General Principles of Diagnosis and Differential Diagnosis in Oral Pathology
The Diagnostic Sequence

1. Examination of the patient
   - Chief complaints
   - Onset and course
2. Detection and examination of the lesion
3. Classification of the lesion
4. Listing the possible diagnosis
5. Developing the differential diagnosis
6. Working diagnosis
7. Re-examination of the lesion
8. Final diagnosis
**History**

- Clinical exam (radiographs if needed)

**Possible Procedures Leading to Diagnosis**

- Biopsy and/or Lab tests
  - Definitive Dx.
  - Tx by experience
    - (Diagnosis ex juvantibus)
      - Response to specific Rx
      - Resolution with no diagnosis
      - No resolution
        - Biopsy and/or Lab tests
          - Definitive Dx.
During procedures, you have also to:

1. **Identify** – undetected systemic disease

2. **Identify** – taking medicine or illegal drugs

3. **Modify** – treatment plan if needed

5. **Communicate** – with other medical consultants

6. **Establish** – good patient-dentist relationship
History Taking

- What, where, when, how
  - Chief complaint
  - Present illness
- Past medical history
  - Family history
  - Social history
  - Occupational history
  - Dental history
- Review of symptoms by system
- Physical examination
  - Radiographic and laboratory examination
Is this diagnostic too?

You are what you eat!

I’m loving it............
...drinker
Eating disorders
Chief complaint(s)

- Pain
- Soreness
- Burning sensation
- Bleeding
- Loose teeth
- Recent occlusal problem
- Delayed tooth eruption
- Dry mouth or too much saliva
- Swelling
- Bad taste or Halitosis
- Parthesia and anesthesia
Pain

Location, sharp or dull, severity, duration, precipitating circumstances

- Teeth
- Mucous membrane diseases
- Salivary gland inflammation or infection
- Lesions of the jaw bone
- LN inflammation and/or inflammation
- TMJ diseases
- Sinus diseases
- Ear diseases
- Psychoses
- Somatic diseases: angina pectoris, neuralgia etc
Soreness
Usually related to mucosa inflammation or ulcers

Burning sensation
Thinning or erosion of the surface epithelium

- Burning mouth syndrome
  - Xerostomia
  - Anemia
  - Vitamin deficiencies
- Psychosis
- Neurosis
- Viral, fungal or chronic bacterial infection
Burning mouth syndrome

- **Gender effects**: F:M = 3:1 ~ 7:1
- **Age**: Middle-aged and elderly-aged

**Local and systemic precipitating factors**:

- Hematologic diseases
- Undiagnosed diabetes
- Oral candida infection
- Xerostomia
- Denture faults
- Mouth breathing
- Allergy
- Psychological state
- Drug induced
- Hypothyroid function
- Cancerophobia
Vit. B$_{12}$ deficiency (Pernicious anemia)

After treatment
Bleeding

- Gingivitis and periodontal disease
- Traumatic incidence, surgery
- Inflammation
- Tumors (traumatized tumor or vascular tumors)
- Diseases associated with deficiencies in hemostasis
Periodontitis
Erythema multiforme
Bleeding
Hematoma
leukemia
Loose teeth

Loss of supporting bone or resorption of roots

- Periodontal diseases
- Trauma (acute or chronic)
- Normal resorption of primary teeth
- Benign tumors (with root resorption)
- **Malignant tumors** (supporting bone destruction)
Ameloblastoma: multilocular radiolucency of the left mandibular body and angle. Significant cortical expansion and extensive resorption of the roots
Recent occlusal problem

Existed teeth don’t bite right or existed teeth are out of line

- Overcontoured restorations
- Periodontal disease, periapical abscess
- Traumatic injury, tooth fracture
- Tumor or cyst of tooth-bearing regions of the jaws
- Fibrous dysplasia
Overcontoured restorations
Delayed tooth eruption

- Malposed eruption or impacted teeth
- Cyst
- Odontomas, mesiodens
- Sclerotic bone
- Tumors
- Developmental anomalies
- Generalized delay: anodontia, cleidocranial dysplasia, hypothyroidism, hypopituitarism
Delayed tooth eruption (dentitio tarda)

