Wanninayake M Tilakaratne
Thomas George Kallarakkal
Editors

Clinicopathological Correlation of Oral Diseases

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Foreword

This comprehensive textbook consisting of 66 chapters is an excellent reference source on oral diseases written by invited experts in the field. The book concisely addresses a range of topics comprehensively covering the curriculum in Oral Medicine, Oral Pathology, Oral Surgery and also includes the broader aspects of Cariology and Periodontology.

This book is unique in its coverage in a number of aspects. Each chapter starts with a guide to history taking based on a patient's complaint to explore the symptomatology of a large range of oral disorders. The reasoning behind the selection of key questions during history taking is explained to the reader, and based on the responses each chapter presents a differential diagnosis that leads to appropriate special investigations. Based on the findings the reader is taken through steps in decision making and is directed to a final diagnosis. This is followed by a comprehensive clinicopathological description of the disorder and the basic clinical management helpful to the clinician. For the practicing Oral Medicine and Oral Surgery specialists and trainees, additional information is included on staging of the disease, an update on the current opinion, and steps in surgical management. This book, in my opinion, will change the way how the readers will approach history taking in their clinical practice.

In the recent decade there has been some tremendous advances in our understanding of the biology and genetics of oral diseases. The molecular biology sections presented in some chapters in this textbook summarise the important achievements made on this rapidly expanding topic. These scientific advances are presented in a clear and understandable way that the reader would find it easy to grasp rather than having to grapple through journals or very extensive published literature.

I found the overall presentation of the book very pleasing. The individual chapters are presented in a reader friendly manner. The core information is presented in an easily accessible format that is ideally suited to student understanding and to help in revision when preparing for examinations. Each chapter is well illustrated with photographs, to convey to the reader clinical presentations and the intricate details from pathological processes to surgical techniques.

The contributors are well-known teachers in dental schools mostly from South and Southeast Asia, and this book has drawn them together in a unique collaboration to provide an all-encompassing review of the current state of knowledge on oral diseases. The textbook is edited by an eminent globally recognised academic in the field of Oral and Maxillofacial Pathology and Medicine together with another experienced academic colleague. Professor Wanninayake M Tilakaratne, former Dean of the Faculty of Dental Sciences, University of Peradeniya and currently Professor and Senior Consultant in Oral Pathology Faculty of Dentistry Universiti Malaya, is a world-renowned Professor who has contributed to teaching Oral Pathology in several universities including Queen Mary University and Guy's and St Thomas Hospitals in the United Kingdom. His in-depth knowledge from his widely published research in Oral Pathology and Medicine has indeed helped to raise the didactic standard of this textbook. Co-editor Associate Professor Thomas George Kallarakkal is a dedicated teacher and a researcher at the Universiti Malaya with years of experience in Oral Pathology and Medicine. He has recently contributed to the WHO book on Head and Neck Tumours. His areas of interest include verrucopapillary oral lesions, epithelial dysplasia, testing for HPV, and developing large databases for image analysis of high-risk oral lesions.

The book will appeal to a wide variety of readers including undergraduate students in dentistry, general dentists, and primary care practitioners. I would also especially recommend this book to higher trainees who are seeking specialisation in Oral Medicine, Oral Pathology, Maxillofacial Surgery, and other branches of dentistry.

With very best wishes!

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20 March 2023

Preface

Clinicopathological Correlation of Oral Diseases is a book aimed at undergraduates, early-stage postgraduates, and practitioners. This book differs from most conventional clinical textbooks at present in many aspects. Clinicopathological correlation is the most widely accepted concept in teaching clinical students on how to arrive at a rational and accurate diagnosis.

The book discusses case-based scenarios, which help in case-based learning and clinical reasoning. Every chapter consists of a detailed approach to the definitive diagnosis of a given disease starting from history taking, clinical examination, and investigations. A detailed account is included in each chapter as a justification for differential diagnosis and necessary investigations. Moreover, a well-designed format of asking questions in order to gather information about a patient's history and examination findings has been proposed in each chapter. A detailed and up-to-date account on each specific disease is described after the section featuring a case-based scenario in every chapter. Salient features of the disease are embedded in a table for easy reference and understanding. One of the unique features in the book is the inclusion of a diagnostic and management algorithm, which imparts a broader knowledge to the reader on related entities to a particular disease and the ways in which they can be differentiated from each other. Finally, a self-assessment exercise is included, covering all major aspects of the disease.

