggered, for example, by nickel or balsam of Peru.

Another clinical manifestation is **airborne allergic contact dermatitis**, which arises when allergens present in the air come into contact with the skin. Lesions typically appear on exposed areas, such as the face, hands, and forearms. Common airborne allergens include substances from plants or preservatives used in paints.

Photoallergic contact dermatitis (PACD) is a form of allergic contact dermatitis that occurs due to the interaction between a topically applied chemical (e.g. ingredients in cosmetics, sunscreens, topical medications) and exposure to usually UVA radiation. It affects sun-exposed areas while often sparing shaded regions such as under the chin or behind the ears.

Connubial allergic contact dermatitis is a rare form that arises from allergen transfer due to close contact with another person This can occur, for example, when a product from a partner’s lips comes into contact with the cheek of the affected individual. Common triggers in consort ACD include cosmetic products such as lipsticks, moisturizers, and aftershaves, as well as topical medications.

Occupational allergic contact dermatitis (OACD) develops after workplace exposure to specific allergens. It occurs when a worker becomes sensitized to a substance used or encountered in their occupational environment, leading to recurrent eczema-like lesions upon re-exposure, typically affecting areas of direct contact such as the hands, forearms, or face. Workers at highest risk include hairdressers, healthcare professionals, metalworkers, blacksmiths, painters, construction workers, and food processing employees. Common occupational allergens include thiurams and carbamates (rubber accelerators), epoxy resins, formaldehyde-releasers, and metals.

Patient education and preventive measures:

- **Educational programs and instructions**
- **Avoidance of clinically relevant allergens**
- **Use of personal protective equipment (PPE)**
- **In some cases, occupational change may be necessary**

After confirming which substances trigger ACD, the patient should be informed about the need to avoid these allergens. Providing written materials detailing each allergen is helpful.

These information sheets ought to include the chemical's name, any common synonyms, usual applications, strategies for avoiding contact, and, if applicable, possible alternatives

Treatment

- **Topical anti-inflammatory treatment** (corticosteroids, tacrolimus ointment, JAK inhibitors)
- **Phototherapy**
- **Systemic treatment: short-course systemic corticosteroids, cyclosporine A, methotrexate,**

azathioprine, acitretin (in hyperkeratotic hand/foot eczema), alitretinoin

- **Emollients**

Treatment should follow basic principles, considering the stage of the disease, causes, severity, type and location of skin lesions, other health conditions. Most patients can control sudden flare-ups of ACD with antiinflammatory drugs and moisturizers.

High-potency corticosteroids should not be used for long periods, as they can slow the repair of the outer skin layer, partly by breaking down filaggrin. They may cause skin atrophy and interfere with recovery in the long term. Mometasone seems to be moderately strong and causes fewer side effects. Applying the cream once a day is sufficient and may even be superior to twice daily application. Additionally, clinical experience suggests that using a topical corticosteroid and a topical calcineurin inhibitor alternately or together may help reduce side effects**.**

It is worth emphasizing that **allergic contact dermatitis caused by a topical corticosteroid, or its vehicle**, is not uncommon and should be considered when ACD does not respond to topical treatment .In patients with resistant or refractory ACD, phototherapy may be used as an adjunctive treatment.

Short-term systemic corticosteroids should be reserved for acute and severe inflammatory episodes or as part of a treatment plan, for example cyclosporine A, methotrexate, azathioprine, acitretin (in hyperkeratotic hand/foot eczema), alitretinoin.

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Urticaria

Urticaria (hives) is a mast-cell–mediated skin disorder characterized by the sudden appearance of *wheals*, *angioedema*, or both. Wheals are transient, pruritic swellings of the dermis while angioedema involves deeper dermal or submucosal layers [1,2].

Epidemiology and Prevalence

- Acute urticaria occurs in approximately 20–25% of individuals at least once during their lifetime[2].
- Chronic urticaria (CU) affects ~1% of the population[1].
- Women are affected twice as often as men.
- Peak onset typically occurs between 20 and 40 years of age.
- The disease can persist for years and exerts a significant impact on quality of life, sleep disturbance and work productivity.

Classification

Tab 1. Classification of urticaria by duration and eliciting mechanisms.

Category	Subtype	Duration / Trigger	Key Features
Acute urticaria (AU)	—	< 6 weeks	Often triggered by food, infection, or drugs; typically, selflimited.
Chronic urticaria (CU)	Chronic Spontaneous Urticaria (CSU)	≥ 6 weeks	Recurrent wheals and/or angioedema without an identifiable trigger; autoimmune mechanisms are frequent.

	Chronic Inducible Urticaria (CIndU)	Trigger-dependent	Wheals appear following exposure to specific physical or chemical triggers.
Angioedema (± urticaria)	Acute or Chronic	Variable	Deep swelling, often involving mucosal tissues; may occur with or without wheals.

Each subtype of inducible urticaria is defined by its characteristic provocation factor and clinical response pattern. Recognition of these forms is essential for targeted diagnostic testing and appropriate patient counselling.

Tab 2. Characteristics of Inducible Urticarias [1].

Type of induced urticaria	Characteristics
Symptomatic dermographism	Development of linear wheals at sites of a skin scratch or friction
Cold-induced urticaria	Wheals or angioedema at sites exposed to cold
Delayed pressure urticaria	Painful oedematous lesions 6–8 hours after a long-term pressure; they may be present up to 72 hours
Solar urticaria	Wheals after light exposure
Heat-induced urticaria	Wheals after exposure to heat
Vibratory urticaria	Skin oedema directly after exposure to vibrations
Cholinergic urticaria	Wheals after physical effort or body warmup
Aquagenic urticaria	Wheals or skin oedema after contact with water (independent of temperature)

Contact urticaria	Wheals or oedema at sites where skin has contact with various factors

Clinical Presentation

Wheals (hives) are the hallmark lesions of urticaria and exhibit three defining characteristics [2]:

- A sharply circumscribed, superficial, central swelling of variable size and shape, typically surrounded by reflex erythema.
- An accompanying itching or burning sensation.
- A transient nature, with complete resolution and return to normal skin appearance usually within 30 minutes to 24 hours.

Angioedema is characterized by [2]:

- A sudden, pronounced, erythematous or skin-colored deep swelling involving the lower dermis, subcutis, or mucous membranes.
- Tingling, burning, tightness, and pain rather than itch.
- A slower resolution compared to wheals, lasting up to 72 hours.

Pathogenesis and Immunologic Mechanisms

All forms of urticaria share a common final pathway: activation and degranulation of cutaneous mast cells, leading to the release of histamine, leukotrienes, prostaglandins, and cytokines.

These mediators increase vascular permeability, promote tissue edema, and stimulate sensory nerves, resulting in pruritus and burning sensations[2].

Triggers of Mast Cell Activation[3–5]:

- **Immunologic mechanisms:** IgE-mediated hypersensitivity reactions to foods, drugs, or venoms.
- **Autoimmune mechanisms:**
  - Type I (autoallergic): presence of IgE autoantibodies directed against self-antigens (e.g., thyroperoxidase).
  - Type IIb (cytotoxic): IgG autoantibodies against IgE or its highaffinity receptor FcεRIα.
- **Non-immunologic:** Activation by NSAIDs**,** infections**,** emotional stress**,** hormonal factors, or physical agents (pressure, heat, cold, vibration).

Mediators and Cellular Pathways[3–5]:

- **Histamine** – activates H1 and H2 receptors, causing vasodilation, erythema, and pruritus.
- **Platelet-activating factor (PAF)** and **bradykinin** – contribute particularly to the development of angioedema.
- **Cytokines** such as **IL-6** and **TNF-α** – maintain inflammation and promote basophil recruitment.
- **Complement fragments (C3a, C5a)** – can further enhance mastcell activation and amplify the inflammatory response.

Tab 3. Urticaria Endotypes and Their Key Characteristics[2–5]

Endotype	Mechanism	Laboratory/Clinical Markers
Type I autoallergic	IgE against autoantigens	Elevated total IgE levels; presence of anti-TPO IgG antibodies.
Type IIb autoimmune	IgG to IgE/FcεRI	Low total IgE; positive basophil histamine release test; thyroid autoantibodies

Non-autoimmune	Idiopathic/triggered	Normal IgE; unremarkable autoimmunity

Clinical Assessment

The diagnosis of urticaria is primarily clinical, based on a detailed medical history and physical examination. A thorough assessment of the morphology, duration, and recurrence of wheals or angioedema is essential to differentiate urticaria from other dermatoses and to guide further investigations.

History:	Physical Examination:
A structured history should include: • Onset, duration, frequency of lesions • Potential triggers: cold, heat, pressure, exercise, infection, medications • Response to medications, particularly antihistamines • Personal or family history of atopy, autoimmune or thyroid disease • Associated systemic symptoms.	A focused clinical examination should assess: • Distribution, shape, and duration of wheals • Presence or absence of angioedema • Signs of vasculitis or systemic disease • Provocation tests if inducible urticaria suspected

Tab 4. Summary of laboratory investigations in different forms of urticaria[1].

Diagnostics	Acute urticaria	Chronic spontaneous urticaria	Chronic inducible urticaria
Routine diagnostic tests	None	CBC, CRP and/or ESR	Provocation tests with threshold determination
Non-obligatory diagnostic tests		– Diagnostics of infections: H. pylori, Borrelia burgdorferi, anti-HCV, bacteriological smears – TSH, ft3, ft4; antiTPO, anti-TG, antirTSH antibodies – ASST – Skin Prick test – Provocation tests – Elimination diet – Tryptase – Inh. C1q, C3, C4 – Histopathological tests	– CBC, CRP or ESR – Diagnostics of infections (coldinduced urticaria only).

Tab 5. Standard provocation and threshold tests for chronic inducible urticaria[2].

