Skin reaction Identification Algorithm

Lesion Characteristics

Please note that the algorithm is intended as a guideline for diagnostic purposes only.

Palpable	Hard	Red	Hot	Painful	Size <1 cm	Fades with Pressure	Fluctuates	Itchy	
☑	☑	☒ ☑	☒	☒ ☑	☒	N/A	N/A	N/A	Nodule 
☒	☒	☑	☒ ☑	☒	N/A	☑	N/A	N/A	Erythema 
☒ ☑	☒ ☑	☑	☒	☒	N/A	☒	N/A	N/A	Ecchymosis/ Hematoma 
☑	☒	☒ ☑	☒	☒	N/A	☑	N/A	N/A	Edema (Drug Pooling) 
☒ ☑	☒ ☑	☑	☒	☒	N/A	☒	N/A	☑	Dermatitis 
☒ ☑	☒ ☑	☑	☑	☑	N/A	☒	N/A	N/A	Cellulitis 
☒ ☑	☒ ☑	☑	☑	☑	N/A	N/A	☑	N/A	Abscess 

Nodule

Palpable	Hard	Red	Hot	Painful	Size <1 cm	Fades with Pressure	Fluctuates	Itchy	
☑	☑	☒ ☑	☒	☒ ☑	☒	N/A	N/A	N/A	Nodule 

Characteristics

- **Nodules** are palpable, circumscribed lesions >1 cm in diameter.[1,2]
  - Different from **papules** (<1 cm) and **plaques** (>1 cm) which are usually more superficial and less voluminous.[3]
- Usually involve **dermis and/or hypodermis**, and the greatest portion is typically **beneath the skin surface**.

Management

- Subcutaneous nodules can be minimized by **rotating infusion sites frequently** and **avoiding reuse of previously affected areas.**
- If nodules form, **gentle massage** (by hand or using a spiky rubber massage ball) may assist in resolution.
  - Local massage should proceed slowly and be stopped if discomfort becomes too intense.*
  - If tolerated, massage can be continued for at least a few days after the needle is withdrawn.*
- Persistent or painful nodules may require medical evaluation.

1. Mosby. Mosby's Medical Dictionary. 11th ed. St. Louis, MO: Elsevier; 2021. ISBN-13: 978-0-323-63915-6; 2. Nast A, Griffiths CE, Hay R, et al. The 2016 International League of Dermatological Societies' revised glossary for the description of cutaneous lesions. *Br J Dermatol*. 2016;174(6):1351–1358; 3. Potter PA, Perry AG, Stockert PA, Hall A. Essentials for Nursing Practice. 9th ed. St. Louis, MO: Elsevier; 2019. ISBN: 978-0-323-48184-7.

*Expert Opinion, Dr. Marc-André Doré, August 2023.

Erythema

Palpable	Hard	Red	Hot	Painful	Size <1 cm	Fades with Pressure	Fluctuates	Itchy	
☒	☒	☑	☒ ☑	☒	N/A	☑	N/A	N/A	Erythema 

Characteristics

- **Redness of the skin**. Occurs when the blood capillaries near the skin surface are congested or dilated.[1]
- Can vary from pink to dark red or violaceous.
- Typically blanchable with pressure.
- Often associated with skin inflammation but can also occur in absence of inflammation.

Management

- Erythema may resolve without treatment, but if treatment is needed, it will mainly focus on the underlying cause.[1]
- **Erythema due to drug allergy:** initial management is to remove the drug that caused the reaction.[2]
- **Consider underlying infection if erythema** is associated with fever/pain, swelling, itching, or bruising.
- Ensure **use of aseptic techniques** during infusion setup and consider **rotating the infusion site more frequently** to prevent skin irritation.
- Applying **cool compresses** and using **topical anti-inflammatory creams** such as **topical corticosteroids** can alleviate symptoms if erythema persists.[3]
  - Less potent (e.g., over-the-counter) topical corticosteroids are rarely sufficient for management of local irritation (e.g., contact dermatitis) or allergic reaction.
  - Starting with at least a moderately potent agent is usually indicated.

1. Yang Y, Wu X, Liu W. Scar Symptom: Erythema and Thickness. 2020 Dec 8. In: Téot L, Mustoe TA, Middelkoop E, Gauglitz GG, editors. Textbook on Scar Management: State of the Art Management and Emerging Technologies [Internet]. Cham (CH): Springer; 2020. Chapter 11. PMID: 36351101.

