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Treatment Of Recurrent Minor Aphthous Stomatitis Using Diode Laser (940nm)

A Dissertation Submitted to the Institute of Laser For Post Graduate Studies - University of Baghdad in Partial Fulfillment of the Requirement for the Degree Diploma of Laser in Medicine(Maxillofacial Surgery)

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(يُؤْتِي الْحِكْمَةَ مَن يَشَاء وَمَن
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سورة البقرة : اية (٢٦٩)

CERTIFICATION

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Dedication

This thesis is dedicated to:

The sake of Allah, my Creator and my Master،

My great teacher and messenger, Mohammed (May Allah bless

and grant him), who taught us the purpose of life،

Hussein

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Praise to Allah, the Almighty, for uncountable help and guidance and peace be upon his messenger Mohammad.

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ABSTRACT

Background –The exact etiology of recurrent aphthous ulcers (RAS) is unknown. The management ofrecurrent aphthous ulcers is not always straightforward.Ulcers in the mouth (recurrent aphthous stomatitis) are very common and may vary in size from very small to very large.

ObjectiveTo evaluate reduction in pain intensity and duration of pain relief, reduction in size of ulcer, duration for healing of ulcer (healing time) in patients with recurrent aphthous stomatitis after application of Low Level Light Amplification by Stimulated Emission of Radiation therapy (LLLT) comparing with topicalAnginovag spray medication and control group.

Materials & Methods- A total number of 21 individuals diagnosed as RAS were divided into three equal groups as follows: Group 1: Minor aphthous ulcer was treated by giving LLLT using Diode LASER; Group 2: Minor aphthous ulcer was treated bytopical Anginovag spray medication.; Group 3: Minor aphthous ulcer was treatedbyconservatively with motivation and re assuranment and fellow up..

Results- In this randomized controlled clinically study LLLT using Diode LASER causes reduction in pain intensity caused byrecurrent aphthous ulcers hence reducing the morbidity, there is also improvement in reduction in the diameter and healing time of the ulcer as compared toAnginovag spray medication and control group.

Conclusion-Although various treatment modalities have been used and LLLT is not commonly used to treat aphthous ulcers but this study is suggestive that using LLLT would be a safe and effective treatment modality forrecurrent aphthous ulcers patients.

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LIST OF ABBREVIATIONS

Abbreviations	Item
°C	Celsius
A	area
AIDS	acquired immunodeficiency syndrome
ANSI	American National Standards Institute
cal	calories
cm	centimeter
CMV	cytomegalovirus
CW	Continuous wave
E	energy
e.g	for example
HLA	histocompatibility antigen
HSV	herpes simplex Virus
Hz	hertz
I	irradiance
J	joule
LLLT	low-level laser therapy
m	meters
MPE	maximum permissible exposure
nm	nanometer
NSAIDs	nonsteroidal anti-inflammatory drugs
P	power
PIs	Principal Investigators
PMNR	periadenitis mucosa necroticarecurrens
PPE	personal protective equipment
RAU	Recurrent aphthous stomatitis
SLS	Sodium Lauryl Sulfate
t	time
TNF-α	tumor necrosis factor-α
UV	utraviolt
VZV	varicella-zoster virus
W	watts
μ	micron

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CHAPTER ONE

INTRODUCTION AND BASIC CONCEPTS

CHAPTER ONE

1.1INTRODUCTION

Recurrent aphthous ulcer: Common ulcerative lesion found in the oral cavity. It is characterized by the appearance of single or multiple ulcerative lesions in the oral mucosa; typically painful, recurrent, small, round or ovoid with circumscribed margins and erythematous haloes. It is usually first observed in adolescence, but it is in adulthood that patients face periods of increased pain and discomfort. Manifestations of RAU impair feeding, swallowing, and speaking, reducing a patient's self-image and quality of life.[1]

The causes of RAU is unknown, but are thought to be multifactorial with many triggers or precipitating factors. Among patient factors are genetic predisposition, local trauma, medications, allergy، hormonal changes, stress, and immunological abnormalities.[1]

RAU has three clinical presentations: minor aphthous ulcers, major aphthous ulcers, and herpetiform ulcers. As RAUwith different size from minor to major with different severity of symptoms and they tend to heal not less than 10-14days.[1]

The treatment is palliative, since most existing therapies only reduce the symptoms and sometimes the duration of the lesion.Local corticosteroids, antiseptic and antibacterial drugs are used singly or in various combinations. Systemic medication is also used in severe cases or those resistant to topical therapies such as steroids and immunosuppressive systemic agents.[1]

However, none of the conventional treatments has been shown to be effective in preventing or even decreasing the incidence of lesions.[1]

Studies have suggested that low-level laser therapy (LLLT) has the potential to treat aphthous ulcer and related lesions In addition to reducing the pain ,discomfort, and stimulates healing of ulcers [1], on the other hand، shown excellent results in the treatment and prevention of RAU.[2]

Low-level laser therapy (LLLT)or cold laser is nondestructive amount of energy that occurs at the periphery of the target tissue. Lowlevel laser therapy (LLLT) was discovered incidentally in attempt to treat cancerous cells with a ruby laser and it was found that it did not kill tumor cells instead it accelerated wound healing From which the concept of photobiomodulation developed.[3]

It has biostimulatingactivating effects, such as increase of cell metabolism and/or tissue regeneration, thereby accelerating healing of the tissue, anti-inflammatory effects on the targeting tissues and cells, as well as reduction of pain of various etiologies. [4]

The principle of biostimulation promoted by therapeutic lasers was introduced > 20 years ago It was first applied in dermatology, especially supplementing the repair process of skin wounds. Later, it was suggested that biostimulation could also be useful in accelerating the healing of wounds inside the oral cavity. Recurrent aphthous stomatitis (RAS) is one among the many that falls into the wide spectrum of clinical applications of a therapeutic laser.[5]

The primary goals of therapy of RAU are relief of pain, reduction of ulcer duration and restoration of normal function.[6]

1.2 STRUCTURE OF ORAL MUCOSA

The oral cavity is lined with stratified squamous epithelium, which is divided into three types of tissue as shown figure(1-1):

- Lining mucosa covers the floor of the mouth and the cheeks, lips, and soft palate. It does not function in mastication and therefore has little attrition.the lining mucosa is soft, pliable, and nonkeratinized.
- Masticatory mucosa covers the hard palate and alveolar ridges and is so named because it comes in primary contact with food during mastication.the masticatory mucosa is keratinized, Indicative of the attrition that takes place during mastication.
- Specialized mucosa, which covers the surface of the tongue, is quite different in structure and appearance from the twoprevious tissues.

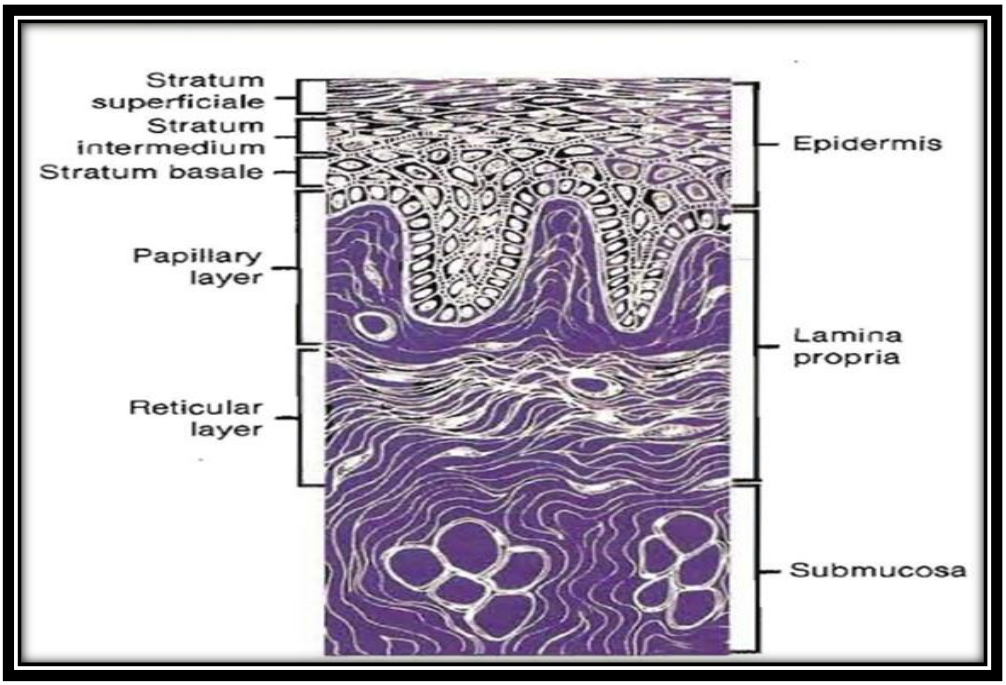


Fig.(1-1)Relationships among oral epidermis, dermis (lamina propria), and submucosal tissue. The names of layers of epidermis and dermis a re noted on the left)[7].

Each type of tissue has structural differences:

The mucosa of the oral cavity has several features common to epithelium elsewhere in the body. One of these features is:

- The lamina propria.
- The connective tissue layer immediately below the epithelium. It is composed of the papillary layer and deeper reticular layer.

In the papillary layer, the connective tissue extends into pockets in the epithelium. This increases the surface of the epithelium for contact with vascular supply and nerves. The reticular layer contains the deeper plexus of vessels and nerves supported by the connective tissue. These two layers, papillary and reticular, contribute the lamina propria or dermis. Beneath this zone is the submucosa or subcutaneous tissue[7].

1.3 RECURRENT APHTHOUS ULCERATIONS ;(CANKER SORES)

Ulceration is a breach in the oral epithelium, which typically exposes nerve endings in the underlying lamina propria, resulting in pain or soreness [8].

although it seems likely that this was oral ulceration as a manifestation of some infectious disease, since they are described as occurring in epidemic-like patterns, with concurrent symptoms such as fever.Aphthous stomatitis was once thought to be a form of recurrent herpes simplex virus infection, and some clinicians still refer to the condition as "herpes" despite this cause having been disproven[9].

The informal term "canker sore" is sometimes used, mainly in North America[63], either to describe this condition generally, or to refer to the individual ulcers of this condition[4] .or mouth ulcers of any cause unrelated to this condition. The origin of the word "canker" is thought to have been influenced by Latin, Old English, Middle English and Old North French[10].

Aphthous stomatitis occurs worldwide, but is more common in developed countries. Within nations, it is more common in higher socioeconomic groups. Males and females are affected in an equal ratio, and the peak age of onset between 10 and 19 years. About 80% of people with aphthous stomatitis first developed the condition before the age of 30[11].

The mucosal destruction appears to represent a T cell–mediated immunologic reaction. Analysis of the peripheral blood in patients with aphthae shows a decreased ratio of CD4+ to CD8+ T lymphocytes, increased T cell–receptor γδ+ cells, and increased tumor necrosis factor-α (TNF-α). generated by these cells, macrophages, and mast cells [11].

Evidence of the destruction of the oral mucosa mediated by these lymphocytes is strong, but the initiating causes are elusive and most likely highly variable[12].

1.4 Causes

Multiple research studies have attempted to identify a causative organism, but aphthous stomatitis appears to be non-contagious, non-infectious, and not sexually transmissible[13].

The following all have been reported to be responsible in certain subgroups of patients and each discounted in other subgroups:

However, common autoantibodies are not detected in most patients, and the condition tends to resolve spontaneously with advancing age rather than worsen. This suggests that there are a number of possible triggers, each of which is capable of producing the disease in different subgroups. In other words, different subgroups appear to have different causes for the condition. These can be considered in three general groups namely

- primary immuno-dysregulation ،
- decrease of the mucosal barrier and
- states of heightened antigenic sensitivity.

One or more of these three factors may be involved in subgroups of patients.Recurrentaphthous stomatitis demonstrates a definite tendency to occur along family lines. When both parents have a history of aphthous ulcers, there is a 90% chance that their children will develop the lesions[11].

In addition, several investigators have shown an association with certain histocompatibility antigen (HLA) types in subgroups of patients. The mucosal barrier appears to be important in the prevention of aphthous stomatitis and might explain the almost exclusive presence of aphthous stomatitis on nonkeratinized mucosa. Numerous factors that decrease the mucosal barrier increase the frequency of Occurrence (e.g.,trauma, nutritional deficiencies, smoking cessation); conversely, those associated with an increased mucosal barrier have been correlated with decreased ulcerations (e.g., smoking, hormonal changes, marked absence of aphthae on mucosa bound to bone[12].

Risk factors in aphthous stomatitis are also sometimes considered as either host-related or environmental. It is obvious that there has been considerable confusion in the past between etiologic factors and precipitating factors[14].

1. Aphthous stomatitis has been associated with other **autoimmune** diseases, namely[11].

- Systemic Lupus Erythematous and[11].
- inflammatory bowel diseases[11].

2. **Allergies[11].**
3. **Genetic predisposition**
4. **Hematologic abnormalities**
5. **Hormonal hormonal changes:** (mostly in women) [15].

It has been recognized for many years that a time relationship exists between the occurrence of the menstrual period and the development of aphthous ulcers. Most series show that the incidence of aphthae is greatest during the premenstrual period. Dolby has similarly shown that ulceration

is maximal in the postovulation period and has related this to the blood level of progesterone [14].

In a small subset of female patients, a negative association was reported between the occurrence of aphthae and the luteal phase of the menstrual cyclea period of mucosal proliferation and keratinization. In addition, these same patients often experience ulcer free periods during pregnancy[11].

6. Immunologic factorsA

Aphthous like ulcerations have occurred in patients with systemic immune dysregulations. Patients with cyclic neutropenia occasionally have cycles of aphthous like ulcerations that correspond to the periods of severe immune dysregulation[12].

In addition, patients with acquired immunodeficiency syndrome (AIDS) have an increased frequency of severe aphthous stomatitis, a fact that is not surprising considering the elevated CD8+/CD4+ ratio as the result of the reduction of CD4+ T lymphocytes[12].

7. Infectious agents

8. Nutritional deficiencies (iron, folate, zinc, B1, B2, B6,B12)

9. Smoking cessation: It is interesting to note that there is negative correlation between aphthous ulcers and smoking. As per Atkin PA and coworkers who measured the nicotine metabolite present inthe blood of smokers, the incidence of recurrent aphthous ulcers is significantly lower in smokers[14].

10. Stress

Stress, with its presumed effects on the immune system, directly correlates with the presence of aphthous stomatitis in some groups. In studies of professional students, recurrences clustered around stressful periods of the academic year; conversely, periods of vacation were associated with a low frequency of lesions[11].

11. Trauma: The traumatic incidents included self-inflicted bites oral surgical procedures, tooth brushing, dental procedures, needle injections, and dental trauma.[14]thermal injury or chemical irritation**.** [16]

12. Poor oral hygiene are proposed factors[17].

13. Systemic Disorders Associated With Recurrent Aphthous Stomatitis[11].

- Behçet's syndrome
- Celiac disease
- Cyclic neutropenia

14. Syndromes cause [11].

- MAGIC syndrome (mouth and genital ulcers with inflamed cartilage
- PFAPA syndrome (periodic fever, aphthous Stomatitis, pharyngitis, cervical adenitis)
- Sweet's syndrome

15. Many systemic medications (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs], various beta blockers, nicorandil), Use of a toothpaste containing Sodium Lauryl Sulfate (SLS) can trigger attacks in some patients[18].