Subtype	Test	Key Notes
Cold urticaria	Ice cube or TempTest	Observe after 5–10 min exposure

Delayed pressure urticaria	Weighted dermographometer	Lesions after 4–6 h
Heat urticaria	Thermal plate or water bath	Lesions within minutes
Solar urticaria	UV/visible light provocation	Differentiate from photodermatoses
Cholinergic urticaria	Exercise or hot bath test	Small punctate wheals post-sweating
Aquagenic urticaria	Water compress at 37°C	Confirm reproducibility
Vibratory angioedema	Vortex mixer test	Swelling after vibration
Contact urticaria	Patch or direct contact	Immediate wheal formation

Differential Diagnosis

The diagnosis of urticaria should always include differentiation from other conditions that can present with wheals, angioedema, or both. The most relevant disorders and their distinguishing features are summarized below.

Tab 6. Key differential diagnoses and clinical [1,2]

Condition	Distinguishing Features
Urticarial vasculitis	Lesions lasting >24 hours, often painful rather than itchy, leaving residual pigmentation.

Mastocytosis	Persistent lesions, positive Darier's sign, and elevated serum tryptase levels.
Bradykinin-mediated angioedema	Absence of wheals; low C4 and/or C1inhibitor levels.
Contact dermatitis	Eczematous, delayed-type lesions rather than transient wheals.
Drug eruption	Fixed lesions with possible systemic symptoms.

Solar urticaria should be distinguished from porphyria, and polymorphous light eruptions [2]. Differential diagnosis is particularly important when the eruption is accompanied by systemic manifestations such as headache, fever, arthralgia, lymphadenopathy, or abdominal symptoms, which may indicate an underlying systemic or autoimmune disease.

Assessment of Disease Activity and Quality of Life

Accurate assessment of disease activity and control is essential for monitoring treatment response and guiding therapeutic decisions in urticaria. Standardized and validated instruments are recommended to ensure objective and reproducible evaluation across clinical visits.

Urticaria Activity Score (UAS7)

The UAS7 is the most widely used tool to quantify urticaria activity. It records the daily number of wheals (0–3) and the intensity of pruritus (0– 3) over seven consecutive days, resulting in a total score ranging from 0 to 42. Higher scores reflect greater disease activity.

Symptom intensity score: 0–3	Wheals	Pruritus
0	None	None
1 – mild	< 20 wheals / 24 hours	Present but not annoying or troublesome
2 – moderate	20–50 wheals / 24 hours	Troublesome but does not interfere with normal daily activity or sleep
3 – intense	> 50 wheals / 24 hours	Severe, sufficiently troublesome to interfere with normal daily activity or sleep

Interpretation:

0 = complete remission; 1–6 = well controlled; 7–15 = mild; 16–27 = moderate; 28–42 = severe.

Urticaria Control Test (UCT)[6]

The UCT evaluates overall disease control using four self-assessment questions**,** each scored from 0 to 4. The maximum score is 16, with a score of ≥12 indicating well-controlled disease.

Question	Response Options

1. How much have you suffered from the physical symptoms of urticaria (itch, hives [welts], and/or swelling) in the last four weeks?	☐ Very much – 0 ☐ Much – 1 ☐ Somewhat – 2 ☐ A little – 3 ☐ Not at all – 4
2. How much was your quality of life affected by urticaria in the last four weeks?	☐ Very much – 0 ☐ Much – 1 ☐ Somewhat – 2 ☐ A little – 3 ☐ Not at all – 4
3. How often was the treatment for your urticaria in the last four weeks not enough to control your urticaria symptoms?	☐ Very often – 0 ☐ Often – 1 ☐ Sometimes – 2 ☐ Seldom – 3 ☐ Not at all – 4
4. Overall, how well have you had your urticaria under control in the last four weeks?	☐ Not at all – 0 ☐ A little – 1 ☐ Somewhat – 2 ☐ Well – 3 ☐ Very well – 4

Angioedema Activity Score (AAS)

The AAS measures the daily severity and frequency of swelling episodes and should be applied when angioedema is the predominant feature.

Score Dimension	Answer Options
Have you had a swelling episode in the last 24 hours?	No / Yes
At what time(s) of day was this swelling episode(s) present? (select all that apply)	Midnight–8 a.m. / 8 a.m.–4 p.m. / 4 p.m.–Midnight
How severe is/was the physical discomfort caused by this swelling episode(s)? (e.g., pain, burning, itching)	No discomfort / Slight discomfort / Moderate discomfort / Severe discomfort

Are/were you able to perform your daily activities during this swelling episode(s)?	No restriction / Slight restriction / Severe restriction / No activities possible
Do/did you feel your appearance is/was adversely affected by this swelling episode(s)?	No / Slightly / Moderately / Severely
How would you rate the overall severity of this swelling episode?	Negligible / Mild / Moderate / Severe

Scoring system:

- Each dimension is scored 0–3, yielding a daily AAS sum score (0–15).
- 7-day sum (AAS7): 0–105
- 4-week sum (AAS28): 0–420

Health-Related Quality of Life (HRQoL) Instruments *(EADV Task Force, 2024)[7]*

Quality of life assessment is an integral part of urticaria management, providing insight into the psychosocial and functional burden of the disease. Validated tools should be used consistently to capture patientreported outcomes.

Instrument	Population	Focus / Domains
DLQI	Adults	General dermatologic QoL
CDLQI	Children	Age-specific dermatology QoL

CU-Q2oL	Adults with CSU	Disease-specific: pruritus, swelling, sleep, appearance, life impact
CU-QOL, CholU-QoL	Subtype-specific	Physical/functional limitation
EQ-5D, SF-36	Generic	Cross-disease comparison

Clinical studies demonstrate a moderate correlation between UAS7 and HRQoL instruments such as DLQI and CU-Q2oL. An improvement of ≥10 points in UAS7 is associated with a clinically meaningful enhancement in quality of life. HRQoL is particularly impaired by nocturnal itching, symptom unpredictability, and visible skin lesions, underscoring the importance of holistic management and patient-reported outcome monitoring[7].

Mangement

The management of urticaria is based on individualized, stepwise therapy guided by disease activity, treatment response, and safety profile.

Key principles include:

- **Identification and elimination of triggers;** · **Evaluation and management of comorbidities**;
- **Use of non-sedating second-generation H1-antihistamines** as first-line therapy and the foundation of treatment.
- **Adherence to a stepwise escalation strategy**.
- **Regular assessment of disease control** (UCT, UAS7) to guide therapeutic adjustment.

Management of chronic urticaria follows a standardized, evidence-based escalation protocol. Each therapeutic step should be

implemented sequentially, with ongoing evaluation of efficacy and tolerability [2].

Treatment Algorithm[1,2]

Step	Medication / Intervention	Comments
1	Non-sedating second-generation antihistamine for exemple Bilastine 20 mg, cetirizine 10 mg, fexofenadine 180 mg, loratadine mg, lewoceterizine 5 mg.	Once daily; avoid firstH1-generation antihistamines due to sedation and anticholinergic effects 10
2	Up-dose non-sedating secondgeneration H1-antihistamine (up to ×4 standard dose)	Supported by clinical evidence for safety and efficacy; monitor for mild sedation.
3	Omalizumab 300 mg subcutaneously every 4 weeks	Typical onset within 1–4 weeks; dose escalation to 600 mg may be considered in partial responders.
4	Cyclosporine A(3–5 mg/kg/day)	Indicated for refractory CSU; requires monitoring of blood pressure, renal function, and cyclosporine levels.
5	Alternative / emerging	Investigational or off-label options include ligelizumab, barzolvolimab, remibrutinib, and dupilumab

Special Populations

Management of urticaria in special populations requires tailored therapeutic decisions to ensure both efficacy and safety. Dosage adjustments, contraindications, and comorbidities must be considered in every case. [2]

Group	Key Notes
Children	Use age-appropriate doses of second-generation antihistamines. Avoid sedating agents. Omalizumab is approved for patients aged ≥12 years.
Pregnancy	Prefer loratadine or cetirizine as first-line agents. Avoid immunosuppressive therapy unless absolutely necessary.
Elderly	Adjust treatment according to renal function and comorbidities. Be cautious of polypharmacy and increased risk of falls with sedating drugs.
Autoimmune disease	Evaluate thyroid function and autoantibodies. Manage the underlying autoimmune condition alongside urticaria treatment.

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Atopic dermatitis

Atopic dermatitis (AD) is a chronic, relapsing, intensely pruritic inflammatory skin disease. Commonly associated with allergic rhinitis (hay fever or seasonal allergies) and asthma. This triad of conditions is collectively known as atopy. The lifetime prevalence of AD is estimated to be 10% to 30% in children and 2% to 10% in adults. Currently, an increasing atopic dermatitis incidence constitutes a serious medical problem. Research studies documented that a higher risk of AD development is associated with areas of industrialization, urbanization, and higher affluent class, whereas living in more tropical latitudes and rural areas are associated with lower risk of AD.

1. Clinical features

Pruritus, dry skin, and a compromised barrier function are characteristic of all stages of AD. Fish-like polygonal scales may appear on the skin, particularly the legs. A decreased skin barrier can also facilitate microorganism overgrowth with bacteria, viruses, and yeasts. There is an increased susceptibility to secondary bacterial colonization and infection with staphylococcus more frequently than streptococcus, often presenting with crusting of involved skin. Hair follicles are often prominent on the extensor aspect of the upper arms and anterior thighs with a surface scale and underlying follicular prominence (keratosis pilaris), occasionally involving the cheeks.

The area around the eyes may also offer clues for atopy. Allergic sensitivity often causes swelling of the periorbital skin that can leave shiners or dark skin with resolution. There is also often a double crease

around the eye (Dennie-Morgan lines) or loss of the lateral third of the eyebrows from constant scratching.
During the first years of life, AD incidence is similar in both sexes, after the age of 6, prevalence of the female sex over male is noted (3 : 2). Atopic dermatitis usually starts in early childhood. It is believed that in 45% of infants symptoms appear before the 6th month of life, and in 50% before they are 1 y/o. In 40–80% of children the disease tends to recede before the age of 5, and in 20% of patients it is present till adulthood.

