**HIV and AIDS**

HIV virus mainly affects lymphocytes,macrophages and certain nerve cells.It affects mainly T lymphocytes.  
The normal CD4 count/mm3 = 800-1200 and T4:T8 = 2:1  
In AIDS patients the CD4 count/mm3<200 and T4:T8 = 1:2

**AIDS prevalence:**  
In our region it is still low.It occurs mainly in South Africa but in our region the prevalence is less than 0.1-0.5 %.

After exposure and getting the infection,there will be presence of antibodies against HIV virus(HIV seropositive) and then there is latency period –which can be few months up to 10 years in some patients-.During that, some features may appear such as persistent generalized lymphoadenopathy(PGL) or AIDS related complex (ARC) including fever,malaise,lymphoadenopathy and diarrhea.In the end,all patients will have full-blown AIDS which is characterized by :  
#Bacterial,viral and fungal infections   
#Tumors mainly Kaposi's sarcomas and lymphomas  
#Neurological manifestations   
AIDS is a fatal disease so HIV patients eventually will die.

**Oral manifestations**:  
No unique condition specific to HIV disease but there are categories of lesions associated with AIDS such as:

1. **Candidal infections**  
   Candidiasis is the most frequent oral lesion in HIV patients.It occurs in 20% of those seropsitive patients and 70% of those who have full-blown disease.  
   -persistent infection, resistant to treatment and refractory .  
   -not localized to oral cavity.It can appear in GIT and other mucous membranes.  
   -not only *Candida albicans* is involved,other species such as *Candida tropicalis* and *Candida glabrata* can be found.

Forms :  
# thrush like on upper lip  
#chronic erythematous candidiasis (red lesion on palate )  
#chronic hyperplastic candidiasis(plaque-like)  
So any form of candidiasis can be seen in AIDS patients and any form can be associated with angular cheilitis.

2**- periodontal disease**: a-**Linear gingival erythema**: appears as red line on marginal gingiva.  
b- **Necrotizing** **Ulcerative Gingivitis (NUG) and Necrotizing Ulcerative Periodontitis.**So periodontal diseases in AIDS patients are more destructive compared with normal patients.  
  
4-**Hairy Leukoplakia**   
It is called hairy because it is a white lesion with hair-like projections. It appears on the lateral border of tongue not on the dorsum of tongue.  
Note: do not mix it with hairy tongue that develops on dorsum of tongue.  
-usually bilateral  
-not always hairy; sometimes it can be flat white lesion  
-not restricted to the lateral border of tongue; it can be found in other sites such as buccal mucosa.   
-precursor of AIDS; when hairy leukoplakia is seen in a HIV patient it is a bad sign as it indicates that CD4 count is very low and the patient will develop full blown AIDS soon.  
**Question**: Does HL affect mucosal sites other than the mouth?  
  
**Is HL specific to HIV patients or not?**  
No, it can appear in other categories of patients.

What is the differential diagnosis?  
\*\*Traumatic Keratosis: as the lateral border of tongue is a common site for this lesion.  
\*\*Leukoplakia  
\*\*Squamous Cell carcinoma  
\*\*lichen planus  
  
Histologically, how to confirm the diagnosis of hairy leukoplakia?

|  |  |  |  |
| --- | --- | --- | --- |
| Traumatic keratosis | leukoplakia | Lichen planus | Squamous cell carcinoma |
| Hyperkeratosis, hyperplasia and inflammation of lamina propria | Hyperkeratosis, hyperplasia, ± dysplasia | Parakeratosis, damage of basal cell region and inflammation of lamina propria (band-like) | Invasion of lamina propria |

But Hairy Leukoplakia appears histollogically as:

a-Hyperparakeratosis,acanthosis and the surface might have hair-like projections.  
 B-koilocyte-like cells in upper part of basal cells which are features of viral infection appear as small nuclei with large cytoplasm.  
**Note**: koilocyte-like cells is a feature in HPV infection too.  
**Do we expect to see inflammation in lamina propria**?  
No, because HIV virus damages the cell-mediate immunity.  
Also, in the epithelial cells we can see the causative organism (EBV) and can see secondary infection with candida; invading the cells as a result of reduced immunity.  
   