We as editors hope that the novel approach we have tried to introduce will help the readership to improve diagnostic skills in oral and maxillofacial diseases. We would like to extend our gratitude to all contributors for accepting our invitation with generosity. Special thanks are due to Dr. Goh Yet Ching and Dr. Nur Fauziani Binti Zainul Abidin for the help extended in providing histopathological pictures. In addition, we would like to thank all our friends and family members for their help and constructive comments.

This book is planned to be published as part of the Golden Jubilee celebrations of the Faculty of Dentistry, Universiti Malaya, Kuala Lumpur, Malaysia.

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Introduction

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Guide to Diagnose Oral Lesions: Principles of Clinicopathological Approach

Thomas George Kallarakkal and Wanninayake M Tilakaratne

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Learning Goals

1. Devise the correct way of compiling the history with appropriate questions.
2. Deduce appropriate procedures in clinical examination.
3. Justify the relevant investigations required to arrive at the diagnosis.
4. Comprehend the importance of clinicopathological correlation in arriving at the correct diagnosis.

A clinician when encountering a patient with oral and maxillofacial disease is faced with vast amount of information pertaining to the patient's chief complaint, personal and medical history. The formulation of a provisional diagnosis or a differential diagnosis is one of the most critical and intellectually challenging aspects of medical reasoning. The clinician must be able to judiciously compare the probabilities of various diseases that could have caused the patient's signs and symptoms using his/her vast knowledge of oral health and disease.

Clinicopathological correlation is a thought process that combines clinical information and findings from microscopic examination of biopsy specimens together with findings from other investigations. It helps to confirm clinical suspicions and provide more information in uncertain clinical cases. Many a time, histopathological examination may not suffice to arrive at a definitive diagnosis but requires correlation with the patient's chief complaint, pertinent clinical examination findings and findings from other relevant ancillary tests such as imaging studies, haemtological, serological and biochemical investigations. In this perspective, a better understanding of the disease, its definitive diagnosis and most importantly, proper and correct management of the patient is not compromised.

Diagnosis is the process of identifying a disease process from its signs and symptoms and other relevant investigations. It requires acquisition of data about the patient and their presenting complaint through observation, hearing, touching and sometimes smelling. In the present age, patients have access to a wide variety of sources of information on health care. This may be used by them for self-diagnosis or to demand a specific treatment. The clinician must be able to allay their concerns and initiate optimal scientific and evidence-based treatment. A correct diagnosis facilitates appropriate and effective treatment as well as prognostication. The diagnostic process comprises three main components:

1. History taking: A thorough history taking usually provides the diagnosis in 80% of the cases.
2. Physical examination.
3. Investigations which may be essential to validate the history and examination findings.

1.1 History Taking

The initial contact with the patient is crucial in establishing good communication between the patient and the clinician. The clinician should be courteous and professional in his approach and should ensure that the patient is the focus of attention. History taking needs to be designed to suit the individual patient. Patients may differ from one another with some being articulate while the others may be nervous or confused. It is very essential to build a good rapport with the patients to elicit useful information. This can be initiated by posing open-ended questions (those questions which do not suggest an answer) to the patient that allows them to open-up and speak at length, thereby helping them to gain some confidence. The clinician should be careful to avoid unwanted use of medical jargon and leading questions (those questions which suggest the answer) that may compel the patients to agree with the clinician. Questions seeking relevant social or psychological history and information on embarrassing medical conditions can be delayed until the patient has gained enough confidence to reveal everything unconditionally to the clinician. The patient should be encouraged to tell their story in their own words, and when required, methodical questioning should be employed to elicit more information. The clinician will be able to assess the psychological status and the patient's expectation from the consultation and the treatment during the history taking. It is important to gauge demographic information such as age, gender and ethnicity of the patient. Certain disease states such as degenerative joint diseases involving the temporomandibular joint tend to occur more commonly in the elderly while mucocutaneous disorders such as lichen planus have a predilection for female patients.

