

The Oral Biopsy: Indications, Techniques and Special Considerations

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Introduction

Accurate diagnosis and treatment of oral disease is an essential component of the patient's comprehensive dental care and the foundation of high-quality dentistry. Inaccurate diagnosis or failure to diagnose oral disease may have profound implications for both the patient and the clinician. A wide array of procedures and techniques is available to assist in the diagnosis of oral disease. Every patient should receive a thorough head and neck examination and appropriate dental radiographs. The clinical and radiographic examinations may provide sufficient information for the diagnosis of certain entities. However, many diseases of the mucosa, other soft tissue and bone require additional information to make a precise diagnosis. This information in many instances may be provided by biopsy and submission of tissue for histopathologic examination. The purpose of this paper is to outline the indications for oral biopsy and other allied techniques and the procedures that will help ensure accurate diagnosis.

Biopsy Indications: Soft Tissue Lesions

For any unknown lesion or condition of the oral mucosa, a scalpel biopsy is the gold standard

for diagnosis. When recognizing tissue abnormalities, the clinician must first attempt to determine the etiology. Evidence of traumatic injury or signs and symptoms of infection (e.g. candidiasis, herpes simplex) may provide the clinician with sufficient information to arrive at a provisional diagnosis. In these cases, the clinician may choose to provide treatment and to monitor the lesion for a period of 1-2 weeks for resolution. Alternatively lesions determined to be self-healing and not requiring any treatment (except palliative therapy) may be followed-up. **After a 2-week period, any remaining abnormality or any lesion that proves refractory to local therapy is indicated for biopsy.**

Leukoplakia, erythroplakia and persistent or widespread ulcerations necessitate biopsy. Persistent changes in color or any new growth noted on examination should also be considered for biopsy. Many submucosal lesions have no diagnostic color or surface changes, and these lesions are rarely distinguishable by palpation alone. For these, biopsy is indicated, especially if recent change in size or symptoms is reported. **No matter how confident the clinician may be with their clinical diagnosis, any tissue removed from a patient should be submitted for histopathologic examination.**

Biopsy Indications: Hard Tissue Lesions

Few bony abnormalities can be accurately diagnosed based on their radiographic features. Idiopathic osteosclerosis, condensing osteitis and cemento-osseous dysplasia are conditions that are radiographically unique, and the expertise of the clinician in diagnosing these conditions using radiographs is paramount.

Most bony lesions cannot be diagnosed exclusively based on their radiographic appearance. Confirmatory diagnosis requires a biopsy and microscopic examination. Periapical inflammatory lesions and intrabony cysts and tumors show radiographic changes that are indefinite beyond a presumptive clinical diagnosis. Given the differences in treatment and prognosis for many of these entities, identification of these lesions mandates biopsy. Further treatment, if necessary, will then be dictated by the definitive histopathologic diagnosis. We have reported twice in this journal on periapical/periodontal inflammatory lesions that upon biopsy and microscopic examination revealed a metastatic breast carcinoma in one and Langerhans cell histiocytosis in the second.^{1,2}

Clinical and radiographic signs and symptoms of bony pathology can

Figure 1



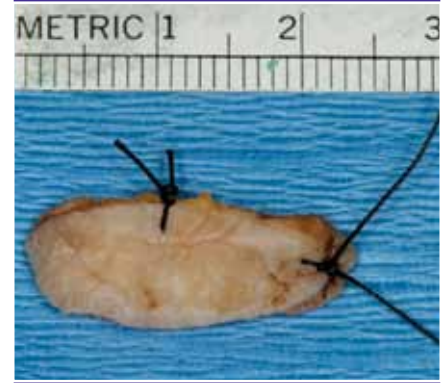
Labeled container of 10% neutral buffered formalin for fixation and transport of routine biopsy specimen.

Figure 2



Labeled container of Michel's solution for transporting tissue for direct immunofluorescence.

Figure 3



An excisional biopsy specimen indicating orientation margins with long and short length sutures.

also alert the clinician to the necessity of biopsy. Rapid bone loss, irregular widening of the periodontal ligament, spiking root resorption and tooth mobility in the absence of trauma or an identifiable source of inflammation is often an ominous sign and should be evaluated carefully. Expansion, pain and paresthesia are some other features of hard tissue lesions that would warrant biopsy and histopathologic examination.