**Question: what is the source of EBV virus? Is it from another patient or the patient himself?  
Why HL affects the lateral border of tongue in specific? Why not the dorsum of tongue, floor of mouth or buccal mucosa?**Special stain (in situ hybridization) by looking for RNA of the virus reveals the presence of virus in upper parts of epithelium (EBV). PAS stain reveals candidal invasion of the superficial part of epithelium; it is a secondary infection not part of the etiology).  
  
5-**Kaposi's sarcoma**:  
It is the most common malignancy of AIDS patients (25% of patients).  
It was found in the past in Africa in an endemic form but with good prognosis (not fatal).  
But in HIV it is a common tumor. It affects mainly males (M:F=20:1)  
-more in whites and homosexuals.  
-affect skin and mucous membranes including the oral cavity.  
-can be multiple; affects many sites in the skin.  
-Painless  
-the nose is the most common area in head and neck to be affected.  
-color is red, brown or violet.  
-it starts as macules then nodules then ulceration and destruction of the region.  
-in oral cavity, most commonly affects the maxilla; palate and maxillary gingiva  
  
Differential diagnosis:  
kissing lesion, erythroplakia, vascular malformation, hematoma and hemangioma, and SCC.

Histologically,how to confirm diagnosis?  
In early stages, it looks like pyogenic granuloma so we see proliferation of endothelium,extravasated RBC's ,hemosiderin,inflammation and spindle-shape cells.So it maybe misdiagnosed with pyogenic granuloma or hemangioma.  
In late satges,mainly composed of spindle-shape cells and abnormally-shaped vascular spaces.  
How to confirm? It is difficult to diagnose and you have to do immunohistochemistry for the Human Herpes Virus-8 which is associated with Kaposi's sarcoma .  
  
6-**Non-Hodgkin lymphoma**:  
The second most common tumor in AIDS patients,mainly in maxilla (upper palate and gingiva)  
Features:  
features of malignancy >>lesion causing mass and destruction to the adjacent structures.  
-mainly B-cell lymphoma and associated with EBV.  
  
**Lesions less commonly associated with HIV infection :**1-atypical ulceration:  
ulcers refractory to treatment,resemble major aphthous ulcers.It can be present in the oropharynx causing problems to the patient.  
It is caused by mycobacterium o CMV or herpes virus or other microorganisms.  
  
2-idiopathic thrombocytopenia purpura:  
bleeding spots in the oral cavity and any trauma can cause heavy bleeding.  
  
3-salivary gland disorders:  
-chronic porotitis  
-Sjogren's like syndrome (enlargement of parotid gland with xerostomia)  
-parotid lymphoepithelial cysts.  
  
4-viral infections such as:  
- recurrent severe herpes simplex and herpes zoster  
-CMV and HPV infection which appears as warts in oral cavity.   
  
**Lesions possibly associated with HIV infection :**  
-bacterial infection other than NUG :syphilis and TB  
-fungal infection other than candida :deep mycosis.  
-melanotic hyperpigmentation :appears as a result of drugs taken by AIDS patients or because of damage of adrenal gland which leads to pigmentations like Addison's disease.  
-neurological manifestions(sensory or motor) such as facial paralysis.  
  
**Oral Ulceration :**  
a-infective  
b-traumatic  
c-associated with systemic disease or a sign of undiagnosed systemic disease such as:  
-hematological deficiencies;anemias  
-GIT disease  
-Bechcet's disease  
-HIV  
d-associated with a dermatological disease:  
-lichen planus  
-chronic discoid lupus  
-vesiculobullous disease: autoimmune disease.  
e-neoplastic: SCC  
f-idiopathic ; Aphthous Recurrent Stomatitis.