16.microbiologic agents (e.g., L forms of streptococci, Helicobacter pylori, herpes simplex Virus [HSV], varicella-zoster virus [VZV], adenovirus, and cytomegalovirus [CMV]).

1**7. Many foods** e.g,. cheese, chocolate, coffee, cow's milk, gluten, nuts, strawberries, tomatoes, dyes, flavoring agents, preservative.[١١]**.**

1.5 Clinical variations of aphthous stomatitis are recognized:

- Minor.
- Major.
- Herpetiform.

Minor aphthous ulcerations (Mikulicz'saphthae) are the most common and represent the pattern present in more than

80% of those affected. Major aphthous ulcerations (Sutton's disease or periadenitis mucosa necroticarecurrens [PMNR]) occur in approximately 10 %of the patients referred for treatment. The remaining patients have herpetiformaphthous ulcerations[12].

The minor and major forms most likely represent variations of the same process, although herpetiformaphthae demonstrate a unique pattern. Some investigators differentiate the herpetiform variant because of supposed evidence of a viral cause, but the proof is weak and does not justify its distinction from the other aphthous ulcerations. Some authors include Behçet's syndrome as an additional variation of aphthous stomatitis[11].

1.5.1 CLINICAL FEATURES

Aphthous ulcerations are noted more frequently in children and young adults, with approximately 80% of affected individuals reporting their first ulceration before the age of 30[11].

Ulceration is a breach in the oral epithelium, which typically exposes nerve endings in the underlying lamina propria, resulting in pain or soreness. The pain inhibits patients' abilities to eat, drink, and maintain oral hygiene[19].

1.5.2 MINOR APHTHOUS ULCERATIONS

Patients with minor aphthous ulcerations experience the fewest recurrences and the individual lesions exhibit the shortest duration of the three variants. The ulcers arise almost exclusively on nonkeratinized mucosa and may be preceded by an erythematous macule in association with prodromal symptoms of burning, itching, or stinging[12].

The ulceration demonstrates a yellow-white, removable fibrinopurulent membrane that is encircled by an erythematous halo as seen in Fig. (1-2)[11].

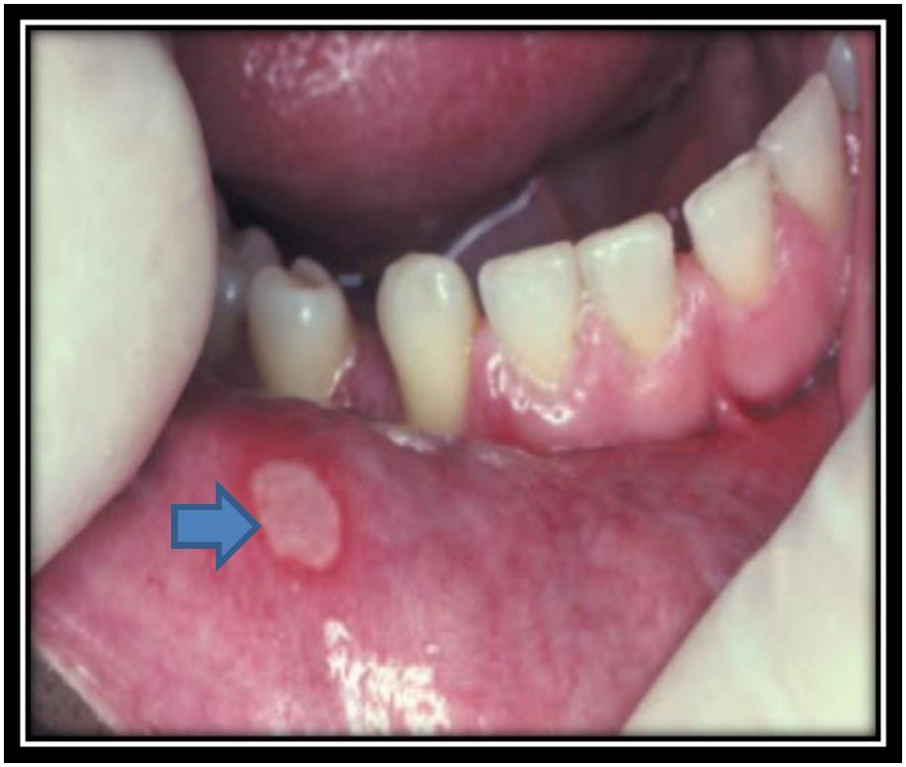


Fig. 1-2 Minor aphthous ulceration. Erythematous halo encircling a yellowish ulceration of the lower labial mucosa. (Courtesy of Dr. Dean K. White.)[11].

Classically, the ulcerations measure between3 and 10 mm in diameter and heal without scarring in 7 to 14 days as seen in (Fig. 1-3)[11]

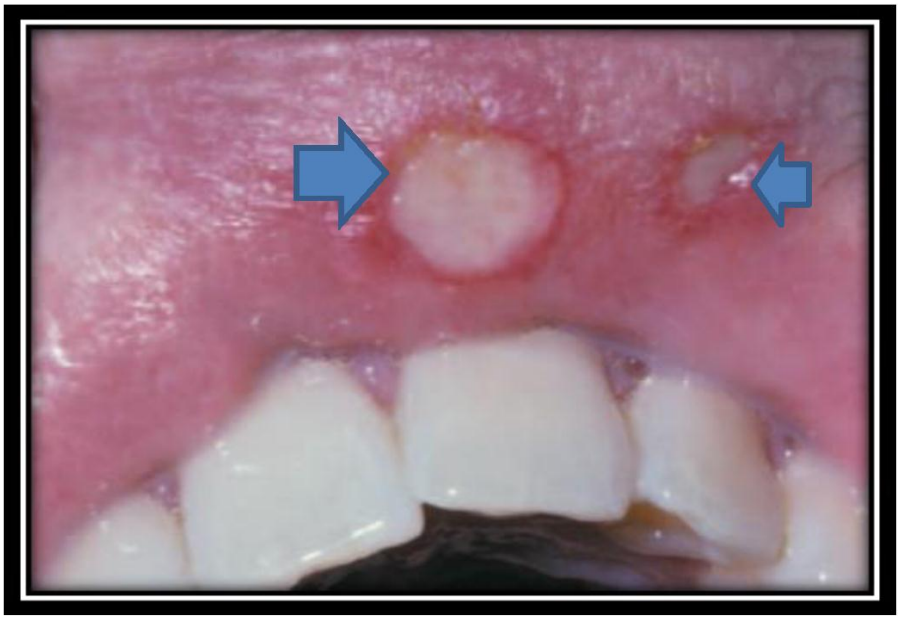


Fig. 1-3 Minor aphthous ulcerations. Two ulcerations of Different sizes located on the maxillary labial mucosa.(Courtesy of Dr. Dean K. White.)[11].

From one to five lesions typically are present during each episode, and the pain often is out of proportion for the size of the ulceration. The buccal and labial mucosae are affected most frequently, followed by the ventral surface of the tongue, mucobuccal fold, floor of the mouth, and soft palate as seen in (Fig.1-4)[12].

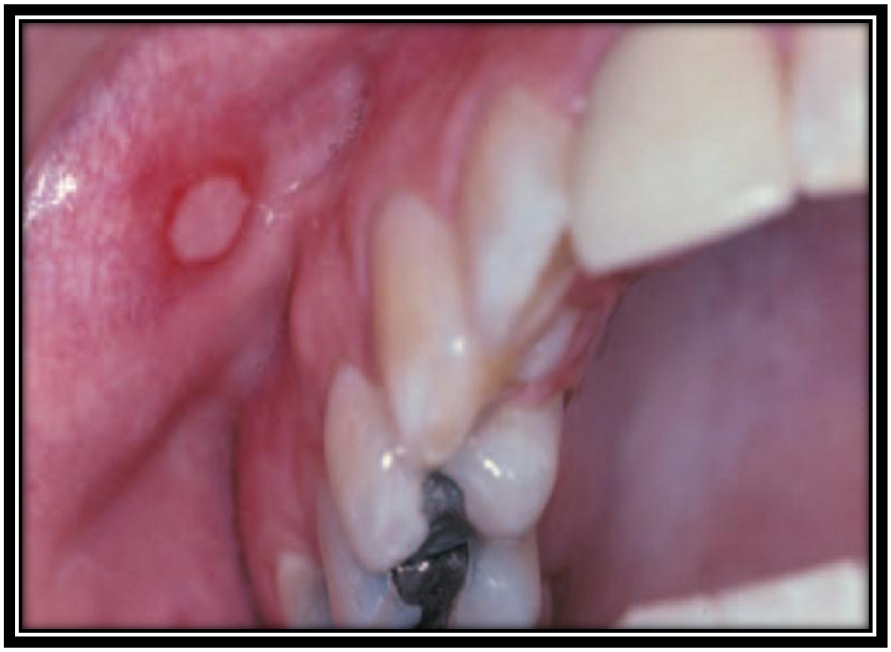


Fig. 1-4 Minor aphthous ulceration. Single ulceration of the anterior buccal mucosa.(Courtesy of Dr. Dean K. White.)[11].

Involvement of keratinized mucosa (e.g., hard palate, gingiva, dorsal surface of the tongue, and vermilion border) is rare and usually represents extension from adjacent nonkeratinized epithelium. The recurrence rate is highly variable, ranging from one ulceration every few years to two episodes per month[11].

1.5.3 MAJOR APHTHOUS ULCERATIONS

Major aphthous ulcerations are larger than minor aphthae and demonstrate the longest duration per episode. The number of lesions usually is intermediate between that seen in the minor and herpetiform variants.The ulcerations are deeper than the minor variant, measure from 1 to 3 cm in diameter, take from 2 to 6 weeks to heal, and may cause scarring as seen in (Fig. 1-5)[12].

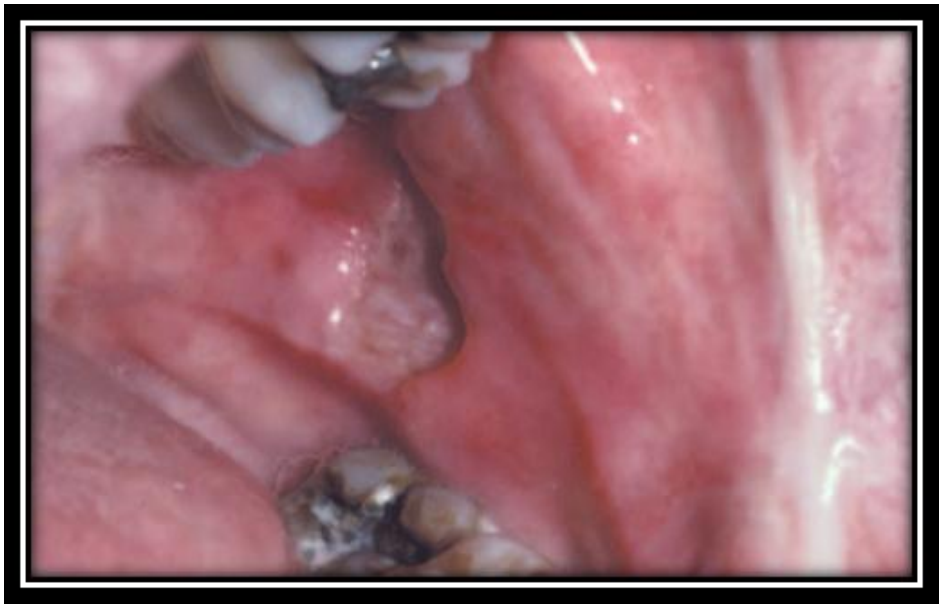


Fig. 1-5 Major Aphthous ulceration. Large, deep, and irregular ulceration of the posterior buccal mucosa.(Courtesy of Dr. Dean K. White.)[11].

Note extensive scarring of the anterior buccal mucosa from previous ulcerations.The number of lesions varies from 1 to 10. Any oral surface area may be affected, but the labial mucosa, soft palate, and tonsillarfauces are involved most commonly as seen in (Fig.1-6)[12].

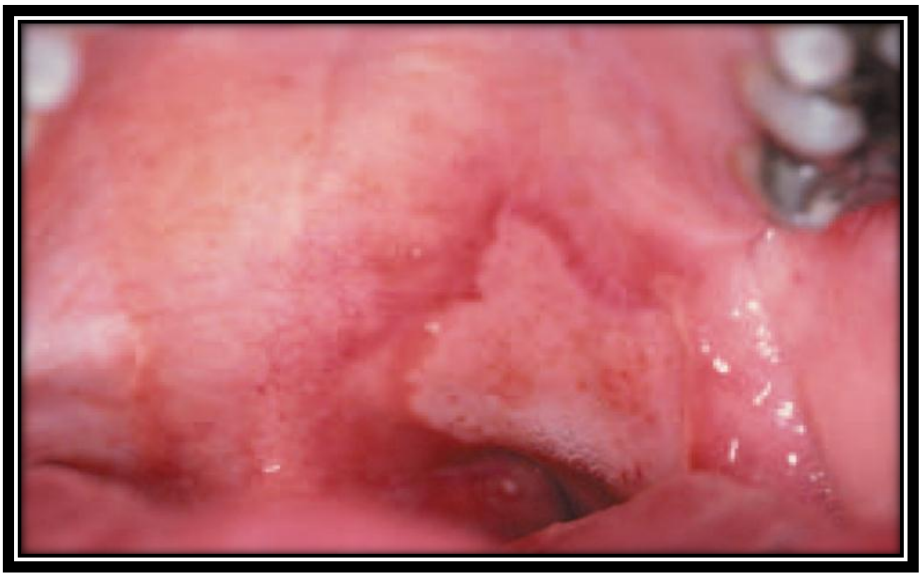


Fig. 1-6 Major aphthous ulceration. Large, irregular ulceration of the soft palate.(Courtesy of Dr. Dean K. White.)[11].

The onset of major aphthae is after puberty, and recurrent episodes may continue to develop for up to 20 years or more. With time, the

associated scarring can become significant, and in rare instances may lead to a restricted mouth opening[20].

Recurrent aphthous stomatitis may result in impairment in feeding and speech, leading to a nutritional deficit and poor quality of life[21].

1.5.4 HERPETIFORM APHTHOUS ULCERATIONS

Herpetiformaphthous ulcerations demonstrate the greatest number of lesions and the most frequent recurrences. The individual lesions are small, averaging ١to 3 mm in diameter, with as many as 100 ulcers present in a single recurrence. Because of their small size and large number, the lesions bear a superficial resemblance to a primary HSV infection, leading to the confusing designation, herpetiform. It is common for individual lesions to coalesce into larger irregular ulcerations as seen in (Fig. 1-7)[12].

