- Histamine is released by mast cells in response to allergic reactions (response to IgE). Examples of conditions/diseases in which histamine is going to be released include:
  - Hives.
  - Hay fever.
- Histamine is also important in the release of gastric acid from parietal cells which are present in gastric mucosa.
- **There are 4 types of histamine receptors:**
  - **H1 receptor (flare and wheal):**
    - It is found in: smooth muscle, endothelium and brain.
    - It causes vasodilatation, increased vascular permeability (leading to edema) and bronchoconstriction.
    - It also causes negative ionotropic effect in the heart (less contraction force of the heart) and diarrhea (by contracting the smooth muscle of the GIT).
    - The mechanism of action of H1-receptor blockers is: competitive antagonists preventing histamine from binding to its receptors.
      - **1st generation blockers:** they are more lipid-soluble so they can cross the blood-brain barrier and cause marked sedation (e.g. diphenhydramine). They are also antiemetic (e.g. promethazine).
      - **2nd generation blockers:** they are less lipid-soluble so they are used only for allergic reactions (they are free of sedation).
  - **Actions caused by blocking H1-receptor:**
    - **Antiallergic.**
  - **Actions not caused by blocking H1-receptor:**
    - **Sedation:** which induces sleep and controls itching in atopic dermatitis but it is unsuitable for day time.
    - **Antiemetic actions:** by the blockade of central acetylcholine receptor + central dopamine receptor.
    - **Antiparkinsonism effects:** blocking central muscarinic receptors.
    - **Anticholinergic actions (atropine-like actions):** resulting in dry mouth, blurred vision, constipation and urinary retention due to the blockade of peripheral acetylcholine muscarinic receptors.
    - **Antiadrenoceptor actions (phenothiazine derivatives):** orthostatic hypotension due to the blockade of α1-adrenergic receptors.
    - **Local anesthetic action (diphenhydramine and promethazine):** reduce nerve action potential by stabilizing nerve membrane through blockade of sodium channels. Diphenhydramine and promethazine are also used for motion sickness, morning sickness in pregnancy. Notice that diphenhydramine and promethazine are from 1st generation (with marked sedation).
  - **H2 receptors:** they are present in gastric mucosa (to increase the secretion of gastric acid from parietal cells), cardiac muscle (to cause positive ionotropic and chronotropic effects: increase in the force of contraction and rate of the heart), mast cells (to cause negative feedback on mast cells themselves) and brain.
  - **H3 receptor:** they are presynaptic (brain, myenteric plexus and other neurons).
  - **H4 receptors:** they are present in eosinophils (causing chemotactic effect) and neutrophils.
- **β-lactamase resistant penicillins:**
  - **Semi-synthetic β-lactamase resistant penicillins:**
    - They include: methicillin, oxacillin, cloxacillin, dicloxacillin and flucloxacillin.
They are relatively acid-stable (except methicillin), rapidly absorbed but incompletely (30%-80%), irregular (naficillin), given 1 hour before meal or 2 hours after it to ensure better absorption.

- Their antimicrobial spectrum is against S.aureus.
- If S.aureus is methicillin-resistant → vancomycin is the drug of choice (cotrimaxazole and linezolid can also be used).

**Topical steroids:**
- They are divided to 4 groups:
  - Mild.
  - Medium.
  - Strong.
  - Very strong.

**Note:** strong and very strong steroids must not be used on the face (thin skin), axilla, groins, perianal skin and submammary region.