1. Traumatic ulcers
2. Mechanical trauma:

* Trauma can be due to teeth
* Fractured restorations
* Rough restorations
* Appliances and dentures (overextended dentures for example)
* Trauma can be induced by the patient himself, if the patient has psychological problems (factitious disorder).
* Dentists can induce trauma in a patient’s mouth, for example when using a polishing disc or a saliva ejector.
* In children who are given local anesthesia, they will keep biting their lip without feeling that they are traumatizing the soft tissues

How to confirm that this ulcer is the result of mechanical trauma: look in the region of the ulcer for any rough restorations, broken teeth, or appliances, or the patient told you that he/she has bitten on that area.

There has to be a consistency in the site and size and shape of the ulcer and the cause of the ulcer; for example, a small rough restoration would not result in an ulcer covering a big part of the tongue, so in this case you’d have to look for another cause of the ulcer.

If the cause of the ulcer was removed, there should be healing within 10 days.

If the ulcer was due to a patient’s bad habit, the patient might not be compliant and there will not be healing of the ulcer.

A biopsy is not taken in the first visit of patient with suspected traumatic ulcer, because it will cause even more trauma to the patient, so we remove the causative factor and we give the patient 2 weeks for ulcer to heal, and if there was no healing we would take a biopsy.

Histopathology of traumatic ulcers:

The epithelium is missing and there is inflamed underlying connective tissue.

Sometimes, the traumatic ulcer may be chronic, meaning that the traumatic cause of the ulcer is persistent. In these cases, we would find a white area of hyperkeratosis or fibrosis around the ulcer. The ulcer itself can be hard as a result of fibrosis (induration). All these feature may lead us to think of malignancy, again remove the cause and wait for 2 weeks if no healing we should take a biopsy to rule out malignancy.

1. Chemically induced:

These are rare in our society.

Most chemically induced ulcers are the result of dentists. These chemicals include:

* Acid etching
* Formocresol
* Irrigation solution for endodontic treatment

Aspirin burns: Some people used to believe that putting an aspirin pill in the labial or lingual sulcus next to a painful tooth will relieve the symptoms more quickly than swallowing the pill. The aspirin is an acid, this will lead to tissue necrosis and an ulcer which we call aspirin burn. This diagnosis can be confirmed when the patient has pain due to irreversible pulpitis near the aspirin burn.

1. Thermally induced

These are the result of eating hot food, and the result is an ulcer in the palate usually.

Thermal trauma can also be cause by dentists, for example when using a hot impression material or hot instrument during endodontic treatment.

1. Radiation

Erosions as a result of radiation appear immediately after the patient is exposed to radiation for therapy of cancers of the head and neck or oral cancer. There will be healing of these erosions and after a while, secondary ulcers will appear in the same area. This is because radiation will cause damage to the blood vessels, and the tissues involved will become ischemic. This might be confused with recurrence of cancer, so a biopsy should be taken to confirm whether this is a recurrence or a traumatic ulcer.

1. Eosinophilic ulcers

Histopathology: Many eosinophils are found

It looks similar to oral cancer.

Question: What is the cause of eosinophilic ulcers and how can they be differentiated from oral cancer?

1. Recurrent Aphthous Stomatitis (RAS) or Aphthous ulcer

Round ulcer which is white in colour and surrounded by red margin.

Unknown etiology

These are one of the most common type of oral ulcers. A study we carried out in the University of Jordan and it was found that 37% of the students had a history of aphthous ulcer in the past year, and 5% had an aphthous ulcer in the time of the study (this is called point prevalence). The lifetime prevalence is 50% (meaning that 50% of the students had an aphthous ulcer at some point in their lives). The average prevalence of aphthous ulcers in different communities is 10-25%.

It is not persistent, it’s recurrent. The duration is usually around 10 days.

Onset: First 3 decades of life. With **increasing** age, the frequency of aphthous ulcers **decreases**. The reason isn’t known for sure but there are **theories** which say that the mucosa will become thicker with age, making it more resistant to aphthous ulcers. Another theory states that aphthous ulcers are immune mediated, and as immunity decreases with age so does the recurrence of aphthous ulcers.

The prevalence of aphthous ulcers in smokers is low, because there is keratosis in the oral mucosa and this mucosa will become more resistant to ulcers. That is why in people who have stopped smoking, the occurrence of aphthous ulcers increases.