1. Merck Manual. Erythema Multiforme. Updated May 2024. Accessed December 3, 2024. https://www.merckmanuals.com/professional/dermatologic-disorders/hypersensitivity-and-reactive-skin-disorders/erythema-multiforme?query=erythema%20multiforme; 2. Ardern-Jones M. Common cutaneous drug reactions. *BMJ Best Practice.* Updated November 22, 2024. Accessed November 27, 2024. https://bestpractice.bmj.com/topics/en-gb/368; 3. Regier L, et al. Topical corticosteroids: comparison chart. Rxfiles. July 2023. https://www.rxfiles.ca/RxFiles/uploads/documents/members/CHT-SteroidClassPotencyCOLOR.pdf

Ecchymosis/Hematoma

Palpable	Hard	Red	Hot	Painful	Size <1 cm	Fades with Pressure	Fluctuates	Itchy	
☒ ☑	☒ ☑	☑	☒	☒	N/A	☒	N/A	N/A	Ecchymosis/ Hematoma 

Characteristics

- **Ecchymosis:** localized, flat discolouration of the skin caused by a collection of clotted blood that accumulated into tissues from ruptured capillaries, appearing as bruising.[1–3]
- **Hematoma:** localized collection of blood outside the vessels, forming a swollen, often firm lump.[1,4]
- Symptoms include discolouration (ranging from red to purple, then yellow-green as they heal), tenderness, and swelling (for hematomas).[1–4]

Management

- Ecchymosis/bruising typically resolves on its own, does not require any specific intervention.[1–4]
- Large hematomas may require medical attention or drainage.[1–4]
- Management of ecchymosis includes applying **cold compresses** initially to reduce swelling, then **warm compresses** to promote healing.[1–4]
  - For existing cases, cold compresses applied immediately post injection can decrease swelling, while warm compresses later can promote healing.

1. Davis CP. Hematoma vs. ecchymosis: differences and similarities. eMedicineHealth. Updated by Cunha JP. Accessed November 27, 2024. https://www.emedicinehealth.com/hematoma_v_ecchymosis/article_em.htm; 2. Asirdizer M, Besik EZ, Kartal E. Non-traumatic ecchymoses: A literature review from a medico-legal perspective. *J Forensic Leg Med*. 2023;95:102490; 3. Mallidi RQ. Ecchymosis. MedIndia. Published August 23, 2017. Accessed November 27, 2024. https://www.medindia.net/patientinfo/ecchymosis.htm; 4. Wedro B. Hematoma. In: Balentine JR, ed. MedicineNet. Published July 5, 2024. Accessed November 27, 2024. https://www.medicinenet.com/hematoma/article.htm.

1. Davis CP. Hematoma vs. ecchymosis: differences and similarities. eMedicineHealth. Updated by Cunha JP. Accessed November 27, 2024. https://www.emedicinehealth.com/hematoma_v_ecchymosis/article_em.htm; 2. Asirdizer M, Besik EZ, Kartal E. Non-traumatic ecchymoses: A literature review from a medico-legal perspective. *J Forensic Leg Med*. 2023;95:102490; 3. Mallidi RQ. Ecchymosis. MedIndia. Published August 23, 2017. Accessed November 27, 2024. https://www.medindia.net/patientinfo/ecchymosis.htm; 4. Wedro B. Hematoma. In: Balentine JR, ed. MedicineNet. Published July 5, 2024. Accessed November 27, 2024. https://www.medicinenet.com/hematoma/article.htm.

Edema (Drug Pooling)

Palpable	Hard	Red	Hot	Painful	Size <1 cm	Fades with Pressure	Fluctuates	Itchy	
☑	☒	☒ ☑	☒	☒	N/A	☑	N/A	N/A	Edema (Drug Pooling) 

Characteristics

- **Edema:** accumulation/retention of fluid within layers of the skin or beneath the skin, leading to noticeable swelling.[1]
- Edema may be generalized or local, and it can appear abruptly or insidiously (more common). If edema develops slowly over time, it may become massive before patients seek medical care.[2]
- Feels soft to the touch and if pressure is applied, may leave an indentation, referred to as "pitting" after pressure is released.[1]
- **Drug pooling** is an accumulation of drug under the skin around the area of infusion. It is typically manifested as an elevated area of the skin, with or without induration and might be a sign of reduced absorption.