The history of the presenting complaint which is recorded in the patient's own words should describe the state of health before the occurrence of the present complaint, the duration of the symptoms, any aggravating or relieving factors and any change in the course of the symptoms over the period of time. Any previous treatment that the patient has had should be detailed. A lack of response to a specific treatment in the past may prompt the diagnosis to be revisited. The patient's medical history will help to understand whether the patient's presenting complaint is an oral manifestation of an underlying systemic disease. Similarly, adequate knowledge regarding the patient's medical history is crucial as it may influence the patient's dental or surgical treatment. A detailed dental history provides comprehensive information on the dental treatment that the patient has had previously. Inappropriate dental treatments in the past such as an ill-fitting denture or a faulty restoration with high bite

may result in pain. A lack of timely dental intervention in the past could have aggravated a carious process eventually resulting in pulpal inflammation or necrosis with resultant severe pulpal pain. A comprehensive subjective review of systems (ROS) (Table 1.1) will help gather information on diseases affecting the different body systems which could either affect the dental treatment or may be a clue to the presenting oral manifestations.

Questions pertaining to the family history will uncover any hereditary disorders such as haemophilia or amelogenesis imperfecta that have a recessive pattern of inheritance. Details of the patient's social history will reveal whether the patient has a partner or a family and the extent of support that can be anticipated as it will influence the implementation of a treatment regimen. Information on patient's habits and sexual history is relevant to the diagnosis of specific oral mucosal lesions.

Table 1.1 Subjective symptoms associated with different body systems

Body systems/ organs	Symptoms
General	Fever, weight loss
Eyes	Changes in vision, photophobia, blurring of vision
Ears	Hearing changes, tinnitus, vertigo
Psychiatric disorders	Changes in mood or sleep pattern, emotional disturbances, anxiety, depression
Skin	Rashes, pruritus, vesicles, bullae
Nervous system	Sensory changes, seizures, unilateral or bilateral weakness, changes in coordination and memory
Respiratory system	Cough, dyspnea, wheezing, chest pain
Cardiovascular system	Chest pain, dyspnea, orthopnea, oedema
Gastrointestinal system	Changes in appetite, constipation, diarrhea, bloating, melena, abdominal pain, hematemesis
Genitourinary system	Changes in urinary frequency or urgency, dysuria, hematuria, nocturia, incontinence
Endocrine system	Skin or mucosal pigmentations, polyuria, polydipsia, polyphagia, temperature intolerance
Musculoskeletal system	Muscle and joint pain, deformities, joint swellings, spasms, changes in range of motion
Circulatory system	Easy bruising, epistaxis, spontaneous gingival bleeding, increased bleeding after trauma
Lymphatic system	Swollen and enlarged lymph nodes

1.2 Clinical Examination

A thorough history and clinical examination will facilitate the clinician to make a provisional diagnosis or a differential diagnosis. The clinician should be able to determine if the patient has any physical difficulties such as abnormal gait, or learning disability as soon as the patient enters the clinic and is greeted by the clinician. Other disabilities such as blindness, deafness, speech or language disorders as well as the patient's mood and general well-being will also be evident. A general examination includes recording of the patient's body weight and vital signs. The vital signs include:

1. Conscious state: An alteration in the conscious state may be a reflection of a head injury or drug abuse.
2. Temperature: The normal body temperature is 36.6 °C (oral). An adult with an oral temperature above 37.8 °C is pyrexic. The fever may be caused due to an underlying infection (bacteria/viral), inflammatory conditions (rheumatoid arthritis) and malignancy besides other causes.
3. Pulse: The normal reference range for pulse rate is 60–80 beats/min in an adult and is elevated due to exercise, anxiety, fever, cardiac disorders and hyperthyroidism among many other factors. Any change in the rhythm, character and the volume of the pulse should be brought to the attention of a medical physician.
4. Blood pressure: The normal systolic/diastolic blood pressure is 120/80 mm of Hg. The blood pressure may be elevated in health conditions such as cardiovascular disease, kidney disease, adrenal disorders and thyroid disease. Several factors including stress, obesity, smoking, excess intake of alcohol, increased salt in the diet, old age and family history can contribute to an elevated blood pressure.
5. Respiration: A reference range of 12–20 breaths/min is considered a normal respiratory rate in an adult. Tachypnea may be caused to several pathological states including asthma, chronic obstructive pulmonary disease (COPD), heart failure and anaemia.