How old is the patient?
Hypopituitarism is the decreased secretion of one or more hormones produced by the pituitary gland. The oral features are dentitio tarda, and follicular cyst formation.
Dry mouth

- Infection and fibrosis of salivary gland
- Dehydration state
- Drug therapy:
  - Tranquilizers
  - Diuretics
  - Antihistamines
  - Anticholinergic
- Autoimmune diseases
- H &N radiotherapy
- Chemotherapy
- Alcoholism
- Psychosis
Hypersalivation

- May be related to psychosomatic problems
- New denture, increased or decreased vertical dimension, oral piercing
Swelling

- Inflammations and infections
- Allergy
- Cysts
- Retention phenomena
- Tumors
Unilateral oral ranula in a young adult manifesting as a purple swelling
## Bad taste

<table>
<thead>
<tr>
<th>Causes</th>
</tr>
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<tbody>
<tr>
<td>Heavy smoking</td>
</tr>
<tr>
<td>Poor oral hygiene</td>
</tr>
<tr>
<td>Dental caries</td>
</tr>
<tr>
<td>Periodontal disease</td>
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<tr>
<td>Dry mouth</td>
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<tr>
<td>Intraoral malignancies</td>
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<table>
<thead>
<tr>
<th>Associated Conditions</th>
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<tbody>
<tr>
<td>Diabetes</td>
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<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Medication</td>
</tr>
<tr>
<td>Uremia</td>
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<tr>
<td>Neurogenic disorder</td>
</tr>
<tr>
<td>Psychosis</td>
</tr>
</tbody>
</table>
Paresthesia and anesthesia

- Injury to regional nerve
  - Anesthesia needles
  - Jaw bone fracture
  - Surgical procedure

- Malignancies

- Medication
  - Sedatives, Tranquilizers, Hypnotics

- Diabetes

- Pernicious anemia

- Acute infection of the jaw bone

- Psychosis
Ptosis in this patient with a right-sided facial paralysis.
1. Masses increase in size just before eating
   - ex. salivary retention phenomena, sialolithiasis

2. Slow-growing masses (duration of months to years)
   1) Reactive hyperplasia
   2) Chronic infection
   3) Cysts
   4) Benign tumors
3. Moderately rapid-growing masses (weeks to about 2-6 months)

1) Chronic infection
2) Cysts
3) Malignant tumors
4. Rapidly growing masses (hours to days)

1) Abscess (painful)
2) Infected cyst (painful)
3) Aneurysm
4) Salivary retention phenomena
5) Hematomas

5. Masses with accompanying fever

1) Infections
2) lymphoma, leukemia
Inspection

- Contours
- Color
- Surfaces
Contours
Normal & Variations

Colors
Masticatory mucosa vs Lining mucosa
White lesions

1. Thickening of epithelium (Hyperkeratosis)
2. Dense fibrous tissue

ex.: leukoplakia, fibroma
Red lesions

1. Thinning of epithelium
2. Inflammation
3. Increased vascularity

ex.: gingivitis, erythroplakia etc
Erythroplakia
Diascopy (is a test for blanchability) is performed by applying pressure with a glass slide and observing color changes.

It is used to determine whether a lesion is **vascular** (hemangioma), **nonvascular** (nevus), or **hemorrhagic** (petechia or purpura).

Hemorrhagic lesions and nonvascular lesions do not blanch; inflammatory lesions do.
Yellow lesions:

1. Adipose tissue
2. Sebaceous gland

ex.: lipoma, Fordyce’s granules
Fordyce’s granules of the upper lip; Histological characteristic
Brownnish, bluish and black lesions

Pigmentation: melanin, hemosiderin, heavy metal, blood vessels, fluids etc
ex: nevus, amalgam tattoo, hemangioma, mucocele

Peutz-Jegher’s syndrome

Mucocele
ORAL TATTOO
Melanoma malignum
Surfaces

Normal: smooth & glistening
Exceptions are dorsal tongue, rugae & attached gingiva
Pathologic mass may be:

1) *Smooth surface*

Arises *beneath epithelium*, originates from *mesenchyme*


( fibroma, osteoma, hemangioma, myoma etc.), *cellulitis, mucocele, etc.*
Mucocele
2) *Rough surface*

Due to trauma, infection and malignant processes;
Originates from the epithelium

Ex: papilloma, V.Ca, ulcerative & exophytic
SCC, polypoid or papillomatous mass
papilloma

SCC
3) **Pebbly surface**

Ex. : Granular cell tumor, lymphangioma

![Image of Lymphangioma]
4) **Flat & raised entities**

Hyperplasia (cell number↑) & hypertrophy (cell size↑)
Ex. papule, nodule, *Epulis fissuratum*
Palpation

A third eye of clinical examination!!!

- Surface temperature
- Anatomic regions & planes involved
- Mobility
- Extent
- Size & shape
- Consistency
- Fluctuance & emptiability
- Painless, tender or painful
- Unilateral or bilateral
- Solitary or multiple
Surface temperature

Temperature↑,

- Inflamed or infected
- Vascular lesions
cellulitis
Anatomic regions & planes involved

- Locates a firm mass, superficial or deep
- Difficult if swelling or painful
lateral cyst of the neck
Mobility

1. **Free movable**
2. **Fixed to skin** but not to the underlying tissue
3. **Free movable to the skin** but fixed to the underlying tissue
4. **bound to both skin or mucosa and to the underlying tissue**

1) **fibrosis** after a previous inflammation

2) **malignancy** from skin or mucosa invade to underlying tissue

3) **malignancy** from deeper tissue invade to surface epithelium

4) **malignancy** from loose CT to both the superficial & the deeper layers
Extent

- Border of a mass:
  (1) Well defined, (2) moderate defined or (2) poor defined
- Depend on:
  - Border of the mass
  - Consistency of surrounding tissue
  - Thickness of overlying tissue
  - Sturdiness of underlying tissue
Size & Shape

Fluctuance & emptiability

- Fluid contented lesions
- Cyst, mucocele, ranuna, hemangioma

Ranula
Consistency

- **Soft**: vein, loose CT, glandular tissue
- **Cheesy**: sebaceous cyst, epidermoid cyst
- **Rubbery**: relaxed muscle, glandular tissue with capsule, arteries
- **Firm**: fibrous tissue, tensed muscle, large nerve
- **Bony hard**: bone, cartilage, tooth structure
Irritating fibroma
Torus palatinus or exostosis
Painless, tender or painful

Pain
1. inflammation-- mechanical trauma or infection
2. painful tumors--some neural tumors
3. sensory nerve encroachment

Tenderness
low-grade inflammation & internal pressure, chronic infection
Unilateral or bilateral

Solitary or multiple

• Solitary: a local benign or early malignancy

• Multiple: systemic, disseminated diseases or syndrome
Aspiration

Investigate the fluid contents of the lesions

1. Cyst
2. Tumor

Content:
- Pus
- Sticky, clear, viscous fluid
- Blood
bilateral nasolabial cysts
Radiographic examination

Intraoral radiography
Extraoral radiographies
Re-examination of the lesion
- Re-evaluate its origin, findings or detailed observation

Classification of the lesion

Soft tissue origin? Bone origin?

- Subclassified: soft tissue → white, exophytic, ulcerative, etc.
- or bone lesion → periapical, cystic like, radiolucency, multiple separate, etc.
Listing the possible diagnosis

- Clinically and/or radiographically

Developing the possible diagnosis

- Sign—symptoms—statistical knowledge relate to the incidence of each disease entity—in order of their relative frequency of occurrence
- Age, gender, race, country of origin, anatomic location
Two or more lesions present

1. Lesions are related
   a. Lesion A and lesion B are identical (ex. 2 aphthous ulcers)
   b. Lesion B is secondary to lesion A (ex. metastatic tumor and primary)
   c. Lesion A and lesion B are both secondary to a third lesion, which may be occult (ex. metastatic tumors and primary)
   d. Lesion A and lesion B are manifestation of a systemic disease (ex. infections, Langerhan’s cell disease. Disseminated malignancy)
   e. Lesion A and lesion B form part of a syndrome (ex. cafe-au-late spots and multiple neurofibromatosis in Von Recklinghausen’s disease)