Management

- When possible, treatment involves resolving the underlying cause.[1,2]
- Mild edema typically resolves spontaneously.
- **Gentle massage** of the area can accelerate the absorption of the edema.
- Persistent or worsening symptoms require further evaluation to rule out infection.
  - If swelling, redness, pain, fever increases after infusion site change, further evaluation from an HCP is required.

Initial recommendations:

- Change infusion site.
- Rotate infusion site more frequently.
- Change cannula size.
- Review patient technique.
  - Ensure 90° angle when inserting cannula.
  - Stretching the skin.
  - Insert cannula in standing/lying position.
- Experience from clinical trials with LDp/CDp suggests that although drug pooling does occur, **it does not typically influence efficacy and tends to resolve after a day to a few days** of switching to a new infusion site.

1. Ellenson S. Subcutaneous edema: symptoms, causes, and treatment. Tactile Medical. Published May 22, 2023. Accessed November 27, 2024. https://tactilemedical.com/resource-hub/cellulitis-and-edema/subcutaneous-edema-symptoms-causes-and-treatment/; 2. Thompson AD, Shea MJ. Edema. MSD Manual Professional Edition. Reviewed/Revised August 2024. Accessed November 27, 2024. https://www.msdmanuals.com/professional/cardiovascular-disorders/symptoms-of-cardiovascular-disorders/edema.

1. Ellenson S. Subcutaneous edema: symptoms, causes, and treatment. Tactile Medical. Published May 22, 2023. Accessed November 27, 2024. https://tactilemedical.com/resource-hub/cellulitis-and-edema/subcutaneous-edema-symptoms-causes-and-treatment/; 2. Thompson AD, Shea MJ. Edema. MSD Manual Professional Edition. Reviewed/Revised August 2024. Accessed November 27, 2024. https://www.msdmanuals.com/professional/cardiovascular-disorders/symptoms-of-cardiovascular-disorders/edema.

CDp, carbidopa prodrug; HCP, healthcare professional; LDp, levodopa prodrug.

Dermatitis

Palpable	Hard	Red	Hot	Painful	Size <1 cm	Fades with Pressure	Fluctuates	Itchy	
☒ ☑	☒ ☑	☑	☒	☒	N/A	☒	N/A	☑	Dermatitis 

Characteristics

- **Dermatitis:** localized skin inflammation caused by irritation, allergens, or immune responses to infusion or delivery system.[1]
- Often presents as **redness, swelling, itching, or a rash** around the injection site and may be accompanied by dryness or flaking. In severe cases, blisters or erosions can develop.[1]
- Symptoms can vary in severity from mild irritation that resolves on its own to persistent inflammation requiring medical treatment.[1]
- **Allergic contact dermatitis** occurs in sensitized individuals who develop an immune response after repeated contact with specific allergens. It typically appears at the site of allergen contact, but the rash can spread beyond the area of contact.
- Patch testing remains the definitive gold standard for diagnosing allergic contact dermatitis.
- **Irritant contact dermatitis:** more common, and may include erythema, scaling, edema, vesiculation, and erosions in acute cases. Erythema, lichenification, hyperkeratosis, and fissures in chronic cases.
- Allergic and irritant reactions may be indistinguishable based solely on visual assessment, as both can present with characteristics similar to eczema.

Management

- Management of dermatitis involves **identifying and removing the irritant** (e.g., switching adhesives or adjusting medication delivery), applying **topical treatments like corticosteroids or emollients, and maintaining proper hygiene** at the site.[1]
- For mild cases, emollients and topical steroids may suffice.
  - After removal, hydrocortisone cream or ointment can be applied to the affected area for a few days to reduce inflammation and itching.
- Severe or recurrent reactions warrant consideration of alternative infusion methods or materials and referral to patch testing.
- Consider use of skin barrier products to create a protective layer between the skin and the adhesive/cannula (e.g., 3M Cavilon No Sting Barrier Film, Skin-Prep, AllKare wipes).
- If dermatitis does not improve with treatment after 2 days or is associated with other symptoms, consider consultation with dermatologist.

1. Forkel S, Buhl T. Allergic Contact Dermatitis After Injection of Local Anesthetic. *J Allergy Clin Immunol Pract.* 2020;8(6):2060-2061.