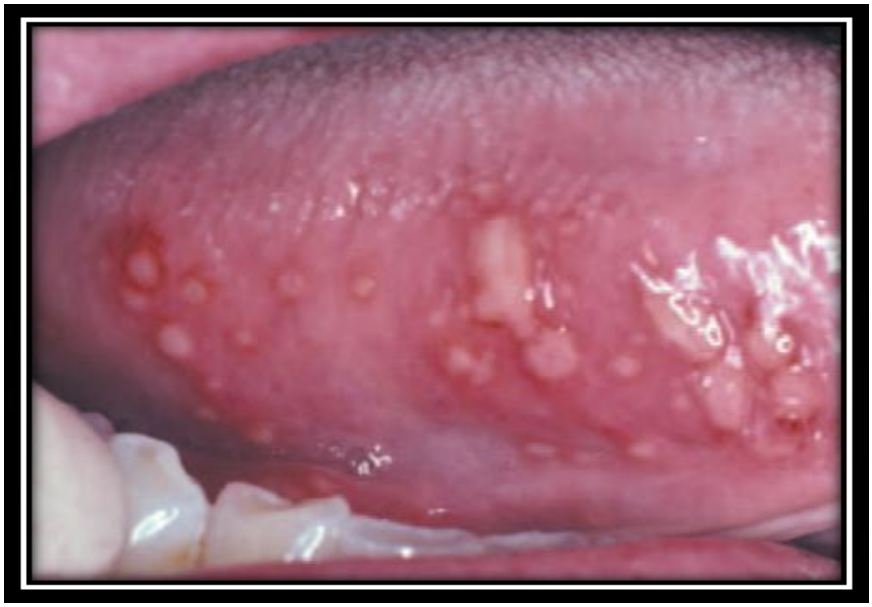


Fig. 1-7 Herpetiformaphthous ulcerations. Numerous pinhead ulcerations of the ventral surface of the tongue, several of which have coalesced into larger, more irregular areas of ulceration.(Courtesy of Dr. Dean K. White.)[11].

The ulcerations heal within 7to 10 days, but the recurrences tend to be closely spaced. Many patients are affected almost constantly for periods as long as 3 years. Although the nonkeratinized, movable mucosa is affected most frequently, any oral mucosal surface may be involved. There is a

female predominance, and typically the onset is in adulthood as seen table (1-1)[22].

(1-1) Table characteristic feature of RUA[22].

% Cases	Minor 80-90%	Major 10-15%	Herpetiform 5-10%
Site of occurrence	Nonkeratinized, moveable mucosa	Nonkeratinized mucosa; some keratinized mucosa (palate, dorsal tongue)	Nonkeratinized mucosa, keratinized mucosa
Color	Red, white Yellow floor but grays as heals Erythematous halo	Red, white Yellow floor but grays as heals Edematous halo Raised erythrocyte Plasma viscosity	Begins with vesiculation that passes rapidly into multiple, coalescing ulcers
Shape	Round, oval	Round, oval	Round, ragged
Size	3-4mm	5mm-1cm	1-2mm (pinhead)
Number of Lesions	1-6	1-6	Coalescing Groups Generally 10 to 40
Duration	7-14 days	10-40 days	10+ days
Scarring	Little to none	Yes	Not normally
Age	10-40 years	10-40 years	Older age groups
Recurrence	2-8 per year	Extremely frequently	Extreme frequency Ulceration may be continuous
Other		Common in immunodeficient patients	Resemble lesions caused by HSV-1 virus More common in females

1.5.5 HISTOPATHOLOGIC FEATURES

The histopathologic picture of aphthous stomatitis is characteristic but not pathognomonic. The early ulcerative lesions demonstrate a central zone of ulceration,which is covered by a fibrinopurulent membrane. Deep to the area of ulceration, the connective tissue exhibits an increased vascularity and a mixed inflamatory cellular infiltrate that consists of lymphocytes, histiocytes, and polymorphonuclear leukocytes.

The epithelium at the margin of the lesion demonstrates spongiosis and numerous mononuclear cells in the basilar one third. A band of lymphocytes

intermixed with histiocytes is present in the superficial connective tissue and surrounding deeper blood vessels[23].

1.6 DIAGNOSIS

No laboratory procedure provides definitive diagnosis. The diagnosis is made from the clinical presentation and from exclusion of other diseases that produce ulcerations that closely resemble aphthae .In patients with complex aphthous ulcerations, a systematic evaluation for an underlying trigger or associated systemic condition is prudent. [11]

The diagnosis of RAUs is based on patient anamnesis and clinical symptoms. There is no specific diagnostic test for RAU, though it is essential to discard possible underlying systemic causes. It is prudent to request a complete series of laboratory tests, including a complete blood count, and evaluation of iron, vitamin B12, and folic acid[24].

An associated triggering condition (e.g., hematologic deficiency,gastrointestinal disease, immunodeficiency, drug reaction) was discovered in almost 60%. Because the histopathologic features are nonspecific. Major aphthous ulcerations are more resistant to therapy and often warrant more potent corticosteroidsas seen in (Fig. 1-8)[11].

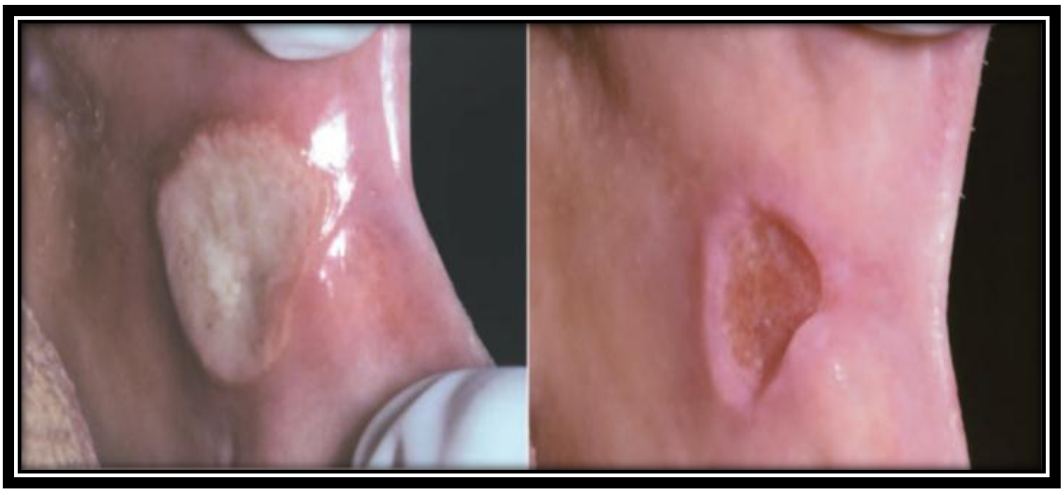


Fig. 1-8 Major aphthous ulceration. A, Large ulceration of the left anterior buccal mucosa[11].

As previously mentioned, the immune attacks are usually a result of immunodysregulation, a decreased mucosal barrier, or an elevated antigenic stimulus. The evaluation for systemic disorders usually eliminates the first two causes. Typically, this is followed by patch tests for antigen stimuli or an elimination diet for possible offending foods. Therapeutic trials might be instituted against the viruses and bacteria that have been implicated in subsets of patients with aphthous stomatitis.[11]

The investigator should explain to the patient that the underlying causation is diverse; even with the most exhaustive search, the answer may be elusive. In many cases, stress appears involved, and all evaluations in these patients will be within normal limits. In spite of the high likelihood of an expensive and negative evaluation,discovery of an underlying abnormality that can be treated often leads to permanent resolution or dramatic improvement in the course of the recurrences. The patient's medical history should be reviewed for signs and symptoms of any systemic disorder that may be associated with aphthous like ulcerations[23].

1.7 TREATMENT AND PROGNOSIS

Treatment modalities are:

1. **Conservative method:** Most patients with mild aphthosis receive either no treatment, therapy with a number of protective bioadhesive products, or periodic topical medicaments that minimize the frequency and severity of the attacks[11].
2. **Medication**

A) Topical: the mainstay of therapy is the use of topical corticosteroids, and the list of possible choices is long. Most patients with diffuse minor or herpetiformaphthae respond well to 0.01% dexamethasone elixir used in a rinse-and-expectorate method. Patients with localized ulcerations can be treated successfully with 0.05% augmented betamethasone

dipropionategel or 0.05% fluocinonide gel. Adrenal suppression does not occur with appropriate use of these medications[11]. Major aphthous ulcerations are more resistant to therapy and often warrant more potent corticosteroids (table. 1-2). The individual lesions may be injected with triamcinolone acetonide or covered with 0.05% clobetasol propionate gel or 0.05% halobetasol propionate ointment'[11]. Triamcinolone tablets also can be dissolved directly over the lesions.In hard-to-reach areas, such as the tonsillar pillars, beclomethasonedipropionate aerosol spray can be used[11].

B) Systemic: Included within the list of therapies are acyclovir, amlexanox, topical 5-aminosalicylic acid, carbenoxolone sodium, chemical cauterizing agents, chlorhexidine, , , dapsone, , gamma globulin, , hydroxypropyl cellulose films, interferon-α, sucralfate, , , tetracyclines, , transfer factor (extract of immunocytes), , and vitamin and mineral supplements especially zinc sulfate. The successes of these Therapies are highly variable. Recurrences often continue, although breaking up the cycle may induce longer disease-free intervals between attacks[11].

In resistant cases, systemic corticosteroids may be required to supplement the topical medications and gain control. In such instances, prednisolone or betamethasone syrup in a swish-and-swallow method is preferable to prednisone tablets. In this way the ulcerations will receive both topical and systemic therapy[12].

3. surgical

A) Simple like cautery: Chemical cautery with silver nitrate continues to be suggested as an effective therapy, but it can no longer be recommended because of the numerous safer alternatives and its rare association with massive necrosis and systemic agrarian. An over-the-counter cautery that uses sulfuric acid and phenolic agents is indicated in certain situations, but

patients must be warned of the potential for significant local tissue necrosis related to its misuse[11].

B) Excision: Surgical removal of aphthous ulcerations has been used but is an inappropriate therapy[11].

4. Low-level laser therapy: A novel treatment modality in the form of **low-level laser therapy (LLLT)** has evolved in recent years. LLLT also known as "cold laser" works on the principle of biostimulation. This biomodulatory effect plays a pivotal role in accelerating the healing process and provides analgesia. Hence, it constitutes an alternative to processes that present pain and inflammatory reaction [5].

Table (1-2) Treatment modalities for recurrent aphthous stomatitis [14.]

Immune enhancement
Levamisole
Vaccine
Immunosuppression, inflammatory suppression
Prednisone
Triamcinolone acetonide
Betamethasone-17-benzoate
Antihistamine
Antibiotics (Tetracycline?)
Suspension, topical
Chloramphenicol
Broad-spectrum antibiotics
Antiseptic
Silver nitrate
Coagulating agent, negatol
Gentian violet
Diet supplementation (Lactobacillus?)
Vitamin B_{12}, folic acid
Iron
Zinc sulfate
Symptomatic treatment
Xylocaine/lidocaine
Silver nitrate
Benadryl, topical
Camphor-phenol

1.8 Laser Basics

Laser Physics – Fundamentals

1.8.1 Laser Light

Light is phenomenon that is characterized by a dual behavior, particle like behavior and wave like behavior. In both photons and Waves, they were considered as energy carriers. Laser systems are devices which are used to amplify light energy to an intense beam of energy of a very pure single color by stimulated emission of radiation.[25]

The word laser is an acronym for light amplification by stimulated emission of radiation[26].

Since this introduction, numerous types of lasers have been produced that generated radiation at various optical frequencies extending from the far infrared to the ultra violet region from the electromagnetic wave spectrum [27].

Electromagnatic spectrum extends from the longest radio wave, whose wavelength are measured in Kilometers ,through the medium and short radio waves to the microwave , infrared and visible regions , beyond the visible ,the ultra -violet merges into the -x-ray region ,while in turn is followed by the shorter wavelength gamma rays and cosmic rays [28], as shown in figure (1-9).

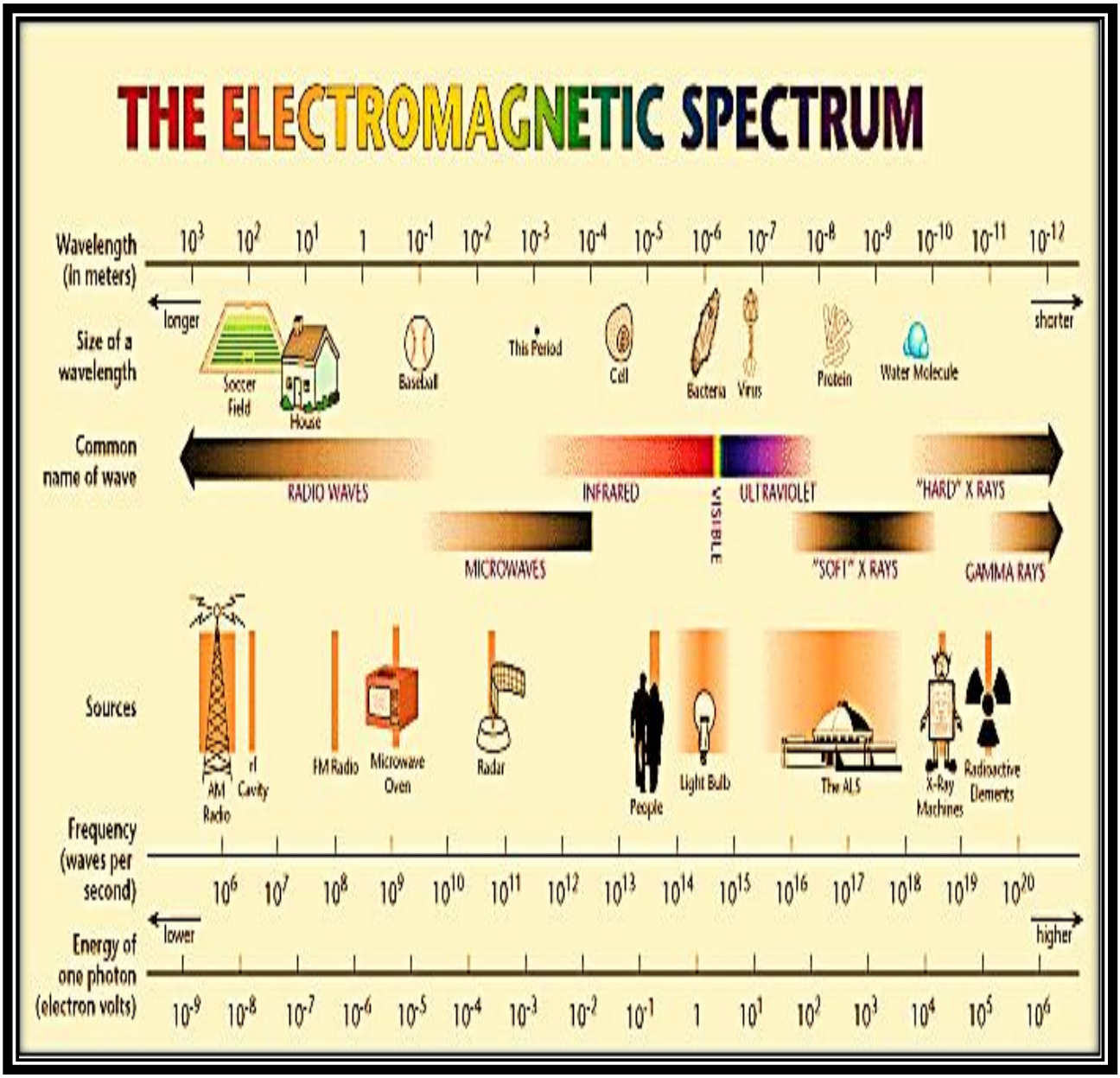


Figure 1-9 the Electromagnetic Spectrum[28].

1.8.2 Properties of the laser beams

- Coherence consists almost exclusively of one wavelength, with is all its wave travelling in the same direction and in phase, with each other [26]**.**
- monochromaticity indicates that the emitted photon are all of the same wavelength (colour)**[26].**
- Directionality this property isconcentration of beam in a narrow width, making the laser highly directional with low divergence and greater coherence**[29].**

1.8.3 Component of laser device

All laser devices have three major components

A) Active Medium

The active medium is a collection of atoms, molecules or ions that absorb energy source and generate laser light by stimulated emission from an outside.The active medium can consist of a solid, liquid, gas or semiconductor material[26].

