Immunological disorders of the oral cavity
Recurrent aphthous stomatitis

Aphthous ulcers
Canker sores
Common condition characterized by development of painful, recurring, solitary or multiple ulcerations of the oral mucosa

Clinically similar to herpetic stomatitis
Etiology

- Bacterial infection
  - A hemolytic streptococci
  - Thought to be immunologic hypersensitivity to streptococcus
Immunologic abnormalities

- Autoimmune response of the oral epithelium
  - Increased binding of IgG and IgM antibodies to the spinous layer of oral epithelium

- Local immune response against antigenically altered mucosa
Nutritional deficiencies

- Iron
- Vitamin B 12
- Folic acid
Hormonal disturbances

- Incidence is greatest during premenstrual and postovulatory period in females
- Remission during pregnancy and eruptions following parturition
- May be related to blood levels of progesteron
Psychological factors
- Emotional and physical stress
- Lack of sleep

Allergic factors
- History of asthma, hay fever, food or drug allergies
Clinical features

Classification

- Recurrent aphthous minor
  - Canker sore

- Recurrent aphthous major
  - Periadenitis mucosa necrotica recurrens
  - Mikulicz’s scarringt aphthae
  - Sutton’s disease

- Recurrent herpetiform ulcerations

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Women
10-30 years

May or may not have prodromal features
- Small nodules
- Generalized edema of the oral cavity
- Paresthesia
- Low grade fever
- Localized lymphadenopathy
- Vesicle like lesions
Single or multiple superficial erosions

- Well circumscribed margins
- Covered by grey membrane
- Erythematous halo
- Extremely painful
- Usually 2-3 mm in size
- Usually seen in mucosa not bound to periostium
- Heal in 7-14 days without scarring

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Recurrent aphthous major

- Large painful ulcers
- 1-10 in number
- Usually about 10mm in diameter
- May persist for upto 6 weeks
- Heal with scarring

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Recurrent herpetiform ulcers

- Crops of multiple, small, shallow ulcers
- Often up to 100 in number
- Gradually enlarge and coalesce
- Any site
- Present almost continuously for one to three years
- Immediate but temporary relief with 2% tetracyclcin mouthwash

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How to differentiate from herpetic stomatitis

- HSV can not be cultured from the lesions
- Cytologic smears fail to reveal Tzank cells
- Microscopic findings are identical to those of aphthous
- Immunofluorescent and serological techniques are negative for antibodies against herpes simplex
Histopathological findings

- Ulcerated epithelium covered by fibrinopurulent area
- Superficial colonies of microorganisms
- Intense inflammatory cell infiltration with considerable necrosis
- Granulation tissue near the base of the lesion
- Intercellular edema with distintegration of epithelium
Ulcerated epithelium with intense inflammatory infiltrate
Ductal ectasia

Periductal fibrosis

Disruption of ductal epithelium
Cytological smears

- Cells with elongated nuclei
- Linear bar of chromatin with radiating processes of chromatin extending towards the nuclear membrane
- Anitschkow cells
Behcet’s syndrome

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Disease of uncertain etiology thought in past to be caused by Pleuropneumonia-like organism (PPLO)

Now thought to have autoimmune etiology
Clinical features

- Between 10 to 45 years
- Males
- Triad
  - Oral and genital ulcers
  - Ocular lesions
  - Skin lesions
- At least 2 should be present
- **Oral lesions**
  - Similar to aphthous
  - Painful
  - Any site

- **Ocular lesions**
  - Photophobia
  - Irritation
  - Conjunctivitis
  - Uveitis

- **Skin lesions**
  - Pustules or papules on trunk, limbs, and genital

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- Arthralgia
- Thrombophlebitis
- CNS, cardiovascular, pulmonary involvement
Histopathologic features

- Nonspecific
- Similar to recurrent aphthous stomatitis
Laboratory findings

- Hypergammaglobulinemia
- Leukocytosis
- Eosinophelia
- Elevated ESR

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Reiter’s syndrome
Disease of unknown etiology

Previously thought to be caused by
- PPLO
- Bedsonia group of virus
- Mycoplasma
- Chlamydia species

Current concept
- Immunodysregulated condition
Clinical features

- Young adults
- Men (9:1)

- Tetrad
  - Nongonococcal urethritis
  - Arthritis
  - Conjunctivitis
  - Mucocutaneous lesions
- Urethritis
  - Urethral discharge
  - Itching
  - Burning sensation

- Arthritis
  - Polyarticular
  - Bilaterally symmetrical

- Conjunctivitis
  - Mild

- Skin lesions
  - Red or yellow keratotic macules or papules
Oral manifestations