There are three stages of AD based on the age of affected individuals:

- The infantile stage is often acute, with papules (raised lesions <1 cm) that develop after the second week of life up to age 2 years. It is classically located on the head and neck with involvement of the extensor skin on the elbows and knees related to the trauma from the crawling posture.
- The infantile stage from age 2 years to puberty is most likely to present with subacute lesions on the trunk and extremities and prominent flexural involvement of the elbows and knees.
- The adult stage may be limited to the hands but can be involved elsewhere on the skin surface.

2. Allergic march

Atopic dermatitis may be concomitant with other IgE-dependent atopic diseases: bronchial asthma, allergic upper respiratory congestion and catarrhal conjunctivitis, and sometimes even food allergies.
Epidemiological studies and clinical observations indicate the existence of a specific sequence of occurrence of atopic diseases. This phenomenon was called an allergic march and does not always have a classic course. About 34% of AD-patients develop allergic rhinitis, 20–35% – asthma,

and 15% – clinical symptoms of food allergies. Genetic factors and external factors such as stress, eating habits, infections, cigarette smoke, or smog, mainly predispose individuals to develop an allergic disease and allergic march.

3. Pathopysiology

The pathophysiology of AD is complex and multifactorial. AD is the results of the interaction between skin barrier dysfunction, immunologic, and environmental factors. Abnormal gene(s) that encode defective skin barrier components (eg, filaggrin, ceramides) lead to increased transepidermal water loss and associated dry skin and surface pH changes. The pathogenesis of AD is also orchestrated through a biphasic inflammatory response typified by a helper T-cell type 2 (TH2) lymphocyte-dominant response with overproduction of TH2 cytokines interleukin 4 (IL-4), IL-5, and IL-13 prior to converting to a T1 response. Interplay of psychological stress and environmental factors has a also a crucial role. The dysregulation of the skin barrier predisposes individuals to colonization of microbial pathogens. Well-established triggers for atopic eczema include environmental aeroallergens (eg, animal dander), along with environmental stressors such as reduced humidity and lower outdoor temperatures. Further, the use of harsh alkaline detergents and soaps over the skin is known to alter the skins acidic pH. When the skin becomes more alkaline, this dysregulates downstream enzyme activity and triggers AD.

4. Diagnostic

Atopic dermatitis often begins in childhood and is characterized by periods of flare-ups and remission. Because there are no definitive laboratory tests, diagnosis of atopic dermatitis is primarily clinical, relying on a combination of patient history, morphology and distribution of skin lesions. Common diagnostic criteria sets include the Hanifin and Rajka. They are applied in both children and adults it is a combination of major and minor features.

Major features (at least 3 are required for diagnosis):

1. Pruritus
2. Typical distribution and morphology of skin lesions depends on the age of patients
3. Chronic and relapsing course
4. Personal or family history of atopy (asthma, allergic rhinitis, atopic dermatitis, conjunctivitis) **Minor features:**

1. Xerosis (dry skin)
2. Ichthyosis or other keratotic disorders
3. Immediate skin test reactivity (positive prick tests, urticaria)
4. Elevated serum ige levels
5. Early onset of the disease
6. Tendency toward cutaneous infections (especially staphylococcus aureus, herpes simplex)
7. Tendency toward nonspecific hand and foot dermatitis
8. Nipple eczema
9. Cheilitis
10. Recurrent conjunctivitis
11. Keratoconjunctivitis
12. Orbital darkening (allergic shiners)

13. Infraorbital fold (dennie–morgan fold)
14. Anterior neck folds
15. Keratosis pilaris
16. Pityriasis alba
17. Scalp scaling
18. Intolerance to wool or lipid solvents
19. Exacerbations due to environmental or emotional factors
20. Food intolerance
21. Course influenced by climate and season
22. White dermographism or delayed blanching response

The most commonly used, validated tools for assessing the severity of AD:

- **SCORAD** (Scoring Atopic Dermatitis) - takes into account the extent and severity of lesions (objective and subjective), allowing for treatment monitoring.
- **EASI** (Eczema Area and Severity Index) - focuses on the extent and severity of eczema in four body areas. A recognized tool for monitoring treatment response and assessing disease severity.

A punch skin biopsy may be necessary for patients with atypical presentations to rule out other skin conditions that may resemble AD. These conditions include other inflammatory dermatoses (seborrheic dermatitis, psoriasis, allergic or irritant contact dermatitis, and pityriasis lichenoides), primary ichthyosis, infestations (scabies), infections (fungal, human immunodeficiency virus [HIV]), malignancies (most commonly cutaneous T-cell lymphoma), and metabolic disorders.

5. Patient's perspective

The burden of disease in atopic eczema does not consist of symptoms only, but it affects life in general, for patients and family. As a well as being a painful and frustrating condition, atopic eczema affects all aspects of life, from sleep disorders to relationships, work/school and social activities. The condition can also negatively impact on self-esteem and psychological well-being, which may lead to anxiety and depression. Therefore the whole burden of the disease needs to be taken into account when treating patients with mild to severe atopic eczema. The treatment of atopic eczema can be laborious, complex and confusing to self-manage. Patients/caregivers require personalised education, guidance and on-going support by health care providers and patient networks. Indeed, in many cases, escalation to more aggressive therapies or referrals to specialist care could be prevented by better self-management skills and adherence to treatment at home.

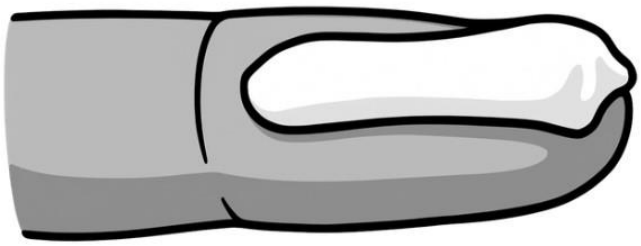
6. Treatment

6.1 Basic emollients and moisturizers

Basic emollient therapy is the essence of every treatment of AD. Throughout this tekst, "emollients" are defined as ‘topical formulations with vehicle-type substances without active ingredients’. Emollients usually contain a humectant or moisturizer (promoting stratum corneum hydration such as urea or glycerol) and an occludent (reducing evaporation such as lipids or petrolatum).

It is recommended to apply emollients immediately after bathing or showering and soft pat drying. Emollients should be free of potentially allergenic substances such as fragrances, especially in children under the age of 2.

The long-term use of maintenance (e.g. twice weekly) emollient therapy after remission may prolong the duration of flare free intervals. The direct, sole use of emollients on inflamed skin is often poorly tolerated, and it is better to treat the acute flare first with anti-inflammatory. Emollients are the mainstay of management. Hydration of the skin is usually maintained by at least twice daily application of emollients with a hydrophilic basecontaining for instance 5 % urea or glycerol. The applied amount is crucial, about 250g/week are recommended. It may follow the finger-tip unit rule: a finger-tip unit (FTU) is the amount of ointment expressed from a tube with a 5 mm diameter nozzle and measured from the distal skin crease to the tip of the index finger (ca. 0.5 g), this is an adequate amount for application to two adult palm areas, which is approximately 2 % of an adult body surface area. The use of pure oil products such as coconut or olive oil instead of emulsions will dry out the skin and increase the transepidermal water loss and thus is not recommended.



LOCATION				
FACE AND NECK	ARM AND HAND	LEG AND FOOT	TRUNK (front)	TRUNK (back)
2.5 FTU	4 FTU	8 FTU	7 FTU	7 FTU

Fig. 1 Recommended number of FTUs to apply to different areas of the body in adults.

The use of emollients is safe, except for occasional cases of contact allergy. Using emollients may be associated with irritative and allergic side effects. In patients for whom topical anti-inflammatory treatment is indicated, the use of emollients alone involves a considerable risk of disseminating bacterial or viral infections typical for AD.
Emollients may contain ingredients eliciting contact sensitisation such as emulsifiers, preservatives or fragrances. There is a high inter-individual variability in skin tolerability of topical preparations, which has to be considered in the management of AD patients. Urea may cause irritation in infants and should be avoided in this age group, while toddlers should be treated with lower concentrations than adults. Glycerol seems to be better tolerated than urea plus sodium chloride. Propylene glycol is easily irritating in young children under two years of age.

6.2 Antiinflammatory treatment

Effective topical therapy depends on three fundamental principles:

- sufficient potency
- sufficient dosage
- correct application

Tab.1 Currently approved topical anti-inflammatory therapies, including available.

Current approved topical anti-inflammatory therapies	
corticosteroids (TCS)	available
calcineurin inhibitors (TCI)	available
phosphodiesterase 4 (PDE-4) inhibitor	approved by EMA, but not yet available

The applied amount of anti-inflammatory topicals should follow the fingertip unit rule.

Topical anti-inflammatory therapy can be done by two approaches: reactive and proactive management.

- **Reactive treatment** regimen, anti-inflammatory topical therapy is applied to lesional skin only and is stopped or rapidly tapered, once visible lesions are cleared or almost cleared.
- **Proactive therapyis** defined as a combination of predefined, longterm, anti-inflammatory treatment applied usually twice a week to previously affected areas of skin in combination with liberal daily use of emollients on the entire body. The proactive regimen is started after the therapy of the acute flare, when lesions have been successfully treated with regular anti-inflammatory therapy.

The duration of the proactive management is usually adapted to the severity and persistence of the disease.

6.2.1 Topical corticosteroids (TCS)

TCS are a first-line anti-inflammatory treatment, typically applied on acutely inflamed skin according to the needs (pruritus, sleeplessness, new flare). The lipophilicity and the low molecular weight of TCS allows good penetration into the skin and binding to a steroid receptor in the cytoplasm. The CS-receptor complex acts as a transcription factor with dual activity decreasing the synthesis of proinflammatory cytokines and increasing the synthesis of anti-inflammatory mediators. The potency of topical corticosteroids is grouped according to Niedner from mild (class I) to super-potent (class IV).