Extra oral examination of the face and the neck can determine whether the patient has anaemia (pallor of the skin and palpebral conjunctiva), jaundice (yellowish sclera), thyroid disease (exophthalmos) and lymphadenopathy. Swellings due to inflammatory or neoplastic disorders and malar rash indicative of lupus erythematosus will be easily apparent. The parotid and submandibular salivary glands and the lymph nodes in the neck should

be palpated. Lymphadenopathy is a common manifestation of infection or a lymphoreticular malignancy. The character (site, size, shape, consistency and tenderness) of the enlarged lymph nodes should be recorded. Evaluation of the temporomandibular joint (TMJ) involves examination for any facial asymmetry indicative of masseteric hypertrophy suggestive of bruxism, mandibular opening and closing paths (straight/corrected deviation/uncorrected deviation), range of mandibular movements (open movements/lateral excursions/protrusive movements), joint noises (click/crepitus) during opening and closing and joint locking. The TMJ and the muscles of mastication should be palpated. The pain induced in the joint and the muscles due to palpation is a classical clinical test to determine if the induced pain replicates the patient's chief complaint of pain if any. Maxillary sinuses should be palpated for tenderness over the maxillary antrum to exclude any sinus infections. The cranial nerves particularly the trigeminal nerve and the facial nerve that guide the facial movement and sensation from the face should be examined for defective function (Table 1.2).

Table 1.2 Signs indicative of defective function of the cranial nerves

Cranial nerve	Signs indicative of defective function
I. Olfactory	Impaired sense of smell for common odours
II. Optic	Visual acuity determined using a hand-held eye chart or a Snellen chart is impaired Visual fields determined by confrontation using the examiner's finger or coloured pen are impaired Pupil responses are impaired
III. Oculomotor	Diplopia (double vision) Strabismus (eye looks down and laterally) Ptosis (drooping of eyelid) Pupil dilated Pupillary reactions: Direct reflex (constriction that occurs when the pupil is exposed to light) is impaired Indirect reflex/consensual reflex (simultaneous constriction of the opposite pupil that occurs when the pupil is exposed to light) is impaired
IV. Trochlear	Diplopia (double vision) Strabismus (eye looks down and laterally) Patients with defective trochlear nerve function will have normal pupillary reactions and not have ptosis contrary to patients with defective oculomotor nerve function
V. Trigeminal	Reduced sensation over the face Impaired corneal reflex Impaired taste sensation Reduced motor power of masticatory muscles Weakness on opening of jaw
VI. Abducens	Diplopia (double vision) Strabismus (eye looks down and laterally) Lateral eye movements impaired to the affected side
VII. Facial	Flattening of the nasolabial groove Impaired motor power of facial muscles (inability to smile, blow-out cheeks, show the teeth) Impaired corneal reflex Impaired taste perception
VIII. Vestibulocochlear	Impaired hearing Impaired balance Nystagmus (an involuntary rhythmic side-to-side, up and down or circular motion of the eyes) Tinnitus
IX. Glossopharyngeal	Reduced gag reflex Deviation of the uvula Reduced taste sensation Voice may have a nasal tone
X. Vagus	Reduced gag reflex Voice may be impaired
XI. Accessory	Impaired motor power of trapezius and sternocleidomastoid muscle
XII. Hypoglossal	Impaired motor power of the tongue Abnormal speech Ipsilateral deviation on protrusion

The muscles of facial expression are innervated by the facial nerve. A lower motor neuron lesion involving the facial nerve results in Bell's palsy characterized by paresis/paralysis of all the ipsilateral muscles. Bell's palsy and stroke are the most common causes of abrupt onset of unilateral facial weakness. The clinical presentation of patients with orofacial pain (OFP) is usually complex and may be driven by many factors. The patients may be well or may have significant comorbidities that may be psychological or related to other medical problems. A clinician consulting a patient with OFP should have excellent communication skills as the pain is invisible, and a diagnosis is based upon what the patients communicate with the clinician. A thorough pain history (Table 1.3) is a cornerstone in establishing a diagnosis in patients with OFP.