Intraoral Biopsy Techniques

An adequate and appropriate tissue sample is critical when obtaining a biopsy. The clinician should strive to remove a reasonably large, intact specimen without causing significant patient morbidity. Specimens that are too small or of inadequate depth may be insufficient for accurate microscopic interpretation and are often difficult to orient properly for sectioning and mounting on a slide. Fragmented specimens create similar difficulties. A mucosal biopsy should be of adequate depth to include the entire layer of epithelium and a portion of the underlying connective tissue.

Of further importance is the instrumentation used in the acquisition of the tissue sample. In order to provide an optimal tissue sample with minimal distortion, a scalpel biopsy is preferable. Heat produced by lasers and electrocautery often distorts the tissue, making diagnosis difficult. It is best

to remove lesions by scalpel, reserving laser or other cautery instruments to control bleeding after the specimen has been obtained. Excessive tissue clamping with forceps may also distort or crush tissue specimens.

A frequent question is whether an incisional or excisional biopsy is indicated. Incisional biopsies sample only a portion of the lesion to establish a diagnosis prior to treatment. This is most appropriate for large lesions where complete surgical removal is impractical. If the lesion is ulcerated, the clinician should strive to include a portion of the adjacent intact epithelium in the specimen. For extensive lesions, sampling of multiple areas is recommended to ensure accurate assessment. A large leukoplakic or erythroplakic patch may demonstrate moderate epithelial dysplasia in one area and a frank, invasive squamous cell carcinoma in an adjoining area.

Incisional biopsy is also indicated for suspected autoimmune disorders such as pemphigus vulgaris. These tissue samples should be submitted for routine histopathologic examination as well as direct immunofluorescence studies. Care must be taken to sample perilesional tissue, with abundant epithelium. If epithelium is lacking or separated from the underlying connective tissue, interpretation and diagnosis are impossible. In this context, any steroid therapy

should be reserved until after the biopsy as presurgical steroid use may alter the histopathologic and direct immunofluorescence findings altogether, rendering the biopsy procedure useless.

Excisional biopsy involves complete removal of the lesional tissue. This is most appropriate for small, accessible lesions that are easily amenable to surgery (e.g. mucocele, pyogenic granuloma and irritation fibroma). Excision of mucoceles must include the few lobules of minor mucous glands that drain into the mucocele. This minimizes the recurrence potential of these lesions.

Specimen Preparation, Placement, and Orientation:

When a biopsy specimen is taken from the oral cavity, immediate immersion into a fixative is imperative. Inadequate fixation results in tissue degeneration, causing difficulty in interpretation. The fixative most commonly used for routine biopsies is 10% neutral buffered formalin (Fig.1). For suspected autoimmune or vesiculobullous disorders, two tissue samples should be submitted: one in formalin for routine microscopy and the other in Michel's solution for direct immunofluorescence (Fig.2). Immunofluorescence studies cannot be performed on tissue submitted in formalin.

All biopsy containers must be appropriately labeled to identify the

patient and the anatomic site if more than one specimen is submitted. Furthermore, a complete and thorough description of the lesion should be provided. Often, a histopathologic diagnosis is based on the provision of accurate clinical information. For example, the histology of a dentigerous cyst is non-specific and in the presence of some inflammation may simulate a periapical cyst. However, in the presence of accurate clinical and radiographic information (radiolucency around the crown of an impacted tooth #17), the diagnosis of a dentigerous cyst is confidently made.

Clinicians may desire to know if a lesion has been adequately excised. It is possible to assess adequacy of removal if the tissue sample is firstly removed in one piece. Adequacy of clear margins may be screened for if the tissue is appropriately tagged with sutures. At least two adjoining margins must be clearly identified to ensure correct orientation once the specimen is received in the laboratory. For example, a short suture may indicate the anterior aspect of a biopsy specimen, with a longer suture indicating the superior aspect (**Fig.3**). Or, the clinician may mark the specimen with one suture at one site and two sutures at another site. After suture placement, the significance of each must be clearly indicated on the history sheet. By providing this information to the pathologist, it is possible to assess anterior, posterior, superior and inferior margins (or medial and lateral, depending on the biopsy site), allowing for the identification of areas that might require further excision. Adequacy of removal may be impossible to interpret if the specimen is fragmented.