In children, low to moderate potency TCS should routinely be used. Adolescent and adult patients can use potent to very potent TCS under specialist supervision in an acute flare of AD for a short period of time. Treatment of the face and especially the peri-orbital region or other sensitive areas (folds, neck) should be restricted to mild-to-moderate TCS (class I and II). With mild disease activity a small amount of TCS twice to thrice weekly (monthly amounts in the mean range of 15 g in infants, 30 g in children and up to 60–90 g in adolescents and adults, roughly adapter to affected body surface area), associated with a liberal use of daily emollients allows for a good weekly maintenance treatment routine. Also, patients with moderate or severe AD can benefit from long-term proactive treatment with a moderate to potent TCS. Twice weekly application of fluticasone proprionate or methylprednisolone aceponate (TCS class III) has shown a significantly reduction of AD-flare recurrence.

Tab. 2 Niedner classification.

	Description of potency	Examples of corticosteroids
Class I	Mild potency	Hydrocortisone, Desonide
Class II	Moderate potency	Triamcinolone acetonide
Class III	Potent	Betamethasone, Mometasone
Class IV	Super-potent	Clobetasol propionate

6.2.2 Topical calcineurin inhibitors

Two topical calcineurin inhibitors (TCI) (tacrolimus ointment and pimecrolimus cream) are licensed for AD treatment. Pimecrolimus 1% cream and tacrolimus 0.03% ointment are approved in the EU from 2 years of age and above. Tacrolimus 0.1% ointment is only licensed in patients age 16 years and above. TCIs have an immunosuppressive effect by inhibiting the activity of the phosphorylase enzyme calcineurin and thus inhibiting the activation of T lymphocytes. The transepidermal penetration of TCI is lower than TCS. TCI are a first line therapy for sensitive areas where TCS use is likely associated with side effects or in areas where TCS had already caused side effects. In adults, long-term proactive treatment with 0.1% tacrolimus ointment has shown good effectiveness for flare prevention, similar to class III TCS. The antiinflammatory potency of 0.1% tacrolimus ointment is similar to a potent corticosteroid (class III) and 0.1% tacrolimus ointment is clearly more effective than 1% pimecrolimus cream. None of the TCI induces skin

atrophy. This favors their use over TCS in sensitive body areas such as the eyelid region, the perioral skin, the anogenital area, the axilla region or the inguinal fold, and makes them suitable for long-term management.

6.2.3 Topical phosphodiesterase 4 inhibitors

The topical phosphodiesterase 4 (PDE-4) inhibitor, crisaborole, is approved for treatment of mildtomoderate AD in patients 2 years of age and older in the United States of America, Canada, Australia, Israel and Hong Kong. Crisaborole has been approved in the European Union in 2020 but is not commercialized in the European market. The inhibition of PDE-4 leads to increased levels of intracellular cAMP, which results in a reduction of inflammatory cytokines.

6.3 Anti-bacterial treatment

- A short course of systemic antibiotics only for patients with atopic eczema who have extensive clinically superinfected lesions.
- Long-term use of topical antibiotics is discouraged due to the risk of resistance development.
- Topical anti-inflammatory treatments are continued during episodes of Staphylococcus aureus superinfection.

6.4 Anti-viral treatment

- Initiate systemic antiviral treatment, such as aciclovir, without delay when managing eczema herpeticum.
- Administer vaccinations according to national recommendations.

6.5 Anti-fungal treatment

- Topical or systemic antifungal therapy may be considered in selected patients with atopic eczema, especially those presenting with the "head and neck" variant and confirmed IgE sensitization to Malassezia species.

6.6 Antipruritic treatment

Itch is the most important clinical symptom in AD with particular impact on emotional dimensions of perception as compared to other pruritic dermatoses.

- UV therapy (narrowband UVB and UVA1) is recommended for the management of pruritus in atopic eczema (AD).
- The use of first and second-generation systemic antihistamines as long-term treatment for pruritus in AD is not recommended.
- The use of selective serotonin reuptake inhibitors for the treatment of pruritus in AD patients is not recommended.
- Emollient therapy is recommended.

6.7 Phototherapy and Photochemotherapy

- Narrowband UVB and medium-dose UVA1 are recommended for patients with moderate-to-severe atopic eczema.
- The use of narrowband UVB or UVA1 may be considered in children and adolescents following assessment of skin type, frequent or prolonged treatment cycles should be avoided.
- Co-treatment with topical emollients is recommended during phototherapy.

- Prolonged or repeated treatment cycles, as well as maintenance regimens with any phototherapy modality, are not recommended.
- All phototherapy modalities should be avoided in patients with a history or increased risk of skin cancer (including those with photodamaged skin or systemic immunosuppressant therapy).

6.8 Systematic treatment

Systemic therapy of AD is deemed necessary if the signs and symptoms of AD cannot be controlled sufficiently with appropriate topical treatments and UV light therapy. Systemic therapy can also be useful to reduce the total amount of topical corticosteroids (TCS) in patients who need large amounts of potent TCS over prolonged periods to control their AD.

6.8.1 Conventional Systemic Drugs ❖

Ciclosporin (CyA)

- Recommendation: Recommended to achieve disease control. Considered a first-line option for severe disease if novel therapies are unavailable or contraindicated.
- Efficacy: Very effective in children and adults. Higher dosages (5 mg/kg/day) lead to a more rapid response than lower dosages (2.5–3 mg/kg/day).
- Safety/Monitoring: Requires close follow-up for blood pressure elevation and signs of renal impairment. Should not be combined with UV light due to potential cancer risk.

❖ **Methotrexate (MTX) [off-label]**

- Recommendation: Suggested for systemic treatment candidates.

- Efficacy: Comparable to Azathioprine but lower than dupilumab and ciclosporin in clearing clinical signs in adults in the short term. In children, MTX may offer more sustained disease control than CyA after initial treatment cessation.
- Safety: Generally well tolerated for long-term treatment. Main side effects include nausea, fatigue, and raised liver enzymes. ❖

Azathioprine (AZA) [off-label]

- Recommendation: Suggested for systemic treatment candidates.
- Efficacy: Comparable to MTX but lower than dupilumab and ciclosporin in clearing clinical signs. Long-term studies show sustained reduction in SCORAD.
- Safety/Monitoring: Serious dose-dependent effects include hepatotoxicity and myelotoxicity. Long-term use raises concerns about potential carcinogenicity (squamous cell skin cancer, nonHodgkin's lymphoma). Monitoring includes TPMT activity (if available), complete blood count, and liver/renal profile. Should not be combined with UV light.

❖ **Systemic Glucocorticosteroids (SCS):**

- Recommendation: Suggested only as rescue therapy for acute flares.
- Strongly recommended against long-term use
- Safety: Long-term use (typically >0.5 mg/kg/day) is associated with serious side effects (skin atrophy, weight gain, osteoporosis, adrenal suppression, high rebound risk).

6.8.2 Modern treatment – biologic drugs ❖

Lebrikizumab:

- New recommendation: Lebrikizumab, an interleukin 13 inhibitor
- Mechanism: High-affinity humanized IgG4 monoclonal antibody that specifically binds to soluble IL-13, preventing the formation of the IL-13Rα1/IL-4Rα receptor complex.
- Licensing: Licensed for patients 12 years of age (with body weight 40 kg).
- Efficacy: Showed clear superiority to placebo in Phase 3 studies. Maintenance doses can be 250 mg Q2W (once every 2 weeks) or Q4W (once every 4 weeks) for patients achieving clear or almost clear skin.
- Safety: The most common adverse events include conjunctivitis, nasopharyngitis, headache, dry eye, and allergic rhinitis. Lebrikizumab currently appears to have lower rates of ocular complications than dupilumab, based on available trial data.

❖ **Dupilumab:**

- Recommendation: Strongly recommended for AD patients who are candidates for systemic treatment.
- Mechanism: Binds to the -subunit of the IL-4 receptor, inhibiting IL4 and IL-13 signaling.
- Licensing: Approved for children aged 6 months and older.
- Safety: Generally well tolerated, but a substantial number of patients develop ocular surface disease. Routine blood tests are not required for monitoring.

❖ **Tralokinumab:**

- Recommendation: Strongly recommended.

- Mechanism: Fully human IgG4 mAb neutralizing IL-13.
- Licensing: Licensed for patients 12 years of age.
- Safety: Appears to have lower rates of ocular complications than dupilumab based on clinical trial data.

6.8.3 JAK Inhibitors

JAK inhibitors target the JAK/STAT pathway.

❖ **Abrocitinib:**

- Recommendation: Strongly recommended.
- Licensing Update: Now recommended for adolescents from the age of 12 years and older.
- Efficacy: The 200 mg dose may provide a higher probability of treatment response compared to dupilumab in severe AD.

❖ **Baricitinib:**

- Recommendation: Strongly recommended.
- Licensing Update: Now recommended for children from 2 years of age and older.

❖ **Upadacitinib:**

- Recommendation: Strongly recommended.
- Efficacy: In a direct head-to-head trial, upadacitinib was superior to dupilumab at 16 weeks regarding EASI75 achievement and improvement in Worst Pruritus NRS.

Monitoring for JAK Inhibitors: Baseline screening and monitoring are recommended for all JAK inhibitors, including full blood count, renal, liver, and lipid profiles, as well as creatinine phosphokinase levels, and screening for Hepatitis, HIV, and TB.

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Hymenoptera stings

Aims/Course objectives:

- Recognition of life-threatening reactions
- Management of anaphylaxis
- Identify common errors

Introduction

Insects from the Hymenoptera order that can sting humans include bees, wasps, yellowjackets, hornets, and ants. While most individuals experience only localized reactions—either right away or after some delay—some people with venom allergies may suffer systemic allergic responses, such as anaphylaxis. These severe reactions can be life-threatening, and venom allergy remains one of the main causes of fatal anaphylaxis.