B) Excitation Mechanism

Excitation mechanisms pump energy into the active medium by one or more of three basic methods; optical, electrical or chemical[29].

C) Optical Resonator

1. Reflect the laser beam through the active medium for amplification. It is consisting of:-

   High Reflectance Mirror: A mirror which reflects 100% of the laser light[29] .
2. Partially Transmissive Mirror: A mirror which reflects less than 100% of the laser light and transmits the remainder (The output coupler). Different energy sources can be used in medical laser systems but the most common is the flash lamp or electric current as seen in fig. (1-10)[29].

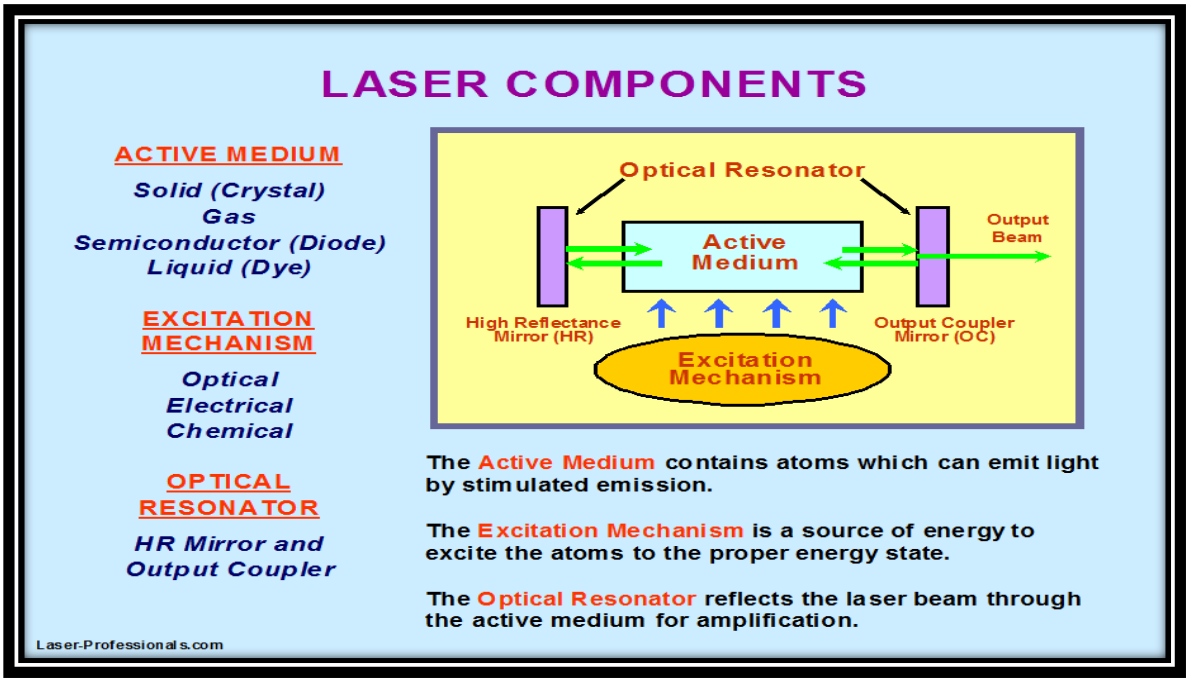


Fig. (1.10) Basic elements of the laser[30].

The light beam produced by stimulated emission, during the multiple passage of light between the mirror of the laser cavity have special properties which result from the fact that the characteristics of each stimulating photon are maintained in the emitted photons[30].

1.8.4 Delivery system

There are various ways to transfer radiation from the laser device to the tissue. In practice only two beam handling systems are used articulated arms are utilized where transmission by fiber is not possible, either due to wavelength range [far UV or mid infrared] or because pulse power is so high that it would destroy the fiber[30].

Whenever possible, fiber transmission is utilized because of the high flexibility offered by various fiber diameters [between 200—600 micrometers].For the applications on tissue surface an articulated arm, a focusing hand piece or a bare fiber can be used as a light transmission system. For interstitial or endoscopic applications the use of flexible fibers is generally necessary[30].

1.8.5 Mode of operation[28].

- Continuous A CW laser is one whose power output undergoes little or no fluctuation with time. It exhibits a steady flow of coherent energy.
- Pulsed A group of lasers has output beam that undergo marked fluctuations, that is the beam's power change with time in a very noticeable fashion.

1. Normal pulse mode.
2. Q- Switched mode.
3. Mode – locked.

1.8.6 Laser parameters

- **Wave lenghth(λ):** the horizontal distance between any two corresponding points on the wave. This measurement is important to both how the laser light is delivered to the surgical site and how it reacts with tissue. Wavelength is measured in meters (m). Dental lasers have wavelengths on the order of much smaller units, using terminology of either a nanometer (nm), one billionth (10^{-9}) of a meter, or micrometer (also micron, [μ or μm], one millionth(10^{-6}) of a meter[25].
- **Frequency:** As waves travel, they rotate around the zero axes certain number of times per second; this is called oscillation. The number of oscillations per unit time is defined as frequency. Frequency is measured in hertz (Hz); 1 Hz equals one oscillation Per second. Frequency is inversely proportional to wavelength[25]
- **pulse duration:** the time of one pulse[25].
- **Peak power:** peak = E pulse / ₸ pulse …… (J/s or W) average power If energy E is emitted in time t , the average emitted radiant power P (also called flux) is P=E/t. The units commonly used are watts (W), where 1 watt is equal to 1 joule per second[25].
- **Pulse repetition rate:** The number of emitted pulses per second.
  PRR = Number of pulses / second …….. (1/s or Hertz)

- **Spot size:** is the double radius of laser beam (**area =r^2 *22/7)**[25].
- **Power density (irradiance):** Laser emits light in a parallel beam. The ratio of the emitted power (P) to the cross sectional area (A) is called the power density , or irradiance (I). The units of I=P/A are W/cm2 .. If a lens is inserted into the beam , the power does not change but the beam area may be reduced to 0.5 cm2 and the power density doubles. The importance of this will be clarified when we consider the interaction of laser beams and materials[25.]
- **Energy density (fluence):** Standard science textbooks define energy as the ability to do work. This naturally applies to the radiant energy in a laser beam. The energy units which are commonly used are calories (cal) or joules (J) , where 1J=0.24cal. A laser beam may be operated intermittently, or the power delivered by the laser onto a given area may vary with time. The total energy delivered, divided by the area (the energy per unit area) is called flounce[25].

1.9 Laser—Tissue Interactions

The interaction of light at the metastable level produces

1. reflection
2. refraction
3. absorption
4. Scattering.
5. Transmission during the propagation of light through a bulk sample.[31 32]In laser surgery, knowledge of absorbing and scattering properties of a selected tissue is essential for the purpose of predicting successful treatment.

The diagnostic applications of lasers are based on scattered or reemitted light. Surgical and therapeutic applications depend on absorption of light (Figure 1-11) [31].

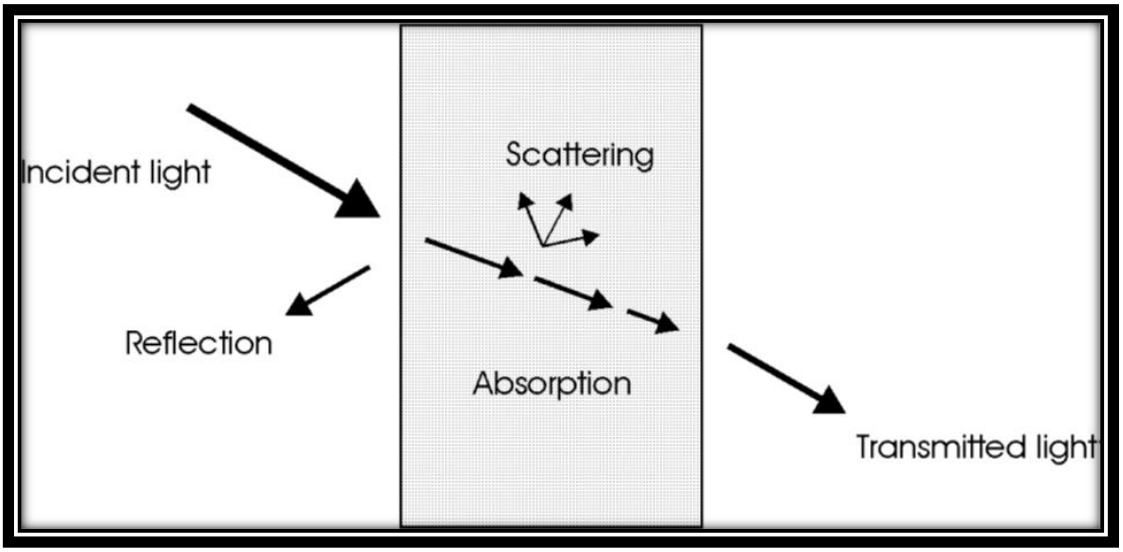


Fig. 1-11. Geometry of reflection, refraction, absorption, and scattering[31] .

1.9.1 Reflection

Is the returning of electromagnetic radiation by surfaces upon which it is incident? In general, a reflecting surface is the physical boundary between two materials of different indices of refraction. Thus the reflected radiation has no effect on the target tissue. There are two types of reflection specular and diffuse reflections. Diffuse reflection is a common phenomenon of all tissues .Reflected light might maintain its collimation in a narrow beam or might become more diffuse. This reflected beam can be dangerous because the energy could be redirected to an unintentional target. The specular reflectance on wet surfaces is approximately 2% of incident radiation. This is a major safety concern for laser operation[31, 33,34].

1.9.2 Refraction

Usually occurs when the reflecting surface separates two media of different indices of refraction. It originates from a change in speed of the light wave. Further interaction of incident light with the tissue is limited to the refracted beam. In medical laser applications, however, refraction plays a significant role only when irradiating transparent media like corneal tissue. In opaque media, usually, the effect of refraction is difficult to measure due to absorption and scattering as seen in fig. (1-12)[31, 32, 34].

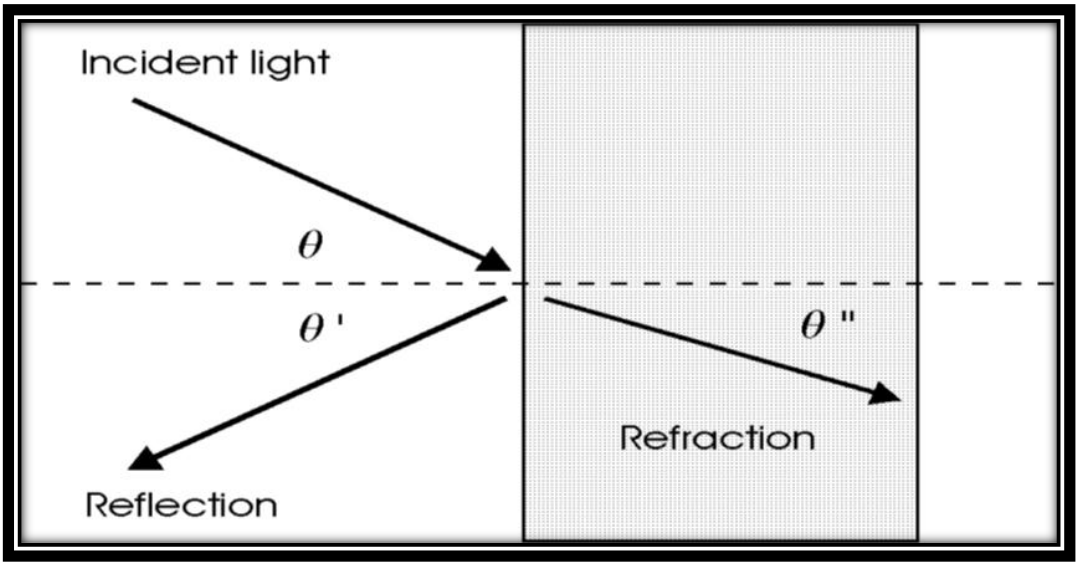


Fig. 1-12. Geometry of specular reflection and refraction[31].

1.9.3 Absorption

It is the attenuation in the intensity of an incident electromagnetic wave in passing through a medium The primary beneficial goal of laser energy is absorption of the laser by the intended biological tissue. It appears obvious that to exert laser effect upon a given tissue, it must first be absorbed[31].

1.9.4 Scattering

It is a change in the direction of propagation of a photon. This results from imprecise absorption of laser energy by a biologic tissue resulting in a diffuse effect on tissue and refers the laser beam in different directions and results in weakening the intended energy. Scattering is the predominant event with the near-infrared lasers in healthy tissue. Also scattering could cause unwanted thermal damage to the tissue adjacent to the surgical site[31, 32].

1.9.5 Transmission

is the inverse of absorption where the laser energy passes directly through the tissue with no effect on the target tissue. This effect is highly dependent on the wavelength. Water is a relatively transparent to the shorter wavelengths (argon, diode and Nd: YAG lasers) whereas tissue fluids

readily absorb the longer wavelengths (erbium family and CO2) at the outer surface so that there is little energy transmitted to adjacent tissues[31].

Depending on these factors the effect of laser could vary from: no effect to complete ablation[31, 32].

1.9.6 Tissue Properties (target cells)

Depending on the nature of tissue like color, pigment content, vascularity, chemical composition, the tissue factors include:

1. optical tissue properties which include the coefficients of reflection, absorption and scattering[31,32].
2. Thermal tissue properties like thermal conductivity and heat capacity.[31,32]
3. Tissue photosensitizes whether endogenous or exogenous (H2O, Hb, melanin, protein)[31,32].