2. Lesions are completely unrelated to each other and occur together only by chance
The lesions are identical (oral papillomatosis)
The lesions are identical (major aphthous ulcers)
Lesions are completely unrelated to each other and occur together only by chance.
Lesion B is secondary to lesion A (metastatic tumor and primary)
Lesion A and lesion B form part of a disease or syndrome (ex. Lichen planus)
Developing the working diagnosis
(=operative diagnosis, tentative diagnosis, clinical impression)

- Further exam. the lesion, more definitive questions to expand the history, additional tests — reevaluating all the assembled pertinent data

Formulating the final diagnosis

- Exfoliative cytology
- Biopsy (microscopic examination) etc
Exfoliative cytology

- Oral exfoliative cytology examines the morphological characteristics of exfoliated (or) scraped off superficial cells of the oral mucosa.

- Fungal or viral disease or **malignant** (appearing cells)

- **Containdications**: smooth-surfaced exophytic lesions, homogeneous leukoplakia, submucosa lesions, unulcerated pigmented lesions, verruca vulgaris, papilloma
Exfoliative cytology

Physiological cell exfoliation
The exfoliative cytology sequence
Exfoliative cytology - modification
modified liquid-based cytology
Differences between:

• Conventional PAP test
• Modified liquid-based cytology
Light-based detection systems and fluorescence visualization
The specific ViziLite TM wavelength is absorbed by normal cells and reflected by abnormal cells due to their higher nuclear-cytoplasmic ratio. As a result, atypical mucosal abnormalities appear bright white.
VELscope technology stimulates epithelial cells and stroma by a blue light (400-460 nm). It is the self-fluorescence of the tissues that allows detection of changes in morphology and composition of the tissues in a non-evasive manner.
Viewed with the unassisted eye

Enhanced view using VELscope® Vx device

(lesion later confirmed as oral cancer)
Toluidine blue staining

- Rinsed with 1% acetic solution then stained with 1% Toluidine blue and washed with water
- Toluidine blue is an acidophilic metachromatic nuclear dye, selectively stains acidic tissue esp. DNA and RNA (affinity DNA > RNA).
- False positive 8-10%, false negative 6-7%
Supravital Toluidine blue (TB) staining
TB stain on a suspicious lesion at the ventral part of the tongue
TB stain on a suspicious lesion at the right lateral border of the tongue
Biopsy

**Artifacts**: improper fixation, freezing, curling of the specimen

**Specimen should be identified with**: patient’s name, clinician’s name, location of the lesion, patient history
Excisional biopsy

- when lesion $\leq 1\text{cm}$, does not necessitate a major surgical procedure
Surgical treatment (excisional biopsy)
Laser biopsy
Фиксиране на биоптата в 10% р-р на формалин (съотношението биоптат:фиксираща течност е 1:10). Хистологичната диагноза е сквамозен папилом.
Incisional biopsy

- Too large to excision, may require multiple tissue samples
- Most suspect area, should be relatively large and deep and include the junction with surrounding normal tissue
- Necrotic tissue, electrosurgery or thermal lasers should be avoided as possible
Incisional biopsy - most suspecteed area, should be relatively large and deep and *include the junction with surrounding normal tissue*
Diagnosis: Leukoplakia without dysplasia
- **Punch biopsies**: used on surface oral tissue (trismus patient)

- **Wedge-shaped biopsies**: used for vesiculoerosive disease

- **Fine-needle aspiration** (fine-needle aspiration FNA, aspiration biopsy): 21-23 gauge.
Punch biopsy
Biopsy of minor salivary gland
Immunofluorescence is a technique uses the specificity of antibodies to their antigen to target fluorescent dyes to specific biomolecule targets within a cell, and therefore allows visualisation of the distribution of the target molecule through the sample. Several oral conditions like *Pemphigus vulgaris* can be diagnosed with the aid of immunofluorescence studies.
Humans have three major salivary glands: parotid, submandibular, and sublingual. These glands, along with additional minor salivary glands, secrete a rich mixture of biological markers.