Examination of the lips is useful to assess cyanosis which is seen in cardiac or respiratory disease. Angular chelitis is observed very commonly in oral candidiasis, iron or vitamin deficiency disorders. Intraoral examination should be performed only with a good light source, mouth mirrors and compressed air for drying the teeth. If the patient is wearing any removable prostheses or appliances, it should be removed first to ensure that all the areas are thoroughly visualized. The fit, function and the relationship of the prosthesis to any lesion if present should be assessed. Evidence of oral dryness as observed by sticking of the mouth mirror to the oral mucosa, absence of normal saliva pooling in the floor of the mouth, presence of lipstick stains on the anterior teeth and food residues on the teeth suggest reduced secretory function of the salivary glands. The soft tissues of the mouth should be examined first in a systematic manner to include all the areas. The floor of the mouth, soft palate and tonsillar areas are high-risk sites for oral squamous cell carcinoma and should not be missed during the examination. The tongue should be held in a piece of gauze and extended from side to side to enable better visualization of the lateral tongue and posterior floor of the mouth. Suspicious areas should be palpated to check for the presence of any induration. The opening of the salivary ducts and the patency of the ducts should be assessed by checking the flow of saliva through the ducts. Dental examination should encompass the status of the periodontal health, caries and restorative state of all the teeth present in the mouth. Teeth vitality must be checked if they are symptomatic and if they are located in the region of jaw swellings or radiolucent jaw lesions.

Table 1.3 SOCRATES—mnemonic for pain assessment

Site—Where is the pain? Or the maximal site of the pain.
Onset—When did the pain start, and was it sudden or gradual? (State whether it is progressive or regressive.)
Character—What is the pain like? An ache? Stabbing?
Radiation—Does the pain radiate anywhere?
Associations–Any other signs or symptoms associated with the pain?
Time course—Does the pain follow any pattern?
Exacerbating/Relieving factors—Does anything change the pain?
Severity—How bad is the pain?

Lumps and swellings are relatively common in the mouth. They may be developmental, inflammatory, traumatic or neoplastic in origin. They may also be caused due to drugs, hormonal imbalances or may be a manifestation of specific disorders such as fibro-osseous lesions. The important features to be assessed when making a provisional diagnosis of a swelling are summarized in Table 1.4.

Oral ulcers may arise as a result of local or systemic factors and are generally very painful. They can be broadly classified into acute and chronic ulcers. Acute oral ulcers have an abrupt onset and persist for a short duration. The more common acute oral ulcers include traumatic ulcers, recurrent aphthous stomatitis and ulcers due to viral infections. It is generally agreed that an ulcer which persists for more than 2 weeks is a chronic ulcer. Examples of chronic ulcers are drug-induced ulcers, ulcers due to altered immunity as seen in pemphigus vulgaris, mucous membrane pemphigoid and erosive oral lichen planus. A persistent ulcer that shows no evidence of healing could be highly suspicious of a mucosal malignancy such as squamous cell carcinoma. Vital information that is essential when making a diagnosis of an oral ulcer is whether the ulcers are a) acute or chronic, b) primary or recurrent and c) single or multiple. Features that need to be assessed during examination of an ulcer are summarized in Table 1.5.

The diagnosis and the optimal treatment plan may be deduced from the history and examination findings. Very often, there are various possible diagnoses which should be recorded in their order of probability based on their prevalence and likelihood of causing the signs and symptoms. The types of diagnosis include:

Clinical diagnosis: made from the history and examination.

Provisional diagnosis: an initial diagnosis from which further investigations need to be planned.

Differential diagnosis: the process of making a diagnosis by considering the similarities and differences between similar conditions.

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Table 1.4 Important features to be assessed in reviewing a swelling