1.10 Laser—Tissue Interaction Mechanisms

❖ wavelength **dependent** interaction mechanisms which include:

A. photochemical reactions

B. photothermal interactions as seen in fig.(1-13)[26].

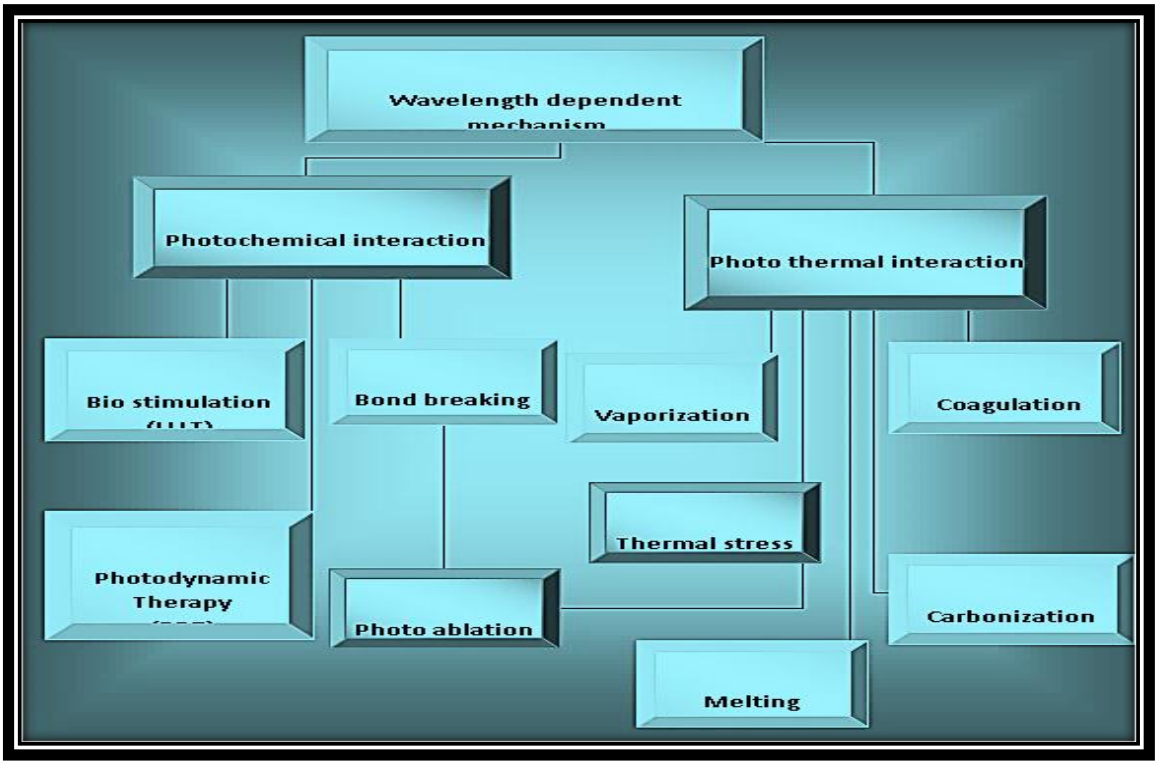


Figure 1- 13: Interaction of light with biological tissue

❖ wavelength **independent** interaction mechanisms which include

A. plasma_ induced photo ablation

B. photo disruption as seen in fig.(1-14)[26]

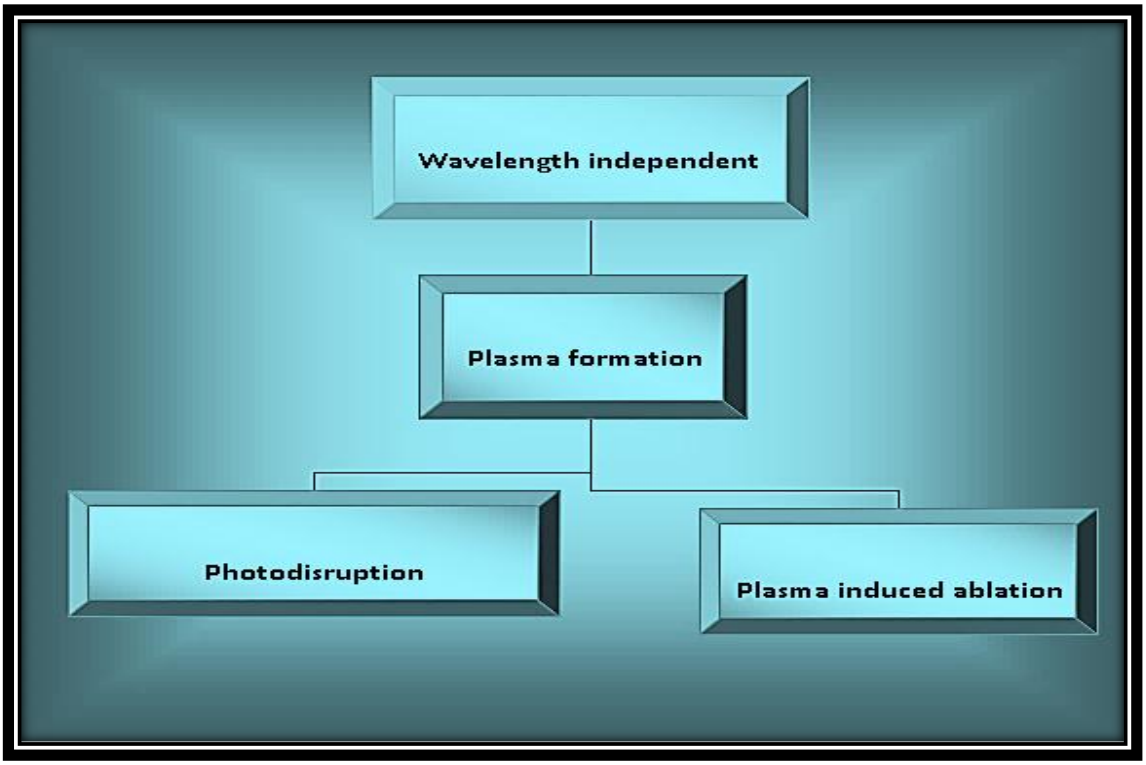


Figure 1-14: Interaction of light with biological tissue

(Wave length independent mechanism)

As seen in Fig. 1-15. Map of laser–tissue interactions. The circles give only a rough estimate of the associated laser parameters. [31, 32.]

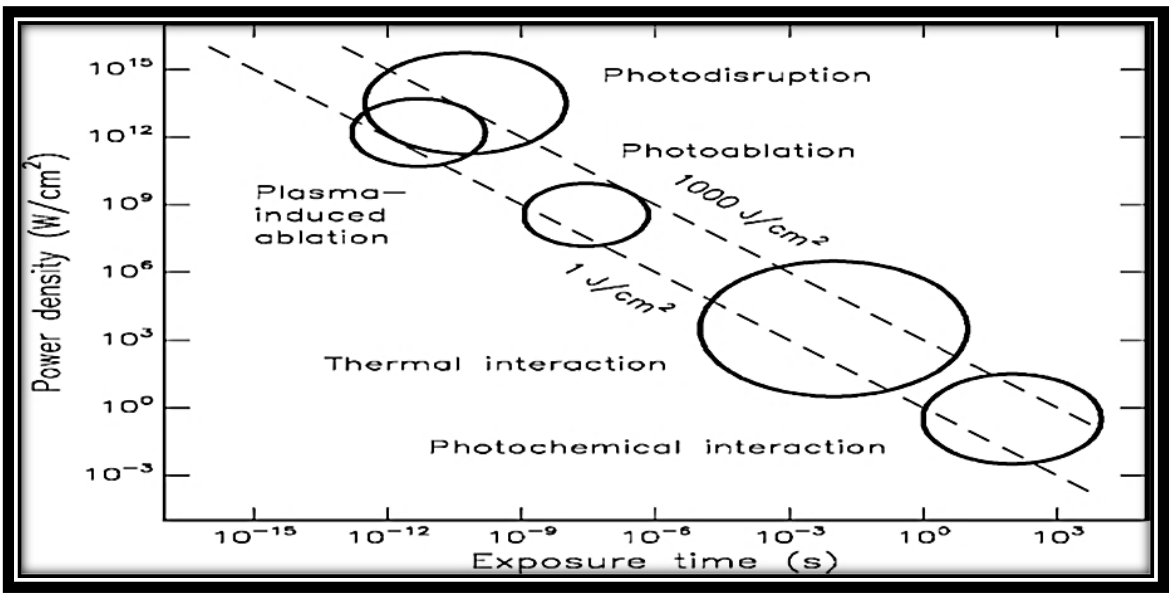


Figure (1-15) the different laser tissue interaction mechanisms [32].

1.10.1 Wavelength—Dependent Interactions

Wavelength-dependent interactions of radiant energy depend largely on the laser wavelength that has impacted the tissue. Because the wavelength is a very important parameter that determines the index of refraction (governs the overall reflectivity of the target) as well as the absorption and scattering coefficients [31, 32].

1.10.1.1 Photochemical Interactions

Photochemical interactions take place at very low power densities (0.01-50W/cm^2) and long exposure times ranging from seconds to continuous wave. Careful selection of laser parameters yields a radiation distribution inside the tissue that is determined by scattering. In most cases, wavelengths in the visible range are used because of their efficiency and their high optical penetration depths that are of importance if deeper tissue structures are to be treated[31.32].

1.10.1.1.1 Photodynamic Therapy

During Photodynamic therapy, a spectrally adapted chromophore (photosensitizer) is injected into the body. Resonant excitation by laser irradiation may then trigger the photosensitizer to perform selective photochemical reactions, resulting in certain biological transformations. Several sequential decays result in intramolecular transfer reactions. At the end of these diverse reaction channels, highly cytotoxic reactants (singlet oxygen) are released causing an irreversible oxidation of essential cell structures . Tumor diagnosis can be established by time-gated detection of the fluorescence that depends on the concentration level of photosensitizer, using time-resolved fluorescence technique. The simultaneous diagnosis and therapy of tumors with photosensitizers is one of the key advantages of Photodynamic therapy. The antimicrobial capacity of photodynamic therapy has been used to improvemicrobial reduction during conventional therapy in periodontics, endodontics, restorative dentistry, and implantology[26, 35].

1.10.1.1.2Biostimulation

Wound healing, pain relief and anti-inflammatory properties by red or near infrared light sources such as helium–neon lasers or diode lasers were reported. Typical energy fluences lie in the range 1–10 J/cm^2. Effect of LLLT appears to be increased macrophage activity in injured areas with quicker resolution of haematomata, faster resorption of edema and increased autoimunologic reaction [31,32].

1.10.1.1.3Photothermal Interactions

Most of the surgical applications of lasers exploit laser induced photothermal effect that is a rise in tissue temperature subsequent to absorption of laser radiation. The term thermal interaction stands for a large group of interaction types, where the increase in local temperature is the governing significant parameter of all thermal laser–tissue interactions.

Thermal effects can be induced by either CW or pulsed laser radiation. Different heat effects like coagulation, vaporizati**on,** carbonization, and melting may be distinguished, depending on the type of tissue, the duration and value of the local temperature achieved inside the tissue .In photothermalinteractions, there is no specific pathway, and the photons may be absorbed by any biomolecule and still lead to a thermal effect. At ~ 37◦C is normal body temperature, and for the first 5◦C or so of heating few irreversible changes occur. This small rise in temperature (5-10 °C) can influence the activity of enzymes and lead to changes in blood flow and vessel permeability[31, 32].

- **Hyperthermia:** when tissue temperature is elevated above normal temperature but tissue is not destroyed, ranging from approximately 42–50◦C is the first mechanism by which tissue is thermally affected and can be attributed to conformational changes of proteins and other macromolecules. These effects are accompanied by bond destruction and membrane alterations, are useful in Photobiostimulation[31 ,32].
- **Coagulation:** At 60-70◦C, denaturation of proteins and collagen occurs which leads to coagulation of tissue and necrosis of cells. The corresponding macroscopic response is visible paling of the tissue. Coagulation for hemostasis is best effected by using a lower energy density, which is achieved by enlarging the spot size or lowering the absolute power or exposure duration. At even higher temperatures 70–80°C adherence or stickiness of layers of soft tissue due to heat-induced alterations in collagen (the helical unfolding of the collagen molecules and their intertwining with adjacent segments) in approximation of soft tissue edges (Welding of tissue). At 80°C—85°C, blood vessels shrink. This effect is probably due to the alteration of the collagen within their walls and is a component of the hemostatic effect of lasers as seen in fig.(1-16**)**[31,32].

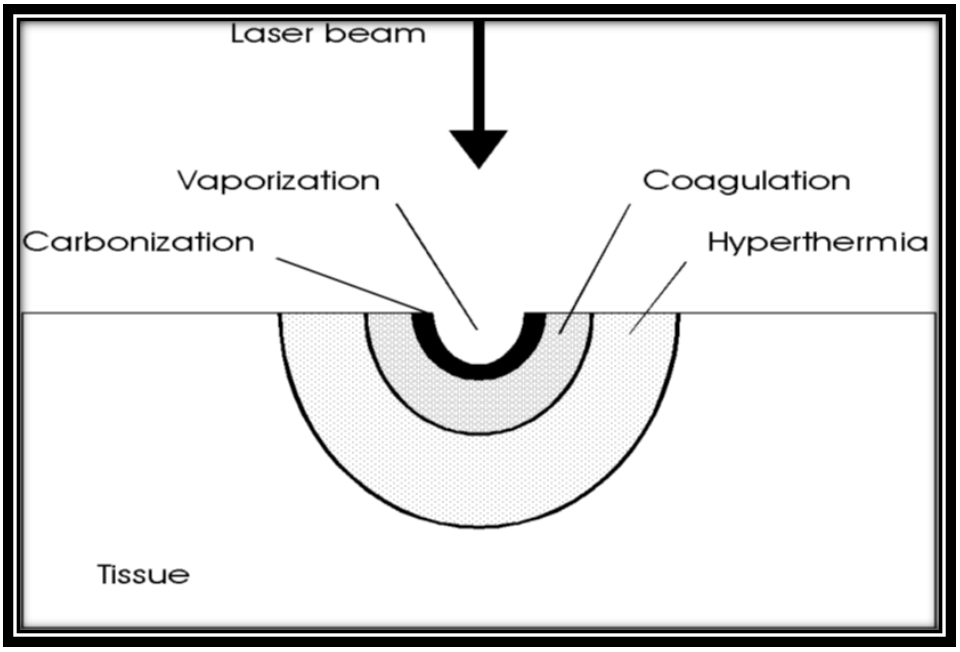


Fig. 1-16. Location of thermal effects inside biological tissue[31, 32].

- **Vaporization:** At 100◦C, inter and intracellular and interstitial water in tissue is vaporized. This destructive phase transfer results in expansive volume change, leading to localized microexplosions resulting in a jet of steam that expands and then explodes the surrounding matter into small particles, which can aid the ablative effect of the laser by dissociating large tissue elements, especially seen in laser use in hard dental tissue ablation, where complete layers of tooth substance are removed. Vaporization is sometimes also referred to as a thermomechanical effect due to the pressure build-up involved. the resulting ablation is called thermal decomposition. The optimum beam conditions are a large spot size and high power density to achieve a higher rate of tissue removal, while cutting with the laser is basically a thin linear vaporization produced by combining a high power density with as small a spot size as possible. Efficient cutting is achieved by moving the beam at a rate that produces the desired cut, yet that minimizes secondary thermal effects in the adjacent tissue[31, 32].
- **Carbonization:** occurs when too much energy is applied and only if all water molecules have been vaporized, and laser exposure is still continuing, does the increase in temperature proceed. At temperatures

exceeding 100◦C the tissue starts to carbonize, i.e. carbon is released; leading to the blackening of adjacent tissue and the escape of smoke. The surface carbonized layer prevents normal tissue ablation by absorbing the incident beam causing heat conduction collaterally to a wide area . To avoid carbonization, the tissue is usually cooled with either water or gas. For medical laser applications, carbonization should be avoided in any case, since tissue already becomes necrotic at lower temperatures. Thus, carbonization only reduces visibility during surgery.[31, 32].

- **Melting:** Beyond 300◦C, melting can occur; depending on the target material. At the microscopic level, thermal effects have their origin in bulk absorption occurring in molecular vibration–rotation bands followed by nonradiative decay, transferring photon energy to kinetic energy of a molecule. The spatial extent and degree of tissue damage primarily depend on magnitude, exposure time, and placement of the deposited heat inside the tissue. The deposition of laser energy is a function of laser parameters and strongly depends on optical tissue properties, affecting heat generation and thermal tissue properties, affecting heat transport to unexposed tissue structures as seen in table. (1-3) [31,32].

  For thermal decomposition in tissues, it is important to adjust the duration of the laser pulse to be shorter than the thermal relaxation time in order to confine the heat within the target tissue minimizing thermal damage to the adjacent structures, to have the least possible necrosis. Thermal damage to adjacent tissue also can be kept minimal if the selected wavelength is strongly absorbed by the tissue, having the shortest thermal relaxation time[31, 32].

Table 1-3: Thermal effects of laser radiation[31].