- 1% hydrocortisone (or its equivalents) is used for simple dermatitis. Powerful fluorinated steroids are used for chronic eczema and psoriasis (الصدفية).
- Occlusion of topical steroids in the skin with moisture proof plastic tape (occlusive dressing), enhances their penetration (less evaporation of the drug) and thereby their potencies.
- The penetration rate of topical steroids is increased several folds when applied to inflamed or injured skin instead of normal skin (DUH©!!).
- Chemical modifications (esterification of hydroxygroups at C_{16,17,21}) increase steroids potencies by increasing their lipid-soluble properties.
- Addition of urea (ex. uremol) and salicylic acid (ex. diprosalic) enhance the absorption of topical corticosteroids probably by breaking down the barrier function of the skin.
- **Percutaneous absorption and potency of topical steroids are affected by vehicle in which the drug is dissolved:**
  - The more occlusive the vehicle (W/O emulsion or ointment) → the greater the hydration of S.corneum and the greater the permeability.
  - The more soluble topical steroids in vehicle (optimized vehicle) → the greater the penetration and the greater the potency.
- Some dermatological disorders are unresponsive to topical steroids (least responsive) and this can be overcome by intraleional injection of steroid suspension.

**Systemic side effects from topical steroids are related to:**
- Potency of the agent.
- Site of application and the percentage of the body covered.
- Use of occlusion.
- The status of stratum corneum (penetrating diseased skin more rapidly than normal skin).

**Regional differences in penetration of glucocorticoids (in order):**
1. Mucous membrane.
2. Scrotum.
3. Eyelids.
4. Face.
5. Chest and back.
6. Upper arms and legs.
7. Lower arms and legs.
8. Dorsa of hands and feet.
9. Palmar and plantar skin.

- **Valisone = betamethasone valerate**
  - 0.1% ointment: potent.
  - 0.1% cream: mild-strength.
  - 0.1% lotion: mild.

- **Topical side effects of glucocorticoids:**
  - Striae and atrophy.
  - Acne.
  - Perioral dermatitis.
  - Purpura and telangiectesia.
  - Rosacea.
  - Glaucoma.
  - Allergic contact dermatitis.
  - Hypopigmentation.
  - Reduced wound healing.
  - Hirsutism (face).
  - Folliculitis and miliaria.

- **Ointment:**
  - It is semi-solid.
  - Greasy (difficult to remove).
  - Uncomfortable if applied to a large area of skin, particularly in hot climate.
  - Interferes with heat loss.
  - Hydrates stratum corneum.
  - Enhances the percutaneous penetration of a drug.

- **Cream:**
  - W/O Cream
    - Greasy
    - Interferes with heat loss more than O/W cream
    - Enhances the percutaneous penetration of a drug more than O/W cream
  - O/W Cream
    - Non-greasy, easily removable
    - Has a cooling or soothing action

- **Topical antimicrobial agents used in burn care:**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Antimicrobial Coverage</th>
<th>Advantages</th>
<th>Disadvantages/Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacitracin</td>
<td>Gram-positive bacterial; antibiotic</td>
<td>Soothes and moisturizes; good for facial care and epithelializing wounds</td>
<td>Not appropriate for deeper wounds</td>
</tr>
<tr>
<td>Mafenide</td>
<td>Broad-spectrum antibacterial; anticoagulant</td>
<td>Penetrates eschar well; available as solution or cream</td>
<td>Painful on application; causes metabolic acidosis (via carbonic anhydrase inhibition)</td>
</tr>
<tr>
<td>Mupirocin</td>
<td>Anti-MRSA</td>
<td>Effective against MRSA</td>
<td>Narrow (poor gram-negative) antimicrobial coverage</td>
</tr>
<tr>
<td>Nystatin</td>
<td>Anti-fungal (Candida)</td>
<td>Provides fungal prophylaxis with swish-and-swallow solution</td>
<td>May interfere with activity of mafenide</td>
</tr>
<tr>
<td>Silver nitrate</td>
<td>Broad-spectrum antibacterial</td>
<td>Effective for both prophylaxis and treatment of wound infection</td>
<td>Penetrates eschar poorly; causes hypernatremia; stains linen and dressings; induces methemoglobinemia</td>
</tr>
<tr>
<td>Silver sulfadiazine</td>
<td>Broad-spectrum antibacterial; antipseudomonal</td>
<td>Soothes on application and causes no pain</td>
<td>Penetrates eschar poorly; causes leukopenia</td>
</tr>
</tbody>
</table>