Feature
Duration—Reactive lesions such as mucoceles and swellings due to infections arise rapidly within a few days. Benign tumours grow slowly and may be present for many years, while malignant tumours grow rapidly within a period of months
Alteration in size—A mucocele may increase and decrease in size over time, while benign and malignant neoplasms usually do not decrease in size
Position—The anatomical position and the proximity to adjacent structures should be recorded Midline lesions —are usually developmental in origin (e.g. torus palatinius) Bilateral lesions —are usually benign (e.g. dialysis) Unilateral lesions—tend to be neoplastic in nature
Size: The size should always be measured and recorded
Shape—Some swellings have a characteristic shape. A parotid swelling usually fills the space between the posterior border of the mandible and the mastoid process
Colour—The colour of the lesion reflects the content of the swelling. A haemagioma may appear purple or red due to the vascularity of the lesion. A naevus or a melanoma usually appears brown or black due to the presence of the melanin pigment in the lesion
Temperature—Inflammatory swellings such as abscesses are warm to touch
Tenderness—Inflammatory swellings are tender
Mobility—Neoplastic swellings tend to be fixed to the underlying structures or the overlying skin or mucosa
Consistency—They may be soft and fluctuant, firm or stony hard in consistency. Fluctuant swellings contain fluid, while stony hard or indurated swellings are highly suggestive of a malignancy or a lesion with hard tissue formation
Surface texture—The surface characteristics should be recorded. Papillomas have a warty or papillary surface. Malignant neoplasms tend to have a nodular or verrucous surface and may show surface ulceration
Margins—Malignant swellings have ill-defined margins, while benign swellings have clearly defined margins
Number—Multiple swellings are suggestive of an infective or developmental origin. Specific syndromes may have multiple similar swellings

Table 1.5 Important features to be assessed during the examination of an ulcer

Inspection findings:
Site
Size (Extent)
Tender/painful
Margin (Shape)—Regular/irregular
Edge: Sloping (healing ulcer)/punched out (trophic ulcer)/undermined (tuberculous ulcer)/rolled-out (basal cell carcinoma)/everted (squamous cell carcinoma)
Floor—Healthy/granulation tissue (healing ulcer)/slough (necrotic tissue—non-healing ulcer)
Discharge—Serous/serosanguinous/purulent
Palpation findings:
Margin/edge
Base—Marked induration at the base of the ulcer is a characteristic feature of squamous cell carcinoma

1.3 Investigations

Investigations are intended to determine specific answers regarding a probable diagnosis. They should not be employed as a routine procedure. Prior to ordering the investigations, the clinician should explain to the patient: a) the nature of the investigation, b) the potential benefits and possible adverse effects associated with the investigation and c) the implications of not carrying out the investigation. A witnessed and informed consent should be obtained for all invasive procedures. Strict infection control protocols should be in place prior to the procedure as all body fluids are considered potentially infectious. Certain lesions such as a pyogenic granuloma, which manifests as a gingival overgrowth, will need only a biopsy and histopathological examination to determine the diagnosis. There are other disease conditions such as Paget disease of bone which will require a corroboration of imaging, serological and histopathological investigations to determine the definitive diagnosis.

1.4 Imaging

Imaging techniques most commonly employed in the head and neck region are plain radiography, computerized tomography (CT), cone beam computerized tomography (CBCT), magnetic resonance imaging (MRI) and ultrasound. The clinician ordering the imaging investigation should be able to justify the need for the investigation due to the cumulative effect of radiation hazard. A formal radiologist's report should always be requested when the radiographic features appear unusual or beyond the comprehension of a clinician. The imaging modality and their specific applications are detailed in Table 1.6.

Table 1.6 Imaging modalities and their specific applications

Imaging modality	Applications
Intraoral radiography	
Periapical radiograph	• To demonstrate any pathology in the tooth (dental caries), periapical region (such as a granuloma and cyst), periodontium and adjacent bone
Bitewing radiograph	• To reveal any approximal caries and for reviewing the alveolar bone crest
Occlusal radiograph	• To review the facial and lingual bony cortices and adjacent areas such as floor of the mouth and palate
Extraoral radiography	
Dental panoramic tomography	• Valuable for a general full mouth survey including review of the antra and the temporomandibular joint • The radiation dose is significantly lower than a full mouth survey using intraoral periapical films
Sialography	• To assess patients with hyposalivation and salivary gland swelling • To detect salivary gland ductal obstruction • To detect developmental salivary gland disorders such as aplasia
Salivary scintigraphy	• To diagnose patients with salivary gland disorders such as Sjogren syndrome, salivary gland neoplasms, ductal obstruction and aplasia
Arthrography	• To assess patients with suspected internal derangements of the temporomandibular joint
Angiography	• To diagnose vascular anomalies and tumours • To assist in surgical procedures (microvascular surgery or embolization)
Computed axial tomography (CAT/CT)	• To visualize head and neck areas inaccessible to conventional radiographs • To clearly visualize hard tissue lesions • To determine tumour spread • To exclude intracranial or cranial base pathologies • To plan surgery and implant placement
Cone beam CT (CBCT)	• Similar to CT for imaging of jaws and related structures, but the scanning time and radiation dosage are significantly lower than a conventional CT.
Positron emission tomography (PET)	• To detect second primary tumours and metastasis. This is facilitated by mapping tissue metabolic activity based either on blood flow or glucose utilization.
Magnetic resonance imaging (MRI)	• To visualize soft tissues and lesions • To detect bone invasion • To review the temporomandibular joints
Ultrasound scanning (US)	• To review soft tissues including subcutaneous tissues, tendons, muscles, vessels and internal organs such lymph nodes and salivary glands