Temperature °C	Biological effect
37	Normal
<43	Biostimulation
43-45	Hyperthermia
50	Reduction in enzyme activity
60	Protein denaturation (coagulation)
70-80	Welding
80	Permeabilization of cell membranes
100 °	Vaporization
>150	Carbonization
>300	Rapid cutting and ablation

- **Ablative Photodecomposition (Photoablation)**

Photoablation occurs when material is decomposed when exposed to high intense ultraviolet laser irradiation. Typical threshold values are 107–108 W/cm^2 at laser pulse durations in the nanosecond range. The geometry of the ablation pattern itself is defined by the spatial parameters of the laser beam. The main advantages of this ablation technique lie in the precision, its excellent predictability, and the lack of thermal damage to adjacent tissue . Only when photons from ultraviolet laser (wavelength < 350 nm) are absorbed, the energy gain is usually high enough to access an electronic state which exceeds the bond energy dissociating chemical bonds at the very next vibration. Therefore, this interaction is limited to the application of ultraviolet light31, 32.

1.10.2 Wavelength—Independent Interactions

These interaction mechanisms rely on plasma generation, at high power density 1011 -1016W/cm^2 associated with lasers operating in short pulse duration (nanosecond, picosecond). At high intensities, the electric field strength of radiation is also very large, which is sufficient to cause dielectric breakdown in the tissue. The generation of plasma with laser

pulses in the nanosecond range is thermionic emission and in the picosecond or femtosecond range is multi-photon ionization[31, 32].

1.10.2.1 Plasma—induced Ablation

Plasma-induced ablation is primarily caused by plasma ionization itself and is characterized by flashes and popping sounds during laser use. The most important parameter of this ablation is the high peak intensity which determines when optical breakdown is achieved and forces the ionization of molecules and atoms. The important feature of optical breakdown is that it renders possible an energy deposition not only in pigmented tissue but also in nominally weakly absorbing media. This is due to the increased absorption coefficient of the induced plasma. Thereby, the field of potential medical laser applications is considerably widened. Especially in ophthalmology, transparent tissues become potential targets of laser surgery. With ultrashort pulse durations, optical breakdown may still be achieved while significantly reducing plasma energy and, thus, disruptive effects[31].

1.10.2.2 Photodisruption

During photodisruption, the tissue is split by mechanical (shock wave and cavitation) effects propagate into adjacent tissue, thus limiting the localizability of the interaction zone. For pulse durations in the nanosecond range, the spatial extent of the mechanical effects is already of the order of millimeters even at the very threshold of breakdown. Two of the most important applications of photodisruptive interaction are posterior capsulotomy of the lens and laser-induced lithotripsy of urinary calculi. In general, photodisruption may be regarded as a multi-cause mechanical effect starting with optical breakdown and plasma formation. The primary mechanisms are shock wave generation and cavitation (bubbles consist of gaseous vapors inside soft tissues or fluids), completed by jet formation if

cavitation bubbles collapse in fluids and near a solid boundary as seen in fig. (1-17) [31, 32].

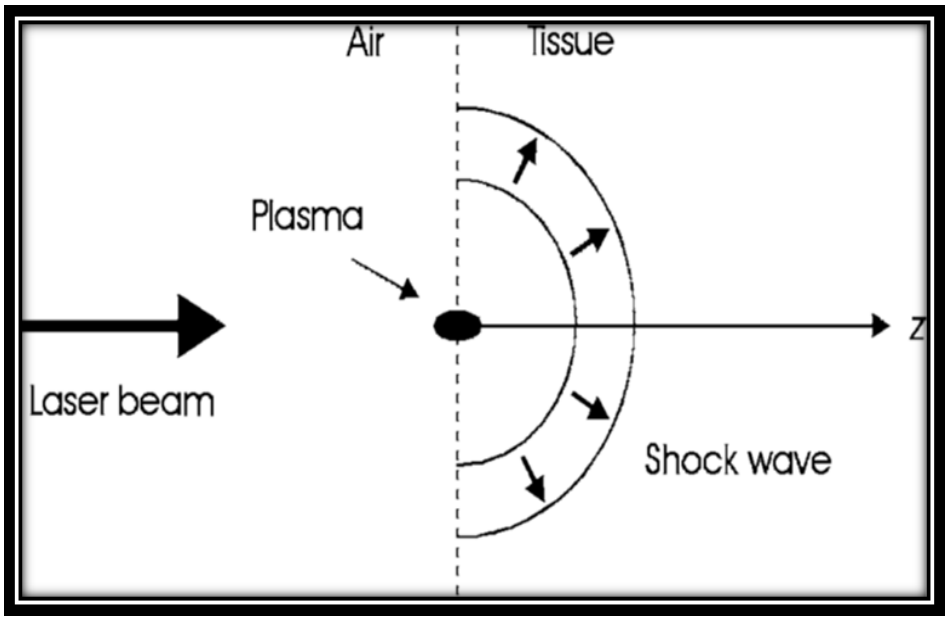


Fig. 1-17 .Geometry of shock wave generation [31].

1.11 Literature Review about the treatment modalities of RAU

1. CONSERVATIVE

A. The oral mucosa functions as a mechanical and immunological barrier. Protective mechanisms are noted in the form of increased capacity for epithelial regeneration and increased keratinization. These epithelial changes are reactive and reversible but progressive loss of normal control mechanisms leads to pre-cancerous states and oral ulcers[36].

B. Dietary modifications may also support therapeutic measures. In resistant cases of aphthous ulcers or aphthous ulcers with systemic involvement.

C. Good oral hygiene is important to prevent secondary infection of the ulcers[37].

D. Similarly patch testing may indicate that food allergy is responsible, and the diet modified accordingly[37].

E. Use of nicotine replacement therapy for people who have developed oral ulceration after stopping smoking has also been reported. Starting smoking again does not usually lessen the condition[37].

F. Trauma can be reduced by avoiding rough or sharp foodstuffs and by brushing teeth with care[37].

G. If sodium lauryl sulfate is suspected to be the cause, avoidance of products containing this chemical may be useful and prevent recurrence in some individuals[37].

2. MEDICATION

A. Standard topical treatment options that provide symptomatic relief include analgesics, anesthetics, antiseptics, anti-inflammatory agents, steroids, sucralfate, tetracycline suspension, and silver nitrate[17].

B. systemic treatment can be selected from a wide spectrum of immunomodulators that include dexamethasone,tacrolimus, azathioprine, cyclophosphamide, colchicine, prednisolone, cyclosporine A, interferon-a,tumor necrosis factor-a antagonists, antimetabolites, andalkylating agents[17].

C. Despite the many therapeutic options available for the management of RAS, no treatment is specific and definitive. Systemic and topical tetracycline regimens have been used since several decades in the treatment of RAS Traditionally, the use of doxycycline for the management of RAS was based on its antimicrobial property. However, newer properties of doxycycline such as inhibition of prostaglandin production,[17].

D. Treatment strategies therefore aim at relieving pain, promoting healing and preventing secondary infectionIn severe forms of RAS, systemic agents such as colchicine, dapsone and corticosteroids may be administered to control the symptoms. However most of these therapies are associated with side-effects or unwanted reactions. Several topical agents are available for symptom relief in less severe forms of RAS. These include antibacterial, anti-inflammatory, anti-histaminic agents, as

well as analgesics, local anesthetics and glucocorticoids ,Amlexanox 5%, a topical anti-inflammatory and antiallergic drug was found to play a significant role in the management of minor aphthous ulcers[37].

E. Amlexanox potentially inhibits the formation and release of histamine and leukotrienes from mast cells, neutrophils, and mononuclear cells. It has been shown to accelerate healing of aphthae and decrease pain, erythema and size of the lesion. Amlexanox oral paste has been specifically formulated to adhere to the oral mucosa, thus limiting the likelihood of the drug being rubbed or rinsed away with saliva [37].

F. Occasionally, in females where ulceration is correlated to the menstrual cycle or to birth control pills, progestogen or a change in birth control may be beneficial[37].

G. In cases of folate deficiency, daily folic acid supplements may prevent or reduce aphthous stomatitis reoccurrence[37].

H. If investigations reveal deficiency states, correction of the deficiency may result in resolution of the ulceration. For example, there is some evidence that vitamin B12 supplementation may prevent recurrence in some individuals[37].

I. Apart from the mainstream approaches detailed above, there are numerous treatments of unproven effectiveness, ranging from herbal remedies to otherwise alternative treatments, including aloe vera, myrtuscommunis, Rosa damascena, potassium alum, zinc sulfate, nicotine, polio virus vaccine and prostaglandin E2[37].

J. The use of natural products, including medicinal plant preparations for pain reduction and shortening of healing time of oral aphthous ulcers are gaining more attention due to their decreased side effects and drug resistance. Acacia nilotica (A), commonly known as Indian gum Arabic tree is rich in flavonoids, simple phenolics, saponins, quinines, tannins, coumarins and polysaccharidesand is used in the treatment of many diseases In India and Africa it is customarily for treating cancers, and the

plant has been also reported to be used in treatment of dental pain. Extracts of A was found to exhibit an antifungal property against candida albicans and also inhibited S. mutans. A was found to be the most active plant against bacteria as well as fungal pathogens when compared with other medicinal plants. Licorice (L), the name given to the roots and stolons of Glycyrrhiza species, has been used since ancient times as a traditional herbal remedy. L contains several classes of secondary metabolites that have numerous human health benefits and many studies have demonstrated[37].

K. Silver nitrate has also been used as a chemical cauterant[37].

L. Surgical excision of aphthous ulcers has been described, but it is an ineffective and inappropriate treatment[37].

3. LOW-LEVEL LASER THERAPY (LLLT)

A. The principle of biostimulation promoted by therapeutic lasers was introduced more than ٢٠years ago. It was first applied in dermatology, especially supplementing there pair process of skin wounds. Later, it was suggested that biostimulation could also be useful in accelerating the healing of woundsinside the oral cavity. Recurrent aphthousstomatitis (RAS) is one among the manythat falls into the wide spectrum of clinicalapplications of a therapeutic laser[5].

B. Low-level laser therapy (LLLT) was discovered incidentally in attempt to treat cancerous cells with a ruby laser and it was found thait did not kill tumor cells instead it accelerated wound healing from which the concept of photobiomodulation developed. Since then, laser therapy has been used in dentistry fordifferent applications, wound healing, aphthous stomatitis،mucositis, neural regeneration, postherpetic neuralgiasynovitis, arthritis, tempromandibular joint pathology،acute abcesses, periapical granulomas, chronic orofacial pain, and bone regeneration LLLT analgesic effects are obtained by stimulating the synthesis of endogenous

endorphins (β-endorphin), decreasing the inflammatory cytokines and enzymes, altering the pain threshold،inducing morphological neurons changes, reducing the mitochondrial membrane potential, and blocking the fastaxonal flow leading to neural conduction blockage. The anti-inflammatory effect is due to an increase of the phagocytic activity, the number and diameter of lymphatic vessels, decrease in the permeability of blood vessels and restoration of microcapillary circulation, normalizing the permeability of the vascular wall, and decreasing the edema [3].

C. On the other hand laser therapy constitutes an alternative therapy to oral diseases that present with pain and inflammatory reactions and that require tissue regeneration, since a laser provides better anti-inflammatory responses with edema reduction, pain reduction and cellular bio-stimulation. Apart from RAS, Low level laser therapy (LLLT) has been used in treatment of other mucosal ulcers as lichen planus, pemphigus vulgaris, mucous membrane pemphigoid, etc...[37].

1.12LASER SAFETY

INTRODUCTION

The purpose is to protect personnel, guests, and property from the hazards associated with lasers and laser systems[38, 39, 40].

1.12.1 PRINCIPAL INVESTIGATORS

The primary responsibility for ensuring the safe use of lasers belongs to Principal Investigators (PIs). Specifically, PIs are responsible for ensuring:

- Only authorized individuals operate lasers or have access to controlled areas during laser operations.
- Individuals authorized to use lasers have received adequate training.

- Appropriate personal protective equipment (PPE) is available and worn when necessary.
- Operating procedures include adequate safety measures.
- Lasers manufactured or modified at Caltech are properly classified and labeled.
- Proper laser warning signs are posted.
- All class 3b and 4 lasers have been registered with the Safety Office[38], [39], [40].

1.12.2 OPERATORS

Persons operating lasers are responsible for following proper operating and safety procedures and only performing operations authorized by the PI. Operators are also responsible for restricting access to controlled areas during operations[38, 39, 40].

1.12.3 SAFETY OFFICE

Members of the Safety Office are available to provide support in all aspects of laser safety, including:

- Providing training and/or training materials to laser operators.
- Classifying lasers and providing appropriate signs and labels.
- Determining proper protective eye wear and other PPE.
- Reviewing operating and safety procedures[38, 39, 40].

1.12.4 LASER HAZARDS

1.12.4.1 EYE

Different structures of the eye can be damaged from laser light depending on the wavelength. Retinal burns, resulting in partial or complete blindness are possible in the visible (400 - 700 nm) and near-infrared (700 - 1400 nm) regions. At these wavelengths, the eye will focus

the beam or a specular reflection on a tiny spot on the retina. This focusing increases the irradiance of the beam by a factor of about 100,000[41].

Laser emissions in the ultraviolet (< 400 nm) and far-infrared (> 1400 nm) regions are primarily absorbed by and cause damage to the cornea. In the near-ultraviolet range (315 - 400 nm), some of the radiation reaches the lens of the eye[41].

1.12.4.2 SKIN

Skin damage can occur from exposure to infrared or ultraviolet light. For infrared exposure, the results can be thermal burns or excessively dry skin depending on the intensity of the radiation. In the 230 - 380 nm range of ultraviolet light, erythema (sunburn), skin cancer, or accelerated skin aging are possible. The most damaging region of ultraviolet is 280 - 315 nm, also known as UV-B [38, 39, 40].

1.12.4.3ELECTRICAL

Many lasers contain high-voltage components which can present a potentially lethal hazard. Proper lockout procedures should be followed when working on high-voltage components[38, 39, 40.]

1.12.4.4FIRE

Many class 4 lasers are capable of igniting combustible materials. Care should be taken when choosing beam stops and shielding material[38, 39, 40.]

1.12.4.5HAZARDOUS MATERIALS

Laser laboratories contain many of the same hazards found in many chemical laboratories and therefore the same precautions should be taken. In addition, most laser dyes are considered to be hazardous materials and

should be handled accordingly. Laser interactions with certain materials may produce toxic fumes which must be properly vented[38, 39, 40].

1.12.5 LASERHAZARD CLASSIFICATION (2007)

Lasers and laser systems are classified by potential hazard according to a system described in the American National Standards Institute (ANSI) standard Z136.1, and in 21 CFR part 1040. A laser's classification is based on several factors including its wavelength, power output, accessible emission level, and emission duration. The level of hazard associated with each class of lasers is listed below[38, 39, 40].

The ANSI Z136.1 standard was updated in 2007 and current classifications are as follows:

CLASS 1 These are low-power lasers and laser systems that cannot emit radiation levels greater than the maximum permissible exposure (MPE). Class 1 lasers and laser systems are incapable of causing eye injury under normal operating conditions. This class may include lasers of a higher class whose beam are confined within a suitable enclosure so that access to laser radiation is physically prevented[42].

CLASS 1M Class 1M lasers produce large-diameter beams, or beams that are divergent. The MPE for a Class 1M laser can not normally be exceeded unless focusing or imaging optics are used to narrow down the beam. If the beam is refocused, the hazard of Class 1M laser may be increased and the product class may be changed[42].