Classification of Allergic Reactions After Hymenoptera Stings

1. Local (Mild) Reactions

Definition: Reactions limited to the area around the sting site.

Features:

- Pain, redness, and swelling confined to the sting area.

- Itching or warmth at the site.
- Sometimes a **large local reaction** may occur — swelling >10 cm in diameter lasting up to 24–48 hours, but still **without systemic symptoms**.

Management:

- Cold compresses, oral antihistamines, and analgesics.
- Short course of corticosteroids if swelling is extensive.
- No epinephrine needed.

2. Systemic (Severe) Allergic Reactions

Definition: Involvement of organ systems beyond the sting site — mediated by an IgE-dependent allergic mechanism.

1. Symptoms and signs of anaphylaxis

Skin

Feeling of warmth, flushing (erythema), itching, urticaria, angioedema, and "hair standing on end" (piloerection)
Oral
Itching or tingling of lips, tongue, or palate
Edema of lips, tongue, uvula, metallic taste
Respiratory
Nose – Itching, congestion, rhinorrhea, and sneezing
Laryngeal – Itching and "tightness" in the throat, dysphonia, hoarseness, stridor
Lower airways – Shortness of breath (dyspnea), chest tightness, cough, wheezing, and cyanosis
Gastrointestinal
Nausea, abdominal pain, vomiting, diarrhea, and dysphagia (difficulty swallowing)
Cardiovascular
Feeling of faintness or dizziness; syncope, altered mental status, chest pain, palpitations, tachycardia, bradycardia or other dysrhythmia, hypotension, tunnel vision, difficulty hearing, urinary or fecal incontinence, and cardiac arrest
Neurologic

Anxiety, apprehension, sense of impending doom, seizures, headache and confusion; young children may have sudden behavioral changes (cling, cry, become irritable, cease to play); infants may become lethargic
Ocular
Periorbital itching, erythema and edema, tearing, and conjunctival erythema

2. Diagnostic criteria for anaphylaxis

Anaphylaxis is highly likely when any ONE of the following three criteria is fulfilled:
1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg., generalized hives, pruritus or flushing, swollen lips-tongue-uvula)
AND AT LEAST ONE OF THE FOLLOWING:
A. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, hypoxemia)
B. Reduced BP or associated symptoms of end-organ dysfunction (eg, hypotonia, collapse, syncope, incontinence)
2. TWO OR MORE OF THE FOLLOWING that occur rapidly *after exposure to a LIKELY allergen for that patient* (minutes to several hours):
A. Involvement of the skin mucosal tissue (eg, generalized hives, itch-flush, swollen lips-tongue-uvula)
B. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, hypoxemia)
C. Reduced BP or associated symptoms (eg, hypotonia, collapse, syncope, incontinence)
D. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)

3. Reduced BP *after exposure to a KNOWN allergen for that patient* (minutes to several hours):
A. Infants and children - Low systolic BP (age-specific) or greater than 30% decrease in systolic BP
B. Adults - Systolic BP of less than 90 mmHg or greater than 30% decrease from that person's baseline

3. Rapid overview of emergency management

Acute management:
The first and most important treatment in anaphylaxis is epinephrine. There are **NO absolute contraindications to epinephrine** in the setting of anaphylaxis. Epinephrine is given immediately upon recognition of anaphylaxis.
Airway – Early intubation if evidence of impending airway obstruction from angioedema. Delay may lead to complete obstruction. Intubation can be difficult and should be performed by the most experienced clinician available. Cricothyrotomy may be necessary.
Monitoring – Continuous noninvasive hemodynamic monitoring and pulse oximetry monitoring should be performed.
Promptly and simultaneously, give:
IM epinephrine (1 mg/mL preparation) – Give epinephrine 0.3 to 0.5 mg IM in the mid-outer thigh. Can repeat every 5 minutes (or more frequently), as needed. If epinephrine is injected promptly IM, most patients respond to 1, 2, or at most, 3 doses. If symptoms are not responding to epinephrine injections, prepare IV epinephrine for infusion.
If hypotensive, place patient in recumbent position, if tolerated, and elevate lower extremities.

Oxygen – Give with nonrebreather mask at 15 liters/minute flow rate or commercial high-flow oxygen masks (providing at least 70% and up to 100% oxygen), as needed.
Crystalloid (eg, Ringer's lactate or normal saline) rapid bolus

– Establish two large-bore IV lines. Treat hypotension with rapid infusion of 1 to 2 liters IV. Repeat, as needed. Massive fluid shifts with severe loss of intravascular volume can occur. Monitor urine output.
Salbutamol – For bronchospasm resistant to IM epinephrine, give 2.5 to 5 mg in 3 mL saline via nebulizer, or 2 to 3 puffs by metered dose inhaler. Repeat, as needed.
Adjunctive therapies (for residual symptoms after adequate response to epinephrine):
H1 antihistamine – For residual itching or urticaria, give clemastine 2 mg IV
Glucocorticoid – For residual bronchospasm and for patients requiring more than 2 doses of IM epinephrine, give methylprednisolone 80 to 125 mg IV or prednisone 40 to 60 mg orally.
Treatment of refractory symptoms:

Epinephrine infusion – For patients with inadequate response to IM epinephrine and IV saline, give epinephrine continuous infusion, beginning at 0.1 microgram/kg/minute by infusion pump. Titrate the dose continuously according to blood pressure, cardiac rate and function, and oxygenation.

Vasopressors – Some patients may require a second vasopressor (in addition to epinephrine). All vasopressors should be given by infusion pump, with the doses titrated continuously according to blood pressure and cardiac rate/function and oxygenation monitored by pulse oximetry.

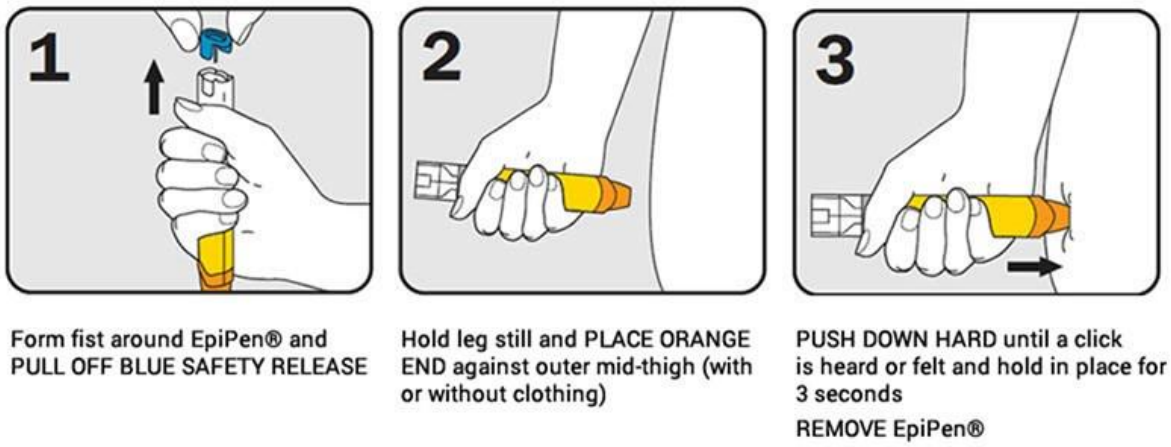
Glucagon – Patients on beta blockers may not respond to epinephrine and can be given glucagon 1 to 5 mg IV over 5 minutes, followed by infusion of 5 to 15 micrograms/minute. Rapid administration of glucagon can cause vomiting.

4. Discharge care and referral

Prior to discharge from the acute care setting, patients should be informed that venom allergy is a potentially fatal disorder, further evaluation will be needed, and that venom immunotherapy (VIT) is available to prevent anaphylaxis to future stings.

They should receive:

- An epinephrine autoinjector(s) (supplying at least two doses of epinephrine)
- Instructions on how and when to use epinephrine
- Clear directions to fill the prescription immediately and carry epinephrine at all times



"How to give EpiPen", *Australian Society of Allergy and Clinical Immunology*

5. Common mistakes

1. Delayed or Missed Diagnosis

- **Failure to recognize anaphylaxis early**, especially when skin symptoms (like hives or swelling) are mild or absent.
- **Underestimating respiratory or cardiovascular symptoms**, thinking they are anxiety-related rather than allergic.

2. Incorrect Use of Epinephrine

- **Delay in administering epinephrine**, waiting until symptoms become severe instead of giving it immediately.
- **Not using epinephrine at all**, substituting antihistamines or steroids instead (these are *adjunctive*, not primary, treatments).
- **Using the wrong route** (e.g., IV push instead of intramuscular [IM] injection in the lateral thigh).
- **Using the wrong dose**, especially in children.
- **Not having epinephrine readily available** (e.g., not prescribed auto-injectors for patients with a known allergy).

Sources and additional reading:

1. EAACI guidelines: Anaphylaxis (2021 update): Antonella Muraro, Margitta Worm, Cherry Alviani, Victoria Cardona, Audrey DunnGalvin, Lene Heise Garvey, Carmen Riggioni, Debra de Silva, Elizabeth Angier, Stefania Arasi, Abdelouahab Bellou, Kirsten Beyer, Diola Bijlhout, Maria Beatrice Bilò, Carsten Bindslev-Jensen, Knut Brockow, Montserrat Fernandez-Rivas, Susanne Halken, Britt Jensen, Ekaterina Khaleva, Louise J. Michaelis, Hanneke N. G. Oude Elberink, Lynne Regent, Angel Sanchez, Berber J. Vlieg-Boerstra, Graham Roberts, European Academy of Allergy and Clinical Immunology, Food Allergy, Anaphylaxis Guidelines Group
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3. Golden DB. Insect sting anaphylaxis. Immunol Allergy Clin North Am 2007; 27:261.
4. Simons FER. Anaphylaxis. J Allergy Clin Immunol 2010; 125:S161
5. Sampson HA, Munoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report-Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol 2006; 117:391.