There is no difference in prevalence between males and females.

Prodromal Symptoms: Burning sensation/tingling sensation

Clinical symptoms: Very painful, which may result in eating and swallowing difficulties. It may also result in anxiety and nutrition problems if it was recurring very frequently.

How to confirm the clinical diagnosis: **Recurrences** and **multiple** ulcers affecting more than one site in the oral cavity.

Histopathology is similar to what is seen with a traumatic ulcer: loss of epithelium with inflamed connective tissue.

Note: There is not specific feature that will allow the histopathologist to say that this is an aphthous ulcer, it just looks like a non-specific ulcer histopathologically.

Forms of aphthous ulcer: major, minor, and herpetiform aphthous ulcers.

Minor aphthous ulcers:

* 80% of all aphthous ulcers
* Usually 1 ulcer, but may reach up to 5 ulcers at the same time
* Intra-oral sites: usually non-keratinized mucosa, so it’s not seen on the gingiva or palate. (It is seen on the buccal mucosa, labial mucosa, floor of the mouth etc.).
* Clinically: round/oval whitish ulcer surrounded by red margin. The redness is due to inflammation.
* Usually not deep
* Size: less than 1 cm (usually 0.5 cm or less)
* Recurrence rate: Variable (in some people it may recur every few months or once every year), but usually the recurrence rate is every 1-4 months.

Major aphthous ulcers:

* Second most common (around 10% of the cases).
* Number: 1 to 10 ulcers at the same time
* Larger than minor aphthous ulcer (more than 1 cm in diameter)
* Deeper than minor aphthous ulcer.
* Duration: can last for up to more than a month because it will take a longer time to heal, so it may be confused with oral cancer because of its large size and long duration.
* Found on the keratinized areas (like the palate). It is frequently found in the posterior part of the palate and the pharynx and tonsils, leading to difficulty and pain during swallowing.
* Its large size will lead to scarring (fibrosis) when the ulcer heals.
* If a patient complained of having an aphthous ulcer previously, we should look for scarring on the mucosae. The presence of scars will indicate that the aphthous ulcer that the patient had was a major aphthous ulcer.
* Recurrence rate: the recurrence rate may be very high so that the patient continuously has an aphthous ulcer, making the patient depressed.

Herpetiform aphthous ulcers:

* Least common type
* Looks similar to herpes ulcers
* Multiple (up to 100 or more ulcers)
* Irregular in shape
* Small (1-2 mm). These small ulcers can fuse together and form larger ulcers. This will lead to fibrosis/scarring after healing
* Can be found on any site in the oral cavity, but it’s found more commonly on the non-keratinized mucosae.
* Recurrence: less than 1 month in severe cases

How to differentiate it from primary herpetic stomatitis:

* Examine the gingiva, in primary herpetic stomatitis there is reddening of the gingiva and edema. This is not seen in herpetiform aphthous ulcers. However, herpetiform aphthous ulcers may affect the gingiva directly and cause reddening and edema, so examining the gingiva isn’t a very reliable way to make a differential diagnosis.
* Systemic manifestations: there are no systemic signs of aphthous ulcers (like fever or lymphadenopathy) but in herpes there are systemic manifestations such as fever, malaise, and lymphadenopathy.
* The clinical presentation of herpes ulcers start out as vesicles. On the other hand, aphthous ulcers do not start out as vesicles; they directly appear as ulcers.
* Primary herpes stomatitis recurs as herpes labialis (it presents the first time as herpes stomatitis and if it recurs, it will be as herpes labialis). Herpetiform aphthous ulcers recur in the same clinical picture as intraoral ulcers.

Until now, the etiology of aphthous ulcers isn’t known so there is no clear management to eradicate the ulcers. The treatment that is given for aphthous ulcers is to relieve the symptoms only, since the main cause of aphthous ulcers isn’t clear.

* Genetic factors: Even though aphthous ulcers are observed to be seen in families, there is no clear pattern of inheritance of the ulcers.
* Mucosal barrier appears to be important in the prevention of aphthous ulcers. An intact mucosa serves as a good prevention of aphthous ulcers, this might explain why most aphthous ulcers appear on non-keratinized mucosa (especially minor aphthous ulcers).