The level of each salivary component varies considerably depending on the health status of the individual and the presence of disease (oral or systemic). By measuring these components in the saliva, it is possible to screen for a variety of infections, allergies, hormonal disturbances, and neoplasms.
Saliva testing

Saliva testing is a diagnostic technique that involves laboratory analysis of saliva to identify markers of endocrine, immunologic, inflammatory, infectious, and other types of conditions. Saliva is a useful biological fluid for assaying steroid hormones such as cortisol, genetic material like RNA, proteins such as enzymes and antibodies, and a variety of other substances, including natural metabolites, including saliva nitrite, a biomarker for nitric oxide status. Saliva testing is used to screen for or diagnose numerous conditions and disease states, including Cushing's disease, anovulation, HIV, cancer, parasites, hypogonadism, and allergies.
“Arborization or ferning phenomenon”

Francois C. Chrétien, Jean Berthou
Crystallographic investigation of the dried exudate of the major vestibular (Bartholin's) glands in women. European Journal of Obstetrics & Gynecology and Reproductive Biology Volume 135, Issue 1, November 2007, Pages 116–122
Oral cancer

In 2010 Jou, et al., found that patients diagnosed with oral squamous cell carcinoma had elevated levels of transferrin in saliva compared to healthy controls and, moreover, that salivary transferrin measurement using ELISA technique was “highly specific, sensitive, and accurate for the early detection of oral cancer.”

A 2009 study reported that the levels of two biomarkers, Cyclin D1 (increased compared to controls) and Maspin (decreased compared to controls), had sensitivities and specificities of 100% for oral cancer detection when measured in saliva.
Xerostomia
SALIVA TESTING

1. pH
2. Buffer capacity
3. Microbiological saliva tests
4. Specific saliva tests
SALIVA TESTING

pH
SALIVA TESTING

Buffer capacity
SALIVA TESTING

Buffer capacity

CRT® buffer
Step by step

Buffer capacity
high  medium  low
Dynamic of oral microbiota
Добрият, лошият и условно патогенният
Bacterial biofilm

> 400 spp microbiota

- Mechanical barrier
- Epithelial antimicrobial peptides
- Adaptive immunity
- Neutrophils
- Saliva
- Langerhans cells
- Bacterial biofilm
Организация на бактериалната екосистема в устната кухина
Динамика на оралната микрофлора през различните възрасти
SALIVA TESTING

Микробиологично изследване на слюнката със селективни хранителни среди
Вземане на слюнчена проба и количествено отчитане в мерителна чаша
Нанасяне на слюнка върху селективна хранителна среда за микробиологично изследване
SALIVA TESTING

Микробиологично изследване на слюнката – пробите се инкубират за 48 часа
Отчитане на пробата чрез визуална скала (като брой колония образуващи единици – CFU)
КЛИНИЧЕН СЛУЧАЙ

Множествен кариеس, пародонтит и големи количества зъбен камък и плака; CFU>10^5
Почистването на максимален брой карисни лезии и премахването на зъбния камък и плака намаляват микробното число; CFU<10⁵
Краен резултат от началната терапия
<table>
<thead>
<tr>
<th>Substance</th>
<th>Short Form</th>
<th>Concentration (ng/ml)</th>
<th>Duration (h/days)</th>
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<tbody>
<tr>
<td>Amphetamone</td>
<td>AMP</td>
<td>50</td>
<td>24</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>mAMP</td>
<td>50</td>
<td>72</td>
</tr>
<tr>
<td>Marijuana</td>
<td>THC</td>
<td>12</td>
<td>3-10</td>
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<tr>
<td>Opiates</td>
<td>OPI</td>
<td>40</td>
<td>10</td>
</tr>
<tr>
<td>Cocaine</td>
<td>COC</td>
<td>20</td>
<td>48</td>
</tr>
<tr>
<td>Phencyclidene</td>
<td>PCP</td>
<td>40</td>
<td>10</td>
</tr>
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</table>
Co-morbidity important for the dental practice

The major reason for dentist to refuse treatment is the fear of infection with contagious diseases like HIV, HBV etc.
Immunological ELISA test for HIV, HCV и HBV status
The accuracy of saliva anti-HIV antibody testing has been demonstrated and both sensitivity and specificity was found to be 100%.