Spirometry

Aims/Course objectives:

- Understand the basic principles of performing spirometry
- Demonstrate proficiency in performing spirometry tests
- Identify common errors and troubleshoot technical issues

Introduction

What is Spirometry?

Spirometry is the **most common pulmonary function test (PFT)** and is fundamental to assessing general respiratory health. It is a physiological test that measures the maximal volume of air an individual can inspire and expire with maximal effort.
The two most relevant indices derived from the Forced Vital Capacity (FVC) maneuver are:

1. **Forced Vital Capacity (FVC):** The volume delivered during an expiration made as forcefully and completely as possible starting from full inspiration.
2. **Forced Expiratory Volume in 1 Second (FEV1):** The expiratory volume delivered in the first second of the FVC maneuver.

Indications for Spirometry

Spirometry provides objective information critical for clinicians, used together with other physical findings, symptoms, and history to reach a diagnosis. Common indications include:

- **Diagnosis:** To evaluate symptoms, signs, or abnormal laboratory test results; to measure the physiological effect of disease or disorder; to screen individuals at risk of having pulmonary disease; to assess preoperative risk; or to assess prognosis.
- **Monitoring:** To assess the response to therapeutic intervention, monitor disease progression, monitor patients for exacerbations of disease and recovery, or monitor adverse effects of exposure to injurious agents or drugs with known pulmonary toxicity.
- **Disability/Impairment Evaluations:** To assess patients as part of a rehabilitation program, for insurance evaluations, or for legal reasons • **Other:** Research and clinical trials, epidemiological surveys, derivation of reference equations, occupational health monitoring, assessment before at-risk physical activities

1. Keys to Reliable Spirometry

1. **Full Patient Engagement**
   Ensure the patient gives their best and sustained effort in every attempt.
2. **Clear, Simple Guidance**
   Use concise instructions that are easy for the patient to understand.
3. **Pre-test Demonstration**
   Show how to perform the maneuver before starting to reduce anxiety and confusion.
4. **Active Encouragement**
   Motivate and coach the patient during the test to maintain effort and accuracy.
5. **Real-time Feedback**
   Monitor and review curves as they appear to identify errors immediately.

6. **Communication Aids**

   Use written or translated materials when language or comprehension barriers exist.

Components of PFT Interpretation

Appropriate interpretation of PFT results involves three distinct, complementary key aspects:

1. **Classification of observed values** as within or outside the normal range with respect to a population of healthy individuals. This requires consideration of the measurement error and the inherent biological variability of measurements.
2. **Integration of physiological knowledge** into a functional classification of the identified impairments (e.g., airflow mechanics, volumes, and gas transfer).
3. **Integration of the identified patterns** with other clinical data to inform differential diagnosis and guide therapy.
   Interpretation must be complemented by **clinical expertise** and consideration of the **inherent biological variability** of the test and the **uncertainty of the test result** to ensure appropriate interpretation

2. Equipment and Quality Assurance

Spirometer Technical Specifications
Spirometers must meet the standards contained in the current update of **ISO 26782**.

Key technical requirements include:

- **Maximum Permissible Accuracy Error:** when tested with a 3-L calibration syringe and using the ISO test profiles.
- **Sampling Rate:** Must be **>100 Hz** for digitization of the flow or volume signal.
- **BTPS Adjustment:** All spirometry outcomes must be reported at **BTPS** (Body Temperature, Ambient Pressure, Saturated with water vapor). The ambient temperature must be recorded with an accuracy of .
- **Display Requirements:** Both volume–time and flow–volume realtime displays are required. Expiratory flow must be plotted upward, and expiratory volume plotted toward the right. A **2:1 aspect ratio** must be maintained between the flow and volume scales.

Device Quality Assurance (QC) Procedures

Minimum requirements for documentation include:

- A log of calibration results.
- Documentation of repairs, alterations, hardware/software updates, or relocation dates.
- Verification of reference value calculations after software updates.

Calibration Verification:

- **Frequency:** Calibration verifications must be undertaken **daily**, or more frequently if specified by the manufacturer.
- **Method:** Use a **3-L syringe**. The syringe must have an accuracy of or of the full scale.
- **Procedure:** The syringe must be cycled at least three times to give a range of flows varying between **0.5 and 12 L/s** (3-L injection times between 0.5 and 6 s).

- **Filters:** If an in-line filter is used, it must also be used during recalibrations and verifications.
- **Failure Alert:** Manufacturers must provide an alert if the new calibration factor varies by more than **\pm 6\%** from the previous calibration factor, as this may indicate a need for cleaning or repair.

Zero-Flow Level Determination

The spirometry system **must determine the zero-flow level** with the spirometer blocked or not moving before calibration, verification, and patient tests.

- If variable flow is detected or if the zero level has changed significantly, the zero-flow setting procedure must be repeated.
- A faulty zero-flow set procedure renders both FEV1 and FVC measurements neither acceptable nor usable

3. Patient Preparation and Safety

Patient Details Required

The following demographic and physical details **must be recorded** accurately:

- **Age:** Reported in years to **one decimal place**. Calculated using date of birth and date of test.
- **Height:** Measured without shoes, standing as tall as possible, and reported in centimeters to **one decimal place**.
- **Weight:** To the nearest **0.5 kg**. BMI should be calculated.
- **Biological Sex:** The use of **biological sex**, not gender, is required to yield a more accurate prediction of lung function. Gender identity should also be recorded and respected.
- **Ethnicity/Ancestral Origin:** The **Global Lung Function Initiative (GLI) reference equations** should be used. Spirometry reference values are available for four specific population groupings (White, African American, North East Asian, South East Asian) and a composite "other" equation. The historical approach of **fixed adjustment factors for race is unequivocally discouraged Pre-Test Avoidance List**

Patients should be instructed to avoid the following activities before testing:

Activity	**Recommended Avoidance Time**	**Rationale**
Smoking/Vaping/Water Pipe Use	Within **1 hour** before testing	To avoid acute bronchoconstriction.

Consuming Intoxicants	Within **8 hours** before testing	To avoid problems with coordination, comprehension, and physical ability.
Vigorous Exercise	Within **1 hour** before testing	To avoid potential exercise-induced bronchoconstriction.
Clothing	Avoid clothing that substantially restricts full chest and abdominal expansion.	To avoid external restrictions on lung function.

Medication Withholding (Bronchodilators): If the test is for diagnosis, the clinician ordering spirometry instructs the patient to withhold bronchodilators before baseline testing.

Bronchodilator Class	Suggested Withholding Time
SABA (e.g., albuterol/salbutamol)	**4–6 hours**
SAMA (e.g., ipratropium bromide)	**12 hours**
LABA (e.g., formoterol/salmeterol)	**24 hours**
LAMA (e.g., tiotropium)	**36–48 hours**

Relative Contraindications

There are no absolute contraindications to spirometry. The forced expiratory maneuver increases intrathoracic, intraabdominal, and intracranial pressures. The potential risks associated with testing should always be weighed against the benefit. **Spirometry should be discontinued if the patient experiences pain** during the maneuver.

Relative contraindications include:

- **Cardiovascular Issues:** Acute myocardial infarction within 1 week, severe hypertension, significant arrhythmia, or uncontrolled pulmonary hypertension.
- **Pressure-Related Issues:** Cerebral aneurysm, brain surgery within 4 weeks, or eye surgery within 1 week.
- **Thoracic/Abdominal Issues:** Presence of pneumothorax, thoracic surgery within 4 weeks, or abdominal surgery within 4 weeks.
- **Infection Risk:** Active or suspected transmissible respiratory or systemic infection (e.g., tuberculosis), hemoptysis, significant secretions, or oral lesions.

4. The FVC Maneuver: Procedure

Operator Role and Coaching

The operator must be trained, competent, and motivated to elicit maximal performance.

Procedure Checklist (Must be performed in order):

1. **Preparation:** Confirm patient details, health status, and medication withholding.
2. **Instruction:** Demonstrate the test procedure (maximal inspiration, blast of expiration, continued expiration, maximal inspiration postEOFE). Confirm patient comprehension.
3. **Positioning:** Patient seated erect, noseclip attached, mouthpiece inserted with lips sealed.
4. **Coaching:** Use continuous and enthusiastic coaching throughout the maneuver.

Four Phases of the FVC Maneuver

For spirometers that measure inspiration and expiration, there are four phases:

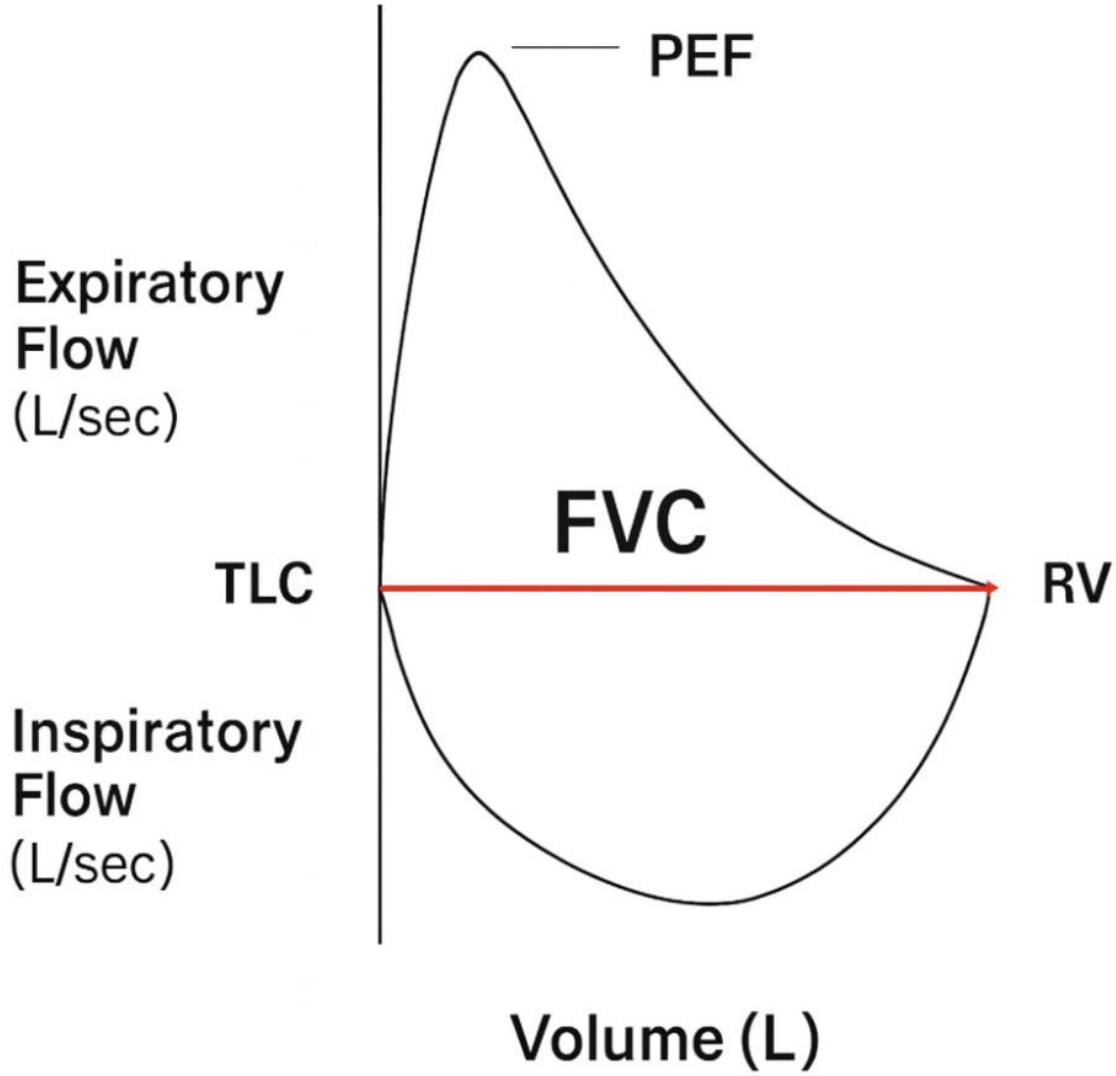
1. **Maximal Inspiration:** Inspire **rapidly and deeply** until completely full. Any pause at full inspiration must be **minimal (<2 s)**. Coaching phrases include “more, more, more”.

2. **The "Blast" (Maximal Expiration Start):** Without hesitation, the patient should be prompted to **"blast"** the air out.

3. **Continued Complete Expiration:** Continue to expire with maximal effort. The operator must continue coaching until reaching plateau. The maximum duration for forced expiration is **15 seconds**.

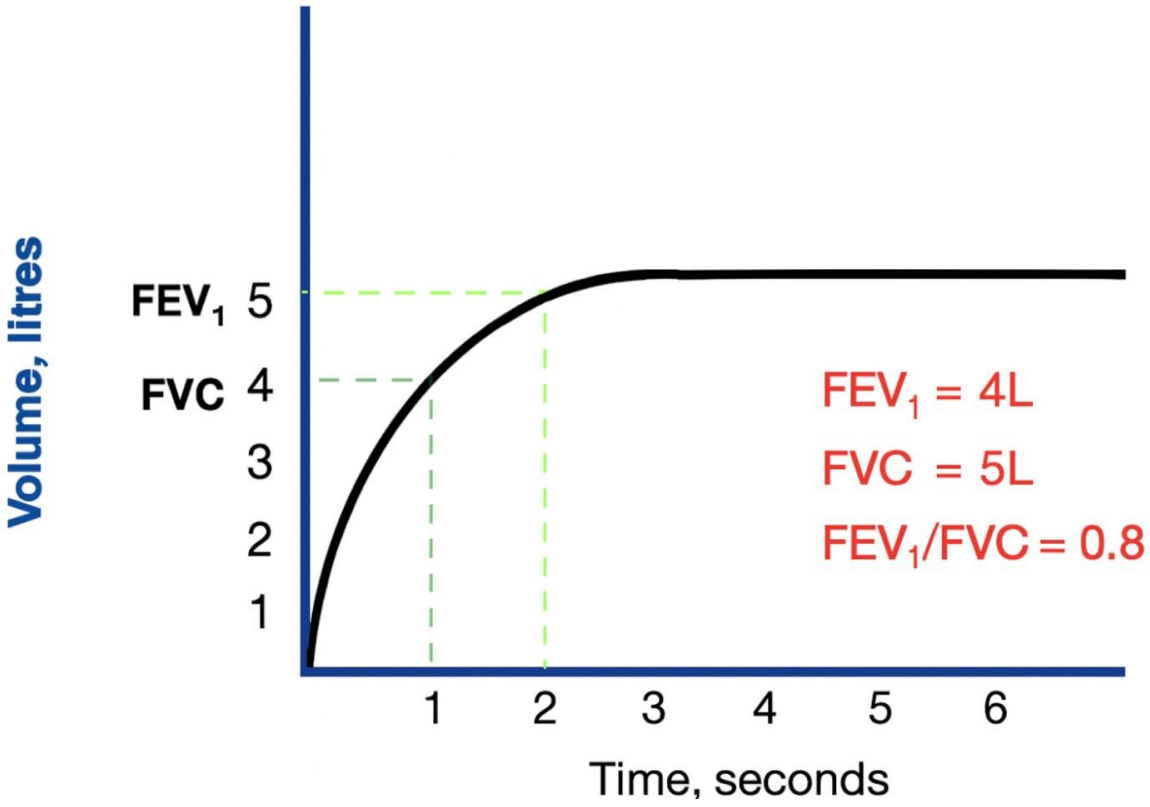
4. **Maximal Inspiration Post-EOFE:** The patient remains on the mouthpiece and rapidly inspires to full inflation, providing the Forced Inspiratory VC (FIVC).

Normal flow-volume loop



- Sharp peak at start of expiration (leading to PEF)
- Smooth descending curve
- Symmetrical inspiratory loop (with volume similar to expiration)

Normal volume/time curve



- Rapid rise, smooth plateau
- FEV_1 and FVC within expected range
- FEV_1/FVC above LLN

6. Within-Maneuver Evaluation (Acceptability)

These criteria determine if a maximal, valid measurement was achieved.
Software must provide explicit feedback to the operator.
Criteria Affecting FEV1 and FVC Acceptability

Criterion	Requirement (For Acceptability)	Impact if Failed

Back-Extrapolated Volume (BEV)	Must be **<5% of FVC or 0.100 L**, whichever is greater. (The tolerance is a reduction from the tolerance in the 2005 standards.)	Renders FEV1 and FVC unacceptable/unusable.
Faulty Zero-Flow Setting	Must be absent.	Renders FEV1 and FVC unacceptable/unusable.
Incomplete Inspiration (FIVC check)	FIVC – FVC must be **<0.100 L or 5% of FVC**, whichever is greater.	Renders FEV1 and FVC unacceptable.
Obstruction/Leak	Must be absent.	Renders FEV1 and FVC unacceptable.

Criteria Affecting Only FEV1

- **Cough/Glottic Closure:** A cough or glottic closure in the **first second** of expiration affects FEV1 and renders it neither acceptable nor usable.
- For children aged 6 years or younger, cough or glottic closure in the first **0.75 seconds** renders unacceptable and unusable.

Glottic Closure/Early Termination

Glottic closure or inspiration (early termination) renders FVC unacceptable. If termination occurs *after* 1 second, FEV1 may still be acceptable, but FVC is not.

Most of the variability in results obtained from spirometry relates to inadequate and variable inspiration to total lung capacity (full lungs), ending the expiration prematurely, and variable effort.

End of Forced Expiration (EOFE)

EOFE criteria must be met to ensure a true FVC measurement.

EOFE Acceptability Criteria

The maneuver must meet **one of the following three indicators**:

1. **Plateau:** Volume change is **<25** ml/s for at least **1 second**. This is the **most reliable indicator** of complete expiration.
2. **Forced Expiratory Time (FET):** Reaches **15 seconds**. FETs seconds will rarely change clinical decisions.
3. **Repeatability Tolerance:** FVC is within the repeatability tolerance (see below), or is greater than, the largest prior observed FVC in the current testing set. (Used when a plateau cannot be reached).

The Absence of Minimum FET

There is **no requirement for a minimum FET**. Previous requirements (minimum 6 seconds) resulted in the exclusion of too many patients, especially those with airflow obstruction or the elderly.

Determining Time Zero

The start of forced expiration (Time 0) is determined by the **backextrapolation method**.

- A tangent equal to PEF is drawn through the point of PEF on the volume-time graph; its intersection with the time axis defines Time 0.
- The **BEV** (volume expired before Time 0) is derived from this calculation.

7. Between-Maneuver Evaluation and Quality Grading

Repeatability Criteria

The goal is to achieve a minimum of **three acceptable FEV1 and three acceptable FVC** measurements. Additional trials (up to eight maneuvers in adults) should be attempted if repeatability criteria are not met.

Age Group	FEV1 Repeatability (Difference between two largest FEV1 values)	FVC Repeatability (Difference between two largest FVC values)
Older than 6 years	**<0.150 L**	**<0.150 L**
6 years or younger	**<0.100 L or 10%** of the highest value, whichever is greater	**<0.100 L or 10%** of the highest value, whichever is greater

Maximum Number of Maneuvers

Eight maneuvers is generally a practical upper limit for most adults. If the FEV1 from an acceptable test drops below the starting value, the test procedure should be terminated in the interest of patient safety.