1.5 Histopathology

Biopsy and histopathological examination are critical for a definitive diagnosis of diseases of the mucosa, soft tissue and bone. Biopsy involves the removal and examination of a part (incisional biopsy) or whole of the lesion (excisional biopsy). An ideal incisional biopsy should be of sufficient size (10 mm × 5 mm × 4 mm) to provide enough information about the lesion and should include the lesional and peri-lesional tissue. For ulcerated lesions, much of the relevant information is obtained from the peri-lesional tissue as the lesion is often entirely denuded off the epithelium. Care should be taken in handling the soft tissues to avoid any crush artefacts that may be caused due to inadvertent squeezing of the tissues. The tissues for histopathological examination should be immediately fixed preferably in tenfold volume of buffered formalin or other fixatives at room temperature. Indications for a biopsy are summarized in Table 1.7.

Fine needle aspiration (FNA) biopsy is a process where a 21-gauge needle is inserted into the lesion and the aspirated cells are smeared on a slide. FNA biopsy does not always provide a definitive diagnosis but provides reliable information to differentiate benign from malignant neoplasms, determine the need for further investigations or initiate treatment. It is usually indicated for lymph node swellings, parotid gland tumours and deep-seated swellings. There are relatively less complications related to the procedure as the small-size needle does not cause any damage to the vital structures of the head and neck. However, the interpretation of the FNA biopsy requires thorough experience.

Table 1.7 Indications for biopsy

Persistent soft or hard tissue lesions that do not respond to treatment
Persistent soft or hard tissue lesions of uncertain origin
Lesions that cause extreme concern to the patient such as a persistent lump or a red/white/pigmented lesion that is increasing in size
Lesions suspicious of a malignancy
Oral potentially malignant disorders such as leukoplakia, erythroplakia and lichen planus
To confirm the clinical diagnosis of conditions such as Sjogren syndrome
Non-healing ulcers and extraction sockets

1.6 Exfoliative Cytology

This is a process that involves the examination of cells scraped from the surface of a lesion. The process is relatively easy and is primarily useful for detecting candidal hyphae, virally damaged cells and acantholytic cells from vesiculobullous diseases such as pemphigus. A major disadvantage of exfoliative cytology is that it samples only the surface cells, while the deeper tissues cannot be assessed and hence, unreliable for diagnosing epithelial dysplasia or cancer.

1.7 Brush Biopsy

This technique utilizes a stiff-bristle brush to collect cells from the surface and the deeper layers by scraping. It is a non-invasive procedure that is relatively painless. The cells obtained are smeared on to a microscopic slide and are screened either manually or using an image analyser to identify the abnormal cells.

1.8 Molecular Tests

Molecular diagnostics are extremely useful for identification of genetic abnormalities and for rapid identification of bacteria and viruses. Malignant neoplasms which harbour characteristic genetic alterations can be detected by cytogenetics, polymerase chain reaction (PCR) or fluorescence in situ hybridization (FISH). The diagnosis of lymphomas is greatly aided with the use of molecular techniques which is otherwise difficult with conventional histopathology and immunohistochemistry (IHC). Specimens for immunofluorescence should not be fixed in formalin but should be sent to the laboratory for freezing or snap frozen on solid carbon dioxide or liquid nitrogen and sent to the laboratory within an hour. Vesiculobullous disorders such as pemphigus and mucous membrane pemphigoid are diagnosed by a direct immunofluorescence (DIF) test. It detects the presence of immune deposits (autoantibodies and/or complement) in the tissues. A fluorescein stain which fluoresces apple green under ultraviolet light is utilized for the DIF test. Indirect immunofluorescence test which