CLASS 2 A Class 2 laser emits in the visible region. It is presumed that the human blink reflex (<0.25 seconds) will be sufficient to prevent damaging exposure, although prolonged viewing may be dangerous. Class 2 lasers are

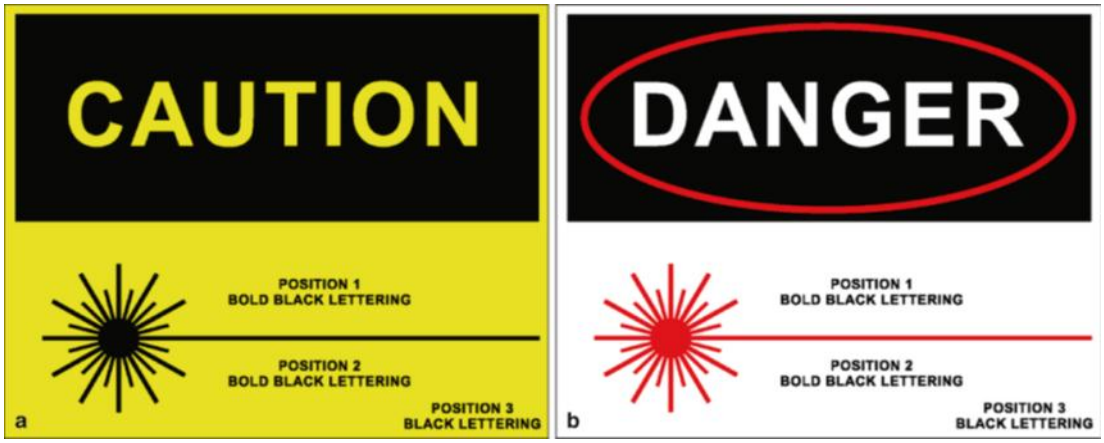
limited to 1 mW when operating in the continuous wave mode, or more if the emission time is less than 0.25 seconds[42].

CLASS 2M A Class 2M laser emits in the visible portion of the spectrum in the form of a large diameter or divergent beam. It is presumed that the human blink reflex will be sufficient to prevent damaging exposure, but if the beam is focused down, damaging levels of radiation may be reached and may lead to a reclassification of the laser[42].

CLASS 3R A Class 3R laser is potentially hazardous under some direct and specular reflection viewing condition if the eye is appropriately focused and stable, but the probability of an actual injury is small. This laser will not pose either a fire hazard or diffused-reflection hazard. Class 3R visible lasers (0.4 to 0.7 um) are limited to 5 mW when operating in continuous wave mode. For other wavelengths and pulse lasers, other limits apply[42].

CLASS 3b Class 3b lasers are capable of causing eye damage from short-duration (< 0.25s) viewing of the direct or specularly-reflected beam. Diffuse reflections from these lasers are generally not hazardous, except for intentional staring at distances close to the diffuser[42].

CLASS 4 Lasers in this class are high powered and capable of causing severe eye damage with short-duration exposure to the direct, specularly-reflected, or diffusely-reflected beam. They are also capable of producing severe skin damage. Flammable or combustible materials may ignite if exposed to the direct beam As Shown in fig. (1-18)[42].



(Fig.1.18) distinction between appropriate laser warning signs for (a) Class 2 and (b) Class 3 and 4 lasers [43].

1.12.6 CONTROL MEASURES

GENERAL This section describes administrative, procedural and engineering measures which can reduce the chance of a laser-related incident. These measures should be considered when evaluating a class 3 or 4 laser facility. Although some items are appropriate for all facilities (e.g. posting proper warning signs), others may not be practical for some operations[38, 39, 40.]

BEAM CONTROL Enclose as much of the beam path as possible. If practical, the entire beam path should be enclosed. As a minimum, beam stops must be used to ensure no direct or specularly reflected laser light leaves the experiment area. Laser beams should be limited to a horizontal plane which is well below or well above normal eye level. Securely fasten the laser and all optics on a level, firm, and stable surface[38, 39, 40].

REFLECTIONS Remove unnecessary reflective items from the vicinity of the beam path. Do not wear reflective jewelry such as rings or watches while working near the beam path. Be aware that lenses and other optical devices may reflect a portion of the beam from their front or rear surfaces. Avoid placing the unprotected eye along or near the beam axis. The probability of a hazardous specular reflection is greatest in this area[38, 39, 40].

POWER LEVEL Operate a laser at the minimum power necessary for any operation. Beam shutters and filters can be used to reduce the beam power. Use a lower power laser when possible during alignment procedures[38, 39, 40].

SIGNS AND LABELS The entrance to a class 3b or 4 laser facility must be posted with the appropriate warning sign. Each laser must be labeled as required by 21 CFR part 1040. These labels show the classification of the laser and identify the aperture(s) where the laser beam is emitted. Signs and labels may be obtained through the Safety Office[38, 39, 40].

WARNING DEVICES Class 4 laser facilities where the beam is not fully enclosed should have a visible warning device (e.g. a flashing red light) at the outside of the entrance which indicates when a laser is in operation[38, 39, 40].

CONTROL OF AREA Except for fully enclosed and interlocked systems, an authorized user must be present or the room kept locked during laser operations[38, 39, 40].

INTERLOCKS Many laser systems have interlocked protective housings which prevent access to high-voltage components or laser radiation levels higher than those accessible through the aperture. These interlocks should not be bypassed without the specific authorization of the Principal Investigator. Additional control measures must be taken to prevent exposure to the higher radiation levels or high voltage while the interlock is bypassed[38, 39, 40].

PERSONAL PROTECTIVE EQUIPMENT Eye protection designed for the specific wavelength of laser light should be available and worn when there is a chance that the beam or a hazardous reflection could reach the eye. Protective eye wear should be marked by the manufacturer with the wavelength range over which protection is afforded and the minimum optical density within that range. Eye wear should be examined prior to

each use and discarded if there is damage which could reduce its effectiveness. Protective eye wear generally will not provide adequate protection against viewing the direct beam of a high-powered laser. Wearing protective eye wear should not be used as an excuse for performing an unsafe procedure[38, 39, 40].

TRAINING All operators must receive training in the safe and proper use of lasers by the PI (or a person designated by the PI) before being allowed to operate a laser[38, 39, 40].

OPERATING PROCEDURES Written operating procedures should be available which include applicable safety measures[38, 39, 40].

MAINTENANCE/SERVICE Maintenance, servicing, or repair of a laser should be performed only by a knowledgeable person who has been specifically authorized by the PI to perform such work. Whenever such work involves accessing an embedded laser of a higher class, the controls appropriate to the higher class must be applied. Any laser which is significantly modified must be reevaluated to determine its classification[38, 39, 40].

1.12.7 EMERGENCY/INCIDENT PROCEDURES

EMERGENCIES follow the emergency response guide posted in the laboratory[38, 39, 40]

EMERGENCIES OR INCIDENTS INVOLVING LASERS In the event of an accident or unusual incident involving alaser:

1. TURN OFF THE LASER.

2. If there is a serious injury or fire, call x5000 and request paramedics or the fire department.

3. Notify the Safety Office. If after working hours and have the operator contact a Safety Office representative.

4. Notify the laboratory supervisor or Principal Investigator.

5. Report all injuries to the Workers' Compensation Administrator[38, 39, 40.]

Aim Of The Work 1.13

The aim of this study

- Comparism between conservative,medication &laser as treatment modalities of RAS.
- Evaluation of 940 nm wave length of the diode laser in treatment of RAU based on decrease in pain,size of the lesion,&decrease in healing time .

CHAPTER TWO

PATIENTS, MATERIALS AND METHOD

Chapter Two

Patients, Materials and Methods

2-1 Introduction

This clinical trial included a total of 21 patients with aphthous stomatitis , attending the Department of Oral and Maxillofacial Surgery, Al –imam Ali (peace upon him) hospital in Baghdad during a period of six months from (June -2018 to November -2018), the patients were examined, with documentation of the following data (table 2-1) of interest in relation to the oral ulcer : patient age and sex,medical history ,Family history, ,oral examination , lesion size ,duration and location.

Table 2-1: Case Sheet for each Patient.

Name: …….
Age: …….
Sex: ……..
Address: …….
Occupation: ……..
Chief complain: ……..
Medical history:……
Laser history ……...……
Family history ……
Present illness: …….
Intra oral examination IO: ……..
Extra oral examination EO: …….
Operation note: …….
Conservatively…….
Medication ……
LLLT……
1-size of ulcer……
2-pain scale…….
3-healing period……..
Follow up notes:
Three days: …….
Six days: ……

2.2 Sample description:

A total of 21 patients of both gender (12 male, 9 female), with age range from 9- 75yrs. were asked to co-operate in the clinical trial, the following criteria were considered during patient's selection:

2.2.1 Inclusion criteria

A. Patients with single Minor recurrent aphthous ulcer

B. Patient should be able and willing to take part in the study, follow all the instructions, and come back during the follow up periods.

C. Patients were advised to improve their oral hygiene from the time of examination till the end of the follow-up period and advised to maintain their oral hygiene habits continuously.

2.2.2 Exclusion criteria

A. Patients with Major and Herpetiform Ulcers**.**

B. Patient with any systemic disease causing oral ulcerations**.**

C. Pregnant and lactating mothers.

D. Patients who are receiving or have received chemotherapeutic drugs, Immune-modulators or systemic corticosteroids**.**

2.3 The patient groups:

A clinical trial on 21 patients between 9 and 75 years old of age was done. They were randomly assigned in 3 groups:

A.7patients treated by low level laser therapy LLLT only .

B.7patients treated by 10 ml solution aerosol (Anginovag spray) medication only .

C.7patients treated by conservatively with motivation and re assuranment and fellow up.

2.4 Sex distribution:

Patient ages ranged from 9 to 75 years (mean, 43 years), with the greatest degree of occurrence (33 %) in the fourth decade. The male was 12 and the female was 9 with male-to-female ratio was 1.33:1 see Table (2-2).

Table 2-2 .Mean Age and Sex distribution of the Study Groups.

	No. of Individuals	**Mean Age**	**Sex distribution (M/F)**	
Group 1(LLLT)	7	37,43	4(19, 04%)	3(4, 76%)
Group 2medication	7	56,43	5(23, 80%)	2(9, 52%)
Group 3control	7	34,85	3(4, 76%)	4(19,04%)
total	21	42,9	12(57, 14%)	9(42,86%)

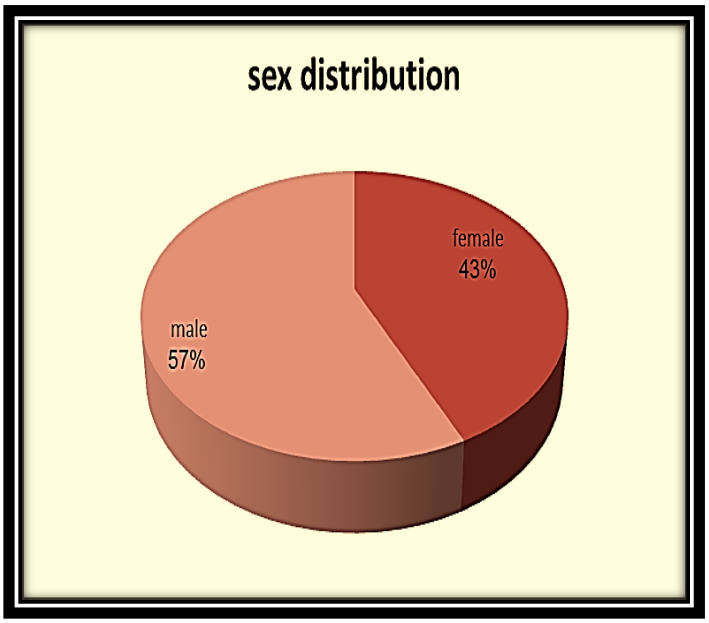


Fig. 2-1 Sex distribution of the Patients treated by Low power laser therapy LLLT only.

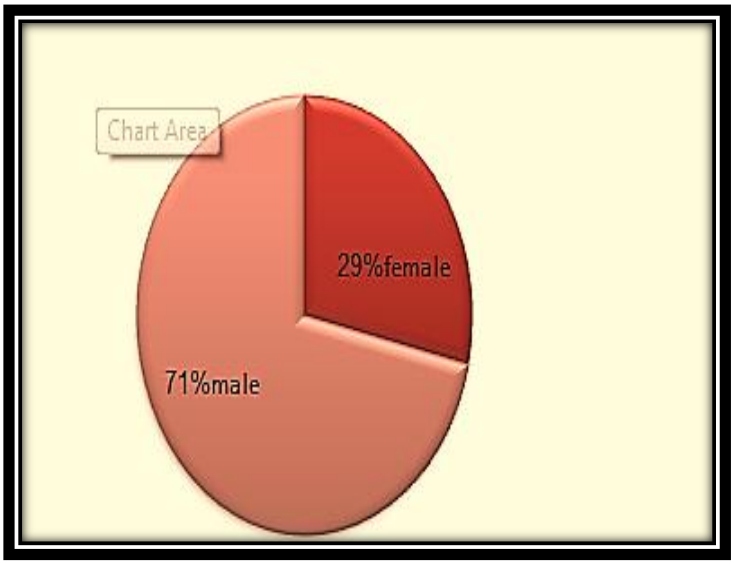


Fig. 2-2 Sex distribution of the Patients treated by Anginovag medication.

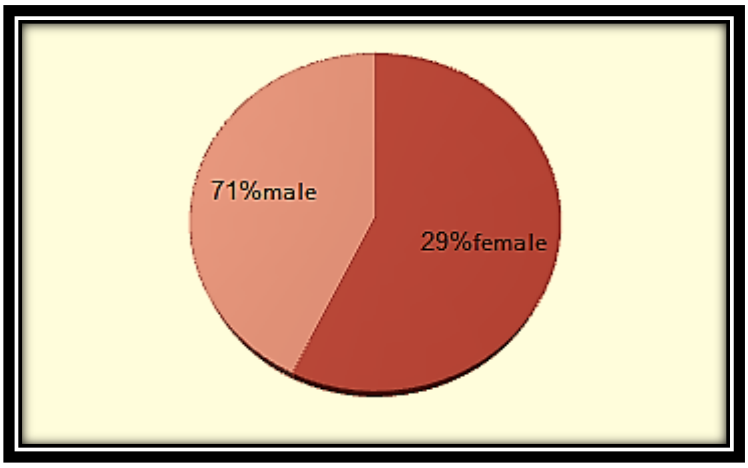


Fig. 2-3 Sex distribution of the Patients control group.

2.5 Site distribution:

The most frequently involved site was the labial mucosa other sites eight case involve the tongue, four casesmucobuccal fold the remain 2 cases involve buccal mucosa.

Table 2-3 site distribution of the Patients study group.

	labial	buccal	floor of mouth	ventral surface of the tongue	mucobuccal fold	soft palate
Group 1(LLLT)	3			2	2	
Group 2 med.	2	2		3		
Group3Control	3			2	2	

2.6Materials

2.6.1 Medications used:

The studied drugs consisted of Anginovag in a form ofAnginovg 10 ml solution aerosol (trade name isAnginovag manufactured by G Ferrrer international ,S.A,, Barcelona Spain).

Anginovag composition each 100ml contain:

i. B-glycyrrhetinic acid, 60mg
ii. Dequalinium chloride ,100mg
iii. Tyrothricin ,400mg
iv. Hydrocortisone acetate,60mg
v. Lidocaine hydrochloride ,100mg
vi. Excipient :sodium saccharin q.s. 100ml

(Fig.2.4) containers containing Anginovag drugs.