Quality Grading System

The grading system (applied separately to pre- and post-bronchodilator sets) informs the interpreter about the confidence level.

Grade	Number of Measurements	Repeatability (Age > 6 years)	Interpretation
A	>3 acceptable	Within 0.150 L	Highest confidence level.

B	2 acceptable	Within 0.150 L	High quality.
C	>2 acceptable	Within 0.200 L	Moderate quality.
D	>2 acceptable	Within 0.250 L	Lower quality.
E	>2 acceptable **OR** 1 acceptable	>0.250 L	Minimally acceptable.
U	0 acceptable **AND** **>1 usable**	N/A	**Usable:** Measurements obtained did not meet acceptability criteria but may be clinically useful.
F	0 acceptable and 0 usable	N/A	Failure to obtain any usable data.

8. Acceptability and usability

All the following eight criteria must be met to have an acceptable FEV1:

1. BEV ≤5% of FVC or ≤0.100L, whichever is greater
2. PEFT ≤0.15s
3. No evidence of a faulty zero-flow setting
4. No cough in the first 1 second of expiration
5. No glottic closure in the first 1 second of expiration
6. No evidence of obstructed mouthpiece or spirometer
7. No evidence of a leak
8. If FIVC > FVC, then FIVC-FVC must be ≤0.100L or ≤5% of FVC, whichever is greater

As soon as just one of these eight FEV1 acceptability criteria on the manoeuvre has failed, the FEV1 acceptability criteria for that manoeuvre have failed and the patient should do the manoeuvre again to replace this manoeuvre until there are at least 3 acceptable FEV1s.

9. Bronchodilator Responsiveness Testing

Terminology and Purpose

- The preferred term is **"Bronchodilator Responsiveness Testing (BDR)"** rather than "reversibility testing," because reversibility implies the complete elimination of obstruction, which is often unwarranted.
- BDR determines the degree of improvement of airflow in response to bronchodilator administration.

Interpretation and Calculation

The recommended strategy is to express BDR as the percent change relative to the individual's **predicted value**. This minimizes sex and height difference bias.

A positive response is classified as a change **>10% of the predicted value** for FEV1 or FVC.

Calculation:

- **Avoided Standard:** The 2005 threshold (relative change from baseline) is **no longer recommended**.
- BDR in FVC, rather than FEV1, may better reflect the physiological processes of air trapping.

Post-BDR Maneuver Timing

Three or more additional post-bronchodilator acceptable FEV1 and FVC measurements are obtained after the specified wait time. The spirometry

system must provide a warning if the time elapsed since bronchodilator administration is less than the wait time specified in the facility protocol.

10. Interpretive Standards: Reference Values and LLN

Required Reference Equations

The **Global Lung Function Initiative (GLI) reference equations** must be used for spirometry. The GLI equations are internally consistent across spirometry, DLCO, and lung volumes, providing a single standard applicable across all ages (3–95 years).

- **Biological Sex:** The interpretation must use **biological sex** for a more accurate prediction of lung function.
- **Ancestry:** If ancestral origins are unknown or uncertain, the GLI "other" equation should be used.

Defining the Limits of Normal

The normal range is defined using the distribution of values in a healthy population.

- **Lower Limit of Normal (LLN):** Defined as the **5th percentile** of the healthy distribution. This corresponds to a **z-score of -1.645**.
- The LLN provides a cut-off to define results that are outside the range of values typically observed in health.

Methods to Avoid

Fixed thresholds are discouraged because they lead to systematic misinterpretation, particularly for children and older adults.

1. **Fixed ratio FEV1/FVC <0.7:** This is **not recommended**. It systematically misclassifies older individuals.
2. **Using 80% of Predicted:** Defining abnormality as of predicted FEV1 is **not recommended**. The LLN for FEV1 varies considerably with age (e.g., predicted at age 10 versus predicted at age 85).

Special Considerations for Children

- Children as young as 2.5 years old can perform acceptable spirometry.
- Specific training is required for operators testing young children.
- Children aged 6 years or younger should have reported. If the Forced Expiratory Time (FET) is second, should also be reported.
- For children aged 6 years or younger, the repeatability difference must be or of the highest value, whichever is greater

10. Classification of Impairments and Severity

Severity Grading using Z-Scores

Severity should be assessed using a **three-level system based on zscore values**, as these provide uniform gradations across age and sex.

Z-Score Range	Severity Classification
>−1.645	**Normal** (Above 5th percentile)
−1.65 to −2.5	**Mild**
−2.52 to −4.0	**Moderate**
< 4.0	**Severe**

Note: The severity of lung function impairment is not necessarily equivalent to disease severity, which encompasses quality of life, functional impairment, etc..

11. Spirometry-Defined Ventilatory Impairments

PFT interpretations should focus on recognizing patterns of altered physiology.

- **Airflow Obstruction:** Defined by FEV1/FVC (or VC) **below the LLN** (5th percentile). Physiologically, this results from premature airway collapse, bronchoconstriction, or airway narrowing.
- **Restriction (Suggested by Spirometry):** May be suspected when FVC is reduced, and FEV1/FVC is normal or increased. **TLC measurement is necessary to confirm restriction**.
- **Non-Specific Pattern (PRISm):** Reduced FEV1 and FVC, but FEV1/FVC is normal. This requires measurement of TLC. If TLC is normal, it remains the non-specific pattern; if TLC is low, restriction is confirmed.
- **Mixed Ventilatory Impairment (Spirometry Suggestion):** Both FEV1 and FVC are reduced, and FEV1/FVC is low. TLC measurement is required for confirmation.

Lung Volume-Defined Impairments

- **Restrictive Impairment:** Confirmed by a reduction in **Total Lung Capacity (TLC) below the LLN** (5th percentile).
  - **Simple Restriction:** TLC, FVC, and FEV1 are typically reduced proportionally. FRC/TLC and RV/TLC are normal.
  - **Complex Restriction:** Low TLC with a disproportionately elevated RV/TLC ratio, suggesting neuromuscular disease, chest wall restriction, or occult obstruction with gas trapping.
- **Mixed Ventilatory Impairment:** Defined physiologically when **both FEV1/FVC and TLC are below the LLN**.

- **Hyperinflation/Air Trapping:** An increase in RV or RV/TLC above the 95th percentile. Hyperinflation/Air trapping often accompanies obstruction.

12. Common errors Patient-related errors

• Obstructing the mouthpiece – biting or blocking with the tongue.

• Poor seal – air leak around the mouthpiece or nose.

• Early termination – stopping the blow before reaching residual volume → underestimates FVC.

• Submaximal effort – not inhaling fully or not blowing forcefully enough → underestimates FEV_1 and FVC.

• Extra breath – taking an additional breath during exhalation → irregular curves, invalid test.

• Hesitant/false start – delay or leak before the forced blow → elevated BEV, falsely high FEV_1.

• Coughing during the first second – disrupts FEV_1 measurement.

• Variable effort between manoeuvres – poor repeatability

Equipment-related errors

• Zero-flow offset error – incorrect baseline → over- or underestimation of FEV_1/FVC.

• Poorly calibrated or uncalibrated device – inaccurate volumes.

• Leaks in the system – e.g. cracked tubing, loose filter, damaged seals.

• Condensation or blockage in the flow sensor → unstable tracings.

Operator/technique-related errors

- Inadequate coaching – weak instructions or not encouraging the patient through the blow.
- Failure to detect errors – accepting curves with coughs, false starts, or early terminations.
- Not checking repeatability – relying on a single effort without confirming reproducibility.
- Incorrect positioning – patient not sitting upright, chin tucked, or head not supported.

13. Key Updates from 2019 Standard

- A new list of relative contraindications was added.
- Spirometers are now required to meet International Organization for Standardization (ISO) 26782 standards, but with a maximum permissible accuracy error of ±2.5%.
- Device quality assurance procedures were updated.
- Operator training as well as attainment and maintenance of competency were addressed.
- The list of activities that patients should avoid before testing was updated.
- There is a focus on the use of devices that measure both expiration and inspiration.
- Manoeuvre acceptability and repeatability criteria were updated. The end of forced expiration (EOFE) was redefined.
- Requirements for spirometry systems to provide uniform cues and feedback to the operator were added.
- New withholding times for bronchodilators before bronchodilator responsiveness testing were developed.
- A new grading system for assessment of spirometry quality was developed.
- Standardized operator feedback options that promote synoptic reporting were developed.
- Preliminary findings derived from an international patient survey were presented.

Spirometry- summary

Correct spirometry essentials:

- Breathe in to fill the lungs completely

- Seal the lips tightly around the mouthpiece
- Ensure nose is closed
- Immediately blast the air out as fast and far as possible. Vigorous effort right from the
- start of the manoeuvre and continuing until absolutely no more air can be exhaled.
- No leaning forward during the test
- Breathe in again fully and completely
- Ensure recovery time between attempts to avoid exhaustion and ensure accurate results
- Obtain at least three acceptable and repeatable FVCs and FEV1s
Sources and additional reading:

1. Graham BL, Steenbruggen I, Miller MR, Barjaktarevic IZ, Cooper BG, Hall GL, Hallstrand TS, Kaminsky DA, McCarthy K, McCormack MC, Oropez CE, Rosenfeld M, Stanojevic S, Swanney MP, Thompson BR. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. Am J Respir Crit Care Med. 2019 Oct 15;200(8):e70e88. doi: 10.1164/rccm.201908-1590ST. PMID: 31613151; PMCID: PMC6794117.

2. Stanojevic S, Kaminsky DA, Miller MR, Thompson B, Aliverti A, Barjaktarevic I, Cooper BG, Culver B, Derom E, Hall GL, Hallstrand TS, Leuppi JD, MacIntyre N, McCormack M, Rosenfeld M, Swenson ER. ERS/ATS technical standard on interpretive strategies for routine lung function tests. Eur Respir J. 2022 Jul 13;60(1):2101499. doi: 10.1183/13993003.01499-2021. PMID: 34949706.