Numerous factors that may decrease the mucosal barrier increase the frequency of aphthous ulcers, like atrophy in the mucosa for example. In contrast, factors that may increase the thickness of the mucosa or cause keratosis of the mucosa will lead to decreased occurrence of aphthous ulcers.

* Hormonal factors: There is no clear evidence that the aphthous ulcer is caused by hormones, since it is found in both males and females. In some females, it was found that the frequency increased in the menstrual period.
* Traumatic factors: Some patients may say that before the aphthous ulcer appeared, the patient bite on that same area and traumatized it. It is thought that trauma helps in determining the location of the aphthous ulcer. This doesn’t mean trauma is an etiological factor, since aphthous ulcers may appear in patients without previous trauma.
* Stress: during exam periods or stressful situations, the occurrence of aphthous ulcers in some patients may increase. For example, when someone stops smoking, the first few weeks of not smoking is stressful which may contribute to the formation of aphthous ulcers in these patients.
* Oral pathology
* 26-10-2014
* Rawan hattab
* The dr was talking about aphthous <https://www.google.jo/search?biw=1366&bih=667&q=aphthous&spell=1&sa=X&ei=zl5NVLTpLKGX7QaEtoGYBw&ved=0CBcQvwUoAA> ulcer :
* He said some researchers connected it to infective agents like H-pylori that cause stomach ulcer or strepto sanguis but there is no evidence that aphthous ulcer is possible to be due to bacterial infection .
* **Hematological deficiencies:**
* All patients with aphthous ulcers undergo for routine hematological screening for iron , folate , and b12 (CBC) "
* A study we conducted to estimate the prevalence of deficiency states in aphthous patients:
* 17% had an iron deficiency
* 5% had folate deficiency and up to 25 % had b12 deficiency .
* They also found after treatment and correction of the deficiency state , aphthous ulcer disappeared in some patients.
* **GIT diseases** like " celiac disease, ulcerative colitis and crohns disease are associated with aphthous like ulcers .
* **Allergy** some patients related it to certain kinds of food and drinks like nuts , others related it to some materials like tooth paste , and food preservatives.
* "Keep in mind there is no clear evidence about all of the above"
* How aphthous ulcer is being induced ?
* It is an immune mechanism not infective agents , for unknown reason cell mediated immunity is triggered causing damage to the epithelium .
* They observed before appearing of ulcers " if they take a biopsy " lymphoid cells infiltrating to lamina propria , later on edema happens , lymphatic infiltration in epithelium then degeneration to the epithelium ..so cell mediated immunity is the main cause of epithelial damage .
* In Pre ulcerative stage they found T4/T8 ration is 2:1
* But during the ulcerative stage the ratio is 1:10 “notice CD8 causing the damage to epithelium ".CD8 is cytotoxic"
* And in healing stage the ratio : 10:1 "t-helper is important for healing "
* Any patient with aphthous ulcer you have to ask about behcet’s syndrome
* How to confirm if the patient has behcet’s disease or not?
* It depends mainly on clinical manifestation, there is no specific test , mainly affects young adult males and some associated with HLA-B51
* what is the components of behcet’s disease ?
* mouth ulcers (recurrent aphthous ulcers) "basic component "
* eye and skin lesions
* genital lesions
* others : cardiovascular , neural and joint disease.
* Dose mouth ulcer differ from aphthous ulcer?
* patients without bechet disease they are the same but they suspected that patients with bechet have more ulcers , variable in size and have irregular peripheries particularly in posterior region and pharynx .
* genital ulcers in genitalia
* eye lesions " chronic inflammation of the eyes " conjunctivitis, Retinitis ,uveitis " "
* skin lesions : like pustular and macular lesions ,they have larger ,red nodules called erythema nodosum and some patients have subcutaneous thrombophelebitis …. ……
* another thing that could help in diagnosis is pathergy test
* "
* minor criteria : joint pain ,CNS LESIONS sensory and motor disturbances ,thrombotic vascular lesions , GIT ULCERS