1. Forkel S, Buhl T. Allergic Contact Dermatitis After Injection of Local Anesthetic. *J Allergy Clin Immunol Pract.* 2020;8(6):2060–2061.

Cellulitis

Palpable	Hard	Red	Hot	Painful	Size <1 cm	Fades with Pressure	Fluctuates	Itchy	
☒ ☑	☒ ☑	☑	☑	☑	N/A	☒	N/A	N/A	Cellulitis 

Characteristics

- **Cellulitis:** bacterial infection involving the inner layers of the skin, specifically affecting dermis and subcutaneous fat.[1]
- Presents as a **red, swollen, warm, and often painful** area of skin. Area of redness increases in size over a few days with borders that are generally round, but the edges of the redness are not always well defined.[1]
- Individual may have a fever and feel tired.[2]
- Lymphatic vessels may occasionally be involved.[1–4]
- Potential complications include abscess formation.[1]
- Infusion-site swabbing discouraged.[5]
  - Swabbing skin will not identify bacterial pathogen and may produce inconclusive results.

Management

- Treating physicians usually prescribe **oral/IV antibiotics**, such as cephalosporin (cephalexin) or penicillin (amoxicillin or cloxacillin)[1,2] depending on their criteria.
- For patients with recurring infections:
  - Test for MRSA.
  - Consider consultation with infectious disease specialist.
    - Do not limit specialist consultation for MRSA only, as it could be various infections.

1. Vary JC, O'Connor KM. Common dermatologic conditions. Med Clin North Am. 2014;98(3):445–485; 2. Mistry RD. Skin and soft tissue infections. *Pediatr Clin North Am.* 2013;60(5):1063–1082; 3. Edwards G, Freeman K, Llewelyn MJ, Hayward G. What diagnostic strategies can help differentiate cellulitis from other causes of red legs in primary care? *BMJ*. 2020;368:m54; 4. Tintinalli JE, Ma O, Yealy DM, Meckler GD, Stapczynski J, Cline DM, Thomas SH, eds. Tintinalli's Emergency Medicine: A Comprehensive Study Guide. 9th ed. McGraw-Hill Education; 2020. Accessed November 27, 2024. https://accessmedicine.mhmedical.com/content.aspx?bookid=2353§ionid=183421313; 5. Fung VSC, and al. Clinical Parkinsonism & Related Disorders. 2024, Vol.10.

1. Vary JC, O'Connor KM. Common dermatologic conditions. *Med Clin North Am*. 2014;98(3):445–485; 2. Phoenix G, Das S, Joshi M. Diagnosis and management of cellulitis. *BMJ*. 2012;345:e4955.
IV, intravenous; MRSA, methicillin□resistant *Staphylococcus aureus*.

Abscess

Palpable	Hard	Red	Hot	Painful	Size <1 cm	Fades with Pressure	Fluctuates	Itchy	
☒ ☑	☒ ☑	☑	☑	☑	N/A	N/A	☑	N/A	Abscess 

Characteristics

- **Abscess:** collection of pus that has built up within the tissue of the body.[1]
- **Abscesses** present as a **localized, swollen, red, and painful area**, often **warm to the touch** and **sometimes with a visible pus-filled centre**.[1]
- Abscess may feel as though it is **filled with fluid or "boggy"** if it is pressed (fluctuates).[1]
- Area of redness is often bigger than the area of swelling.[2]
- Pain, fever and chills may also be present.[1]

Management

- Prompt identification and **cut/drainage of abscesses** are essential to prevent systemic spread.[1]
- **Send sample of drained pus for bacterial cultures**. It is critical for guiding targeted antibiotic therapy, if needed.[1]
- Red flags, such as **fever, chills, worsening redness, or persistent pain**, should prompt immediate medical attention to rule out systemic involvement or complications.

1. Singer AJ, Talan DA. Management of skin abscesses in the era of methicillin-resistant Staphylococcus aureus. *N Engl J Med*. 2014;370(11):1039-1047; 2. Tidy C, Willacy H. Abscess. Patient.info. Last updated September 26, 2023. Accessed November 27, 2024. https://patient.info/infections/abscess-leaflet.

1. Stevens DL, Bisno AL, Chambers HF, et al; Infectious Diseases Society of America. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2014;59(2):e10-e52.