Mucosal biopsies that are superficial and that typically do not include underlying muscle tissue tend to curl and distort. This creates some difficulty in proper measurement and orientation of the specimen for tissue processing. This may be overcome by immediately following the biopsy with spreading the specimen flat onto a piece of stiff card paper or plastic prior to dropping it (mounted on the stiff paper or plastic) into the formalin fixative.

Other Diagnostic Methods

In recent years, a number of new diagnostic adjuncts have been introduced. These techniques, which include cytologic sampling and illumination devices, are designed strictly as screening tools for the assessment of suspected premalignant and malignant mucosal lesions. They are not substitutes for a scalpel biopsy. Furthermore, given the significant potential for false positive results, their findings should be interpreted with caution.^{3,4}

Exfoliative cytology may be a useful diagnostic tool in clinical practice. This technique harvests mucosal cells by means of brushing or scraping, which are then examined microscopically. Suspected cases of candidiasis can be rapidly confirmed through oral cytology. In addition, herpetic lesions sampled within the first 72 hours of appearance will often show diagnostic cytologic features. Lesions of pemphigus vulgaris may show the characteristic Tzanck cells. However, cytology is not a substitute for scalpel biopsy and direct immunofluorescence in the diagnosis of pemphigus vulgaris.

The utility of oral cytology in the diagnosis or screening of suspected premalignant or malignant lesions is limited. Sampling error frequently results in specimens of little diagnostic value.^{3,4} For lesions that are suspicious for malignancy or premalignancy, or for clinical changes of undetermined significance, a biopsy should be performed as soon as clinically feasible.

Conclusion

Ultimately, the screening tool of greatest benefit is careful oral examination and sound clinical judgment. The clinician's knowledge and training may eliminate the need for biopsy in cases where lesions are clinically definable. For entities of uncertain significance or etiology, a biopsy provides the simplest and most rapid means of obtaining the definitive diagnosis. In the interest of the patient's well-being, accurate diagnosis is of utmost importance. When in doubt, one can never go wrong with a biopsy-proven diagnosis. Finally, it would be prudent that a biopsy log be

maintained and a fail-safe mechanism be ensured that each patient be informed of the result of their biopsy. The log may also be used to record the action taken in response to the result.



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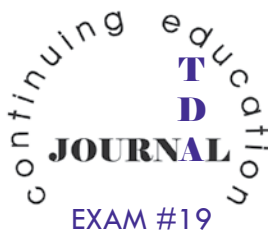
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Questions for Continuing Education Article - CE Exam #19

- For any unknown lesion or condition of the oral mucosa, the gold-standard for diagnosis is:
 - a radiograph
 - an MRI
 - a scalpel biopsy
 - a post-mortem
- A clinician should biopsy an unknown lesion that does not respond to treatment in:
 - a month
 - a year
 - two weeks
 - six weeks
- Lesions exhibiting the following conditions should be biopsied:
 - Leukoplakia
 - Erythoplakia
 - Persistent ulceration
 - All the above
- Unknown submucosal lesions that have no diagnostic color or surface changes should:
 - undergo a scalpel biopsy
 - be treated with silver nitrate
 - have a needle biopsy
 - no biopsy is necessary
- All tissue removed from a patient should be:
 - properly submitted for histopathologic examination
 - discarded in a biohazard container placed in isopropyl alcohol
 - incinerated
 - placed on ice
- Most bony lesions cannot be diagnosed based on their:
 - radiographic features alone
 - pain profile and histopathology
 - cortical expansion and histopathology
 - all the above
- Hard tissue lesions that warrant biopsy and histopathologic examination are:
 - Expansive
 - Painful
 - Those producing paresthesia
 - All the above
- Specimens that are difficult to orient properly for sectioning are those which:
 - are too small
 - are fragmented
 - are of inadequate depth
 - all the above
- The best instrumentation for acquisition of tissue samples is:
 - a scalpel biopsy
 - by laser
 - by electrocautery
 - by hi-volume suction
- When a biopsy is taken from the oral cavity, what is imperative:
 - immediate immersion into a proper fixative
 - placed on ice
 - placed on a 2 X 2 gauze square (filled)
 - placed in India ink

Answer Form for TDA CE Credit Exam #19: *The Oral Biopsy: Indications, Techniques and Special Considerations*

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2. a b c d	7. a b c d
3. a b c d	8. a b c d
4. a b c d	9. a b c d
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