The accuracy of saliva anti-HIV antibody testing has been confirmed by many additional studies, leading to approval of this method by the U.S. Food & Drug Administration in 2004.
INTRAORAL TEST FOR HIV

Advance Awareness™
OraQuick® Rapid Antibody Test
ADVANCE HIV-1/2

Images showing the steps of an intraoral test process.

Images of OraQuick test devices with one showing a negative result and the other showing a positive result.
Други параклинични изследвания

- ЕОД
- ТОД
- Корозионен потенциал (>100 mV е патология)

*Lingua geographica* вследствие патогалванизъм
Microbiological tests

• Candidiasis
• Bacterial infections
Молекулярно-генетични методи – полимеразна верижна реакция (PCR)

Принципът на метода се състои в експоненциално намножаване (амплификация) на специфичен фрагмент ДНК, с използването на къси, изкуствено синтезирани олигонуклеотиди (10 – 30 нд), които се наричат праймери. Те се свързват специфично с определен участък от таргетната ДНК, което е необходимо условие за Taq-полимеразата за започване на синтезата на новата ДНК-верига. След начален етап на денатурация (термично разделяне на двете вериги от изследваната нативна ДНК) следва етап на хибридизация на праймерите и синтез на новата ДНК-верига. В следващия цикъл от реакциата, този новосинтезиран ДНК фрагмент ще послужи като матрица за синтез на нова верига ДНК. Процесът продължава 25 – 50 цикъла, което има като резултат генерирането на милиони молекули ДНК, идентични на целевата молекула.

PCR-базираните методи позволяват видова идентификация на 6-те най-често видове, причиняващи системна кандидоза. Навременното установяване на специфична за етиологичния агент ДНК позволява да се започне превантивна, специфична за конкретния причинител терапия, с която да се избегне развитието на системна инфекция.
Изследване на периферна кръвна картина и биохимичен профил в клинична лаборатория

• СУЕ

• Еритроцити и хемоглобин

• Промени в ДКК (левкопения, лимфоцитоза, моноцитоза, еозинофилия)

• Промени в протеинограмата (намалено количество общ белък и албумин и увеличен процент на глобулините)

• Биохимични изследвания (глюкоза, ензими, желязо, хормони)
Алергологични тестове

- Епикутанно тестване за алергия спрямо материали
- Контактно-алергичен лигавичен тест чрез небцова пластинка
ИЗСЛЕДВАНЕ ЗА АЛЕРГИИ!

“Prick”- тест
“Prick”- тест (отчита се след 20 минути)

СКАЛА ЗА ОТЧИТАНЕ ТЕНЖЕСТТА НА РЕАКЦИЯТА

+ умерена хиперемия (пробата е съмнителна)
++ мехур и оток с размери 2-3мм (слабо положителна реакция)
+++ мехур с големина до 5мм и хиперемия
++++ мехур с големина до 10мм и хиперемия
+++++ мехур с големина над 10мм и изразена обща реакция
1. RECORDING THE IDENTIFYING DATA
2. HISTORY AND PHYSICAL EXAMINATION
3. CHIEF COMPLAINT
4. PRESENT ILLNESS
5. PAST MEDICAL HISTORY
   - Family history
   - Social history
   - Occupational history
   - Dental history
6. REVIEW OF SYMPTOMS BY SYSTEM
7. PHYSICAL EXAMINATION
   - Radiologic examination
8. DIFFERENTIAL DIAGNOSIS
9. WORKING DIAGNOSIS
10. Medical laboratory studies
11. Dental laboratory studies
12. Biopsy
   - Incisional
   - Excisional
   - Fine-needle aspiration
   - Exfoliationg cytology
   - Toludine blue staining
13. Consultation
14. FINAL DIAGNOSIS
15. TREATMENT PLAN