- Buccal mucosa, lips, gingiva
  - Painless, red, slightly elevated areas
  - White borders

- Palate
  - Small, bright red purpuric spots
  - Darken and coalesce

- Tongue
  - Resembles geographic tongue

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Histopathologic features

- Parakeratosis
- Acanthosis
- Neutrophilic infiltration of epithelium forming microabcess
- Lymphocyte and plasma cell infiltrate in connective tissue
Laboratory findings

- Mild leukocytosis
- Elevated ESR
- Pyuria
Sarcoidosis
Multisystem granulomatous disease of unknown origin

Characterized by
  - Depression of delayed type of hypersensitivity
    - Due to impaired cell mediated immunity
  - Raised abnormal serum immunoglobulin levels
    - Due to lymphoproliferation

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Clinical features

- Young and middle aged adults
- Starts with mild malaise and cough
- Hilar lymphadenopathy
- Pulmonary infiltration
- Eye lesions
- Hepatospleenomegaly
- Enlargement of salivary glands
- Cutaneous lesions
  - Multiple, raised, red patches
  - Grow slowly
  - Do not tend to ulcerate or crust
Oral manifestations

- Rare

- Most common site
  - Gingiva, lips, palate, buccal mucosa

- Painless enlargement

- Solitary or multiple nodules having gelatinous consistency

- Diffuse destruction of bone

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Histopathologic features

- Uniform, discrete, compact, non-caseating granulomas
- Nests of epithelioid cells
- Multinucleated giant cells
- No caseation or necrosis
Numerous discrete and compact granulomas

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High power view of single granuloma

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- Multinucleated giant cell with crystalline inclusion
Gingival biopsy

- Compact granulomas within lamina propria
Biopsy of labial mucosa showing granulomas in minor salivary glands

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Angioedema

Angioneurotic edema
Quincke’s edema
Giant urticaria
Diffuse edematous swelling of the soft tissues commonly involving the subcutaneous and submucosal connective tissue
Pathogenesis

- Alteration in vascular permeability

  - **Allergic angioedema** → due to mast cell degranulation caused by IgE mediated hypersensitivity reactions

  - Associated with use of ACE inhibitors → due to increased levels of bradykinin

- Defect in regulation of complement pathway
  - Hereditary or acquired

- Patients with elevated eosinophil counts

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Clinical features

- Soft, nontender, diffuse edematous swelling most commonly involving face
  - Lips and peri oral area
  - Chin
  - Eyes and periorbital area
  - Tongue
  - Pharynx
  - Larynx

- Rapid onset

- Usually resolves within 24-72 hours
- Feeling of tenseness
- Itching and prickly sensation
- Sever cases may show
  - Respiratory involvement
    - Hoarseness of voice
    - Difficulty in breathing
  - GI involvement
    - Vomitting
    - Watery diarrhea
Treatment

- Antihistaminics
- Epinepherine

In severe cases
- Intravenous corticosteroids
- Tracheostomy
Drug allergy

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Sensitivity reaction following exposure to any drug or chemical that is not related to any pharmacologic activity or toxicity of these materials
Clinical features

- Arthralgia
- Fever
- Lymphadenopathy
- Agranulocytosis
- Skin lesions → *dermatitis medicamentosa*
  - Urticaria
  - Fixed drug eruptions

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Oral manifestation

- **Stomatitis medicamentosa**

- **Present as**
  - Erythema multiforme
  - Lichenoid drug reactions
  - Lupus erythematosus like eruptions
  - Pemphigus like eruptions
  - Nonspecific vesiculoulcerative lesions

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Contact stomatitis / dermatitis

Stomatitis/dermatitis venenata
Type of reaction in which skin or oral lesions develop after repeated contact with the causative agent
Clinical features

- Itching or burning sensation at the site of contact
- Erythema
- Vesicle formation
- Erosion

In chronic cases
- Skin becomes thickened and dry
Oral manifestation

- Oral cavity is less sensitive than skin
  - Oral mucosa becomes inflamed and edematous
  - Small vesicles that rupture to form erosions and ulcerations
  - Sever burning sensation, tingling, stinging sensation
  - Plasma cell gingivitis

- Chronic cases
  - Erythematous areas
  - White hyperkeratotic areas

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Histopathologic feature

- Intra and intercellular edema of epithelium
- Intraepithelial or subepithelial vesicle formation
- Engorged and dilated blood vessels
- Edema of connective tissue with dense plasma cell infiltrate
- Increased number of eosinophils