2.6.2 Armamentarium

2.6.2.1 EQUIPMENT

A sterile Tray for the Procedure Placing the following items on a sterile drape:

1-Surgical gloves.

2-Surgical masks.

3-Dental Diagnostic kit

A-mirror

B-probe

C-wiser

4- Sterile Gauze Sponges.

5-A calibrated periodontal probe.

Fig 2-5 sterile tray for the equipment of the procedure.

2.6.2.2 Medical laser system:

2.6.2.2.1 Aiming beam

The aiming beam is a visible laser diode, max 1 mW, 625 nm – 670 nm, continuous or Intermittent.

2.6.2.2.2 Diode laser

The laser used for patients was diode laser (commercial trade mark epic biolase), which emits a wavelength of 940 +/- 10 nm as seen in figure (2-6).

Figure (2-6) Gallium-Aluminum-Arsenide diode laser biolase epic

2.6.2.3 Safety:

During the work, the exposure to the direct or diffuse laser beam to the eye was avoided by using eyeglasses with (OD >5).

☒ The theater was set aside from other rooms, with one inlet to it.

☒ Goggles of optical density> 5 were available and the patient, the surgeon and the stuff wear specified goggle for the use laser.

2.7 METHOD

2.7.1 LASERGROUP

Seven patients treated by low level laser therapy LLLT only.

- Patient set on the dental chair.
- Photograph has been taken preoperative and postoperative.
- Goggle was put on the eyes of the patient also the surgeon and the stuff worn specified goggle for the use laser.

- The LLLT was applied by using Gallium-Aluminum-Arsenide diode laser device (biolase trade mark epic , U.S.A) figure (2.6)
- A power of 0.5W and wavelength 940 nm for 3 minutes (180 seconds) in cw..
- The ulcer exposure for 45second then released for 15second and repeated twice for total time 180 second in each visit and after 3days and according to signs and symptoms of the patients.
- About 2-3mm distance between the tips of the laser fiber optic tube to the surface of the ulcer.
- Perpendicular, circular motion around the ulcer.
- All the patients have been recalled within the 3 days and 6days postoperatively to check the follow-up instructions, and detect the clinical signs and symptoms following the laser therapy, for evaluation of the pain, size of the ulcer.

2.7.2 MEDICTIONGROUP

Seven patients treated by 10 ml solution aerosol (Anginovag spray) medication only.Patientsreceived one spray on the ulcer each 2-3 hour as recommended by manufacture of the drug. All the patients have been recalled within the 3 days postoperatively to check the follow-up instructions, and detect the clinical signs and symptoms following the medication, for evaluation of the pain, size of the ulcer.

2.7.3 CONTROLGROUP

Seven patients treated by conservatively with motivation and re assuranment and fellow up. All the patients have been recalled within the 3 days postoperatively to check the follow-up instructions, and detect the clinical signs and symptoms following theconservative, for evaluation of the pain, size of the ulcer.

Fig.2-7 Gallium-Aluminum-Arsenide diode laser device (biolase trade mark epic, U.S.A)

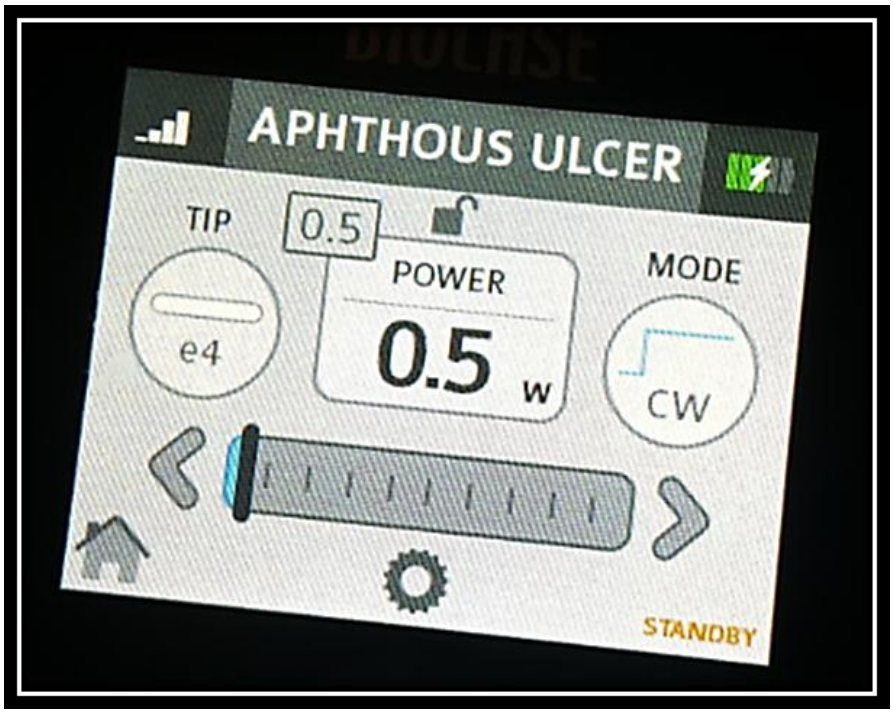


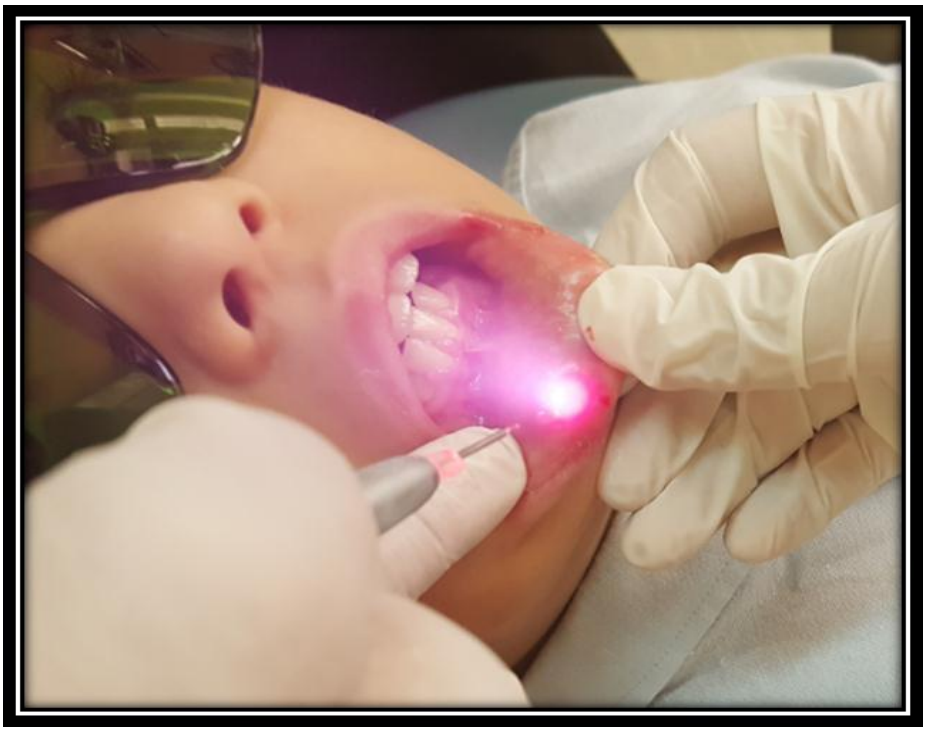
Fig.2-8 for minor recurrent aphthousulcer.A

A-laser dose parameter

B-preoperative

C- intraoperative

B



C

2.7.4 Methods of assessment

2.7.4.1HEALING PERIOD

Both pain and diameter size of ulcer and healing period were evaluated at the baseline, and after three days post treatment and six days.

2.7.4.2 ASSESSMENT OF PAIN:

Post-operative pain has been assessed by simple visual analog scale method. The patient was asked to describe pain intensity as follows:

0= no pain

5=moderate pain

10= sever pain

Visual analog scale (VAS):

It was explained to all patients how to properly register pain perception in a 100 mm visual analog scale. Beginning the day that the lesion appeared (D0) consecutively at the same time, every visit until the lesion completely disappeared.Aphthous lesion healing (ALH): The day that the lesion completely healed was registered on the chart, from the lesion intervention day, until a maximum of 6days.

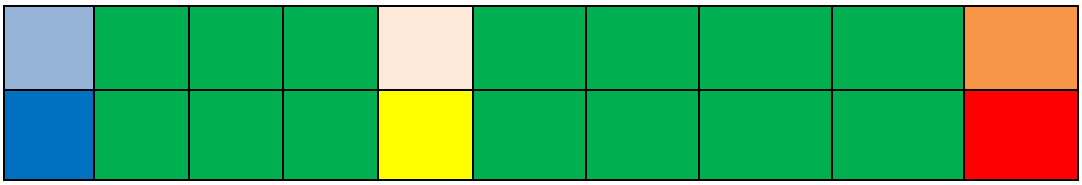


Fig. 2-9 visual analog scale method.

2.7.4.3 APHTHOUS ULCERS DIAMETER MEASURE (AUDM)

A calibrated periodontal probe was used to measure thediameter ulcer's size while the patients were placed in a comfortable sitting position. The probe is a long, tapered, rod like tool that is calibrated in millimeters with a tip.Aphthous ulcers diameter measure (AUDM): It was takenfrom the

first day it appeared Perpendicular to the widest point of lesion diameter and until the day before of its total healing .

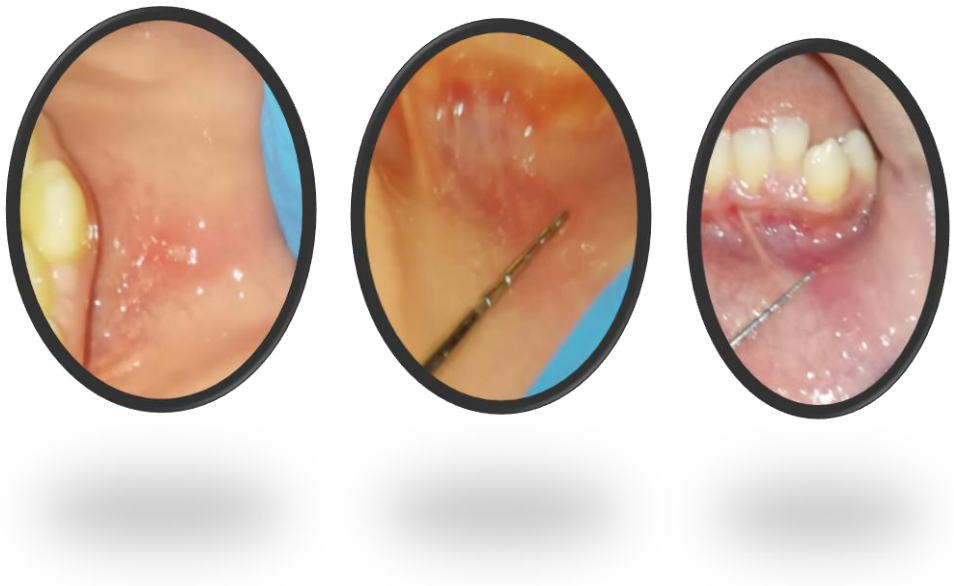


Fig 2-10 A calibrated periodontal probe was used to measure the diameter ulcer's size

2.8 Postoperative Instructions

The patients were given verbal instructions that including:

- ☒ Avoid taking hot, spicy, citrus and hard foods for a few days.
- ☒ Meticulous oral hygiene is practiced.
- ☒ Commitment to follow up appointments in the exact date.

CHAPTER THREE

RESULTS AND DISCUSSION

3.1 Results

The study was depending on comparison between three groups of patients:

a) Patients treated by Low power laser therapy LLLT only .
b) Patients treated by Anginovag medication only.
c) Patients controlgroup (conservatively).

3.1.1 Assessment of treatment result by three parameters as:

A. **Healing time**

There was significant reduction in theHealing time of the ulcer on the subsequent visits. Thus, the results of present study suggest that there was decrease inHealing time of ulcer on subsequent visits more in Group 1 followed by Group 2 and last by Group 3.

B. **Size of Ulcer:**

There was significant reduction in the size of the ulcer on the subsequent visits.Thus, the results of present study suggest that there was decrease in size of ulcer on subsequent visits more in Group 1 followed by Group 2 and last by Group 3.

Table 3-1: Shows Intra-Group comparison of Size ofdiamter Ulcer.

	Day 0	**Day 3**	**Day 6**
Group 1Laser	4.00mm	2. 00mm	0.00mm
Group 2Med.	4.06mm	2.50mm	0.30mm
Group 3Cont.	4.15mm	3.00mm	0.50mm

Figures (3-1) represents lesion at the treatment session, and complete healing of the same lesion without scar after 72 hours.

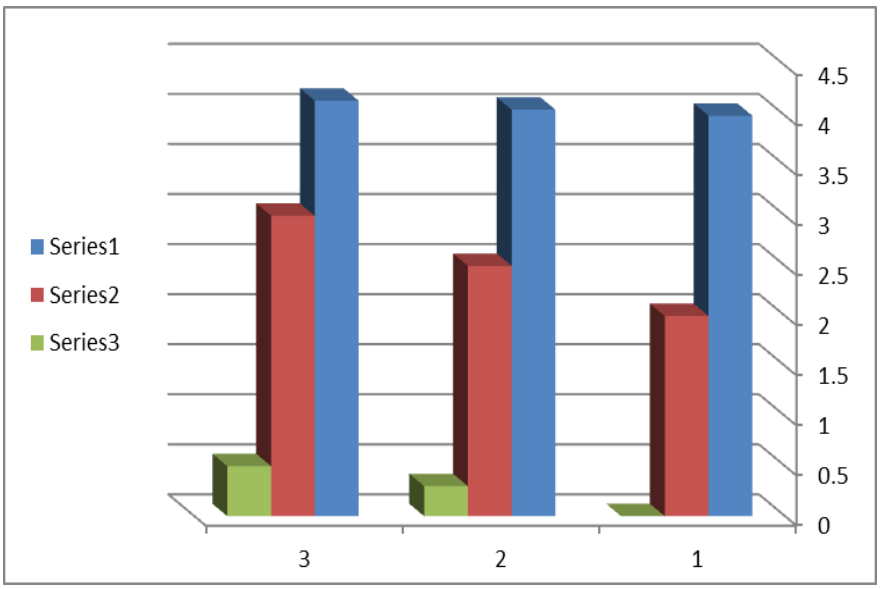


Fig.3-1Shows Intra-Group Size of Ulcer.

There was a highly reduction in the lesions duration in the irradiated ulcers.

Studied the effect of low-power lasers on conditions such as sores and ulcer wounds and concluded that laser therapy is effective at repairing tissue and controlling pain, although the outcomes may be influenced by the wavelength of the laser.

C. Pain VAS score:

Table3-1 and figure 3-2 Shows Intra-Group comparison of Pain VAS score at Day 0 - Before and after treatment. There were immediate changes in the pain scores of the laser group just after diode laser application. The patient felt pain relief and decreased pain scores in a range (6-8) and the mean reduction in the pain scores is as high as 6 in a scale of (1-10) in table (3-2).

Table 3-2 .Shows Intra-Group comparison of Pain VAS score

	Day 0 Before Treatment	Day 0 After Treatment
Group 1	8.02	4.00
Group 2	8.67	6.50
Group 3	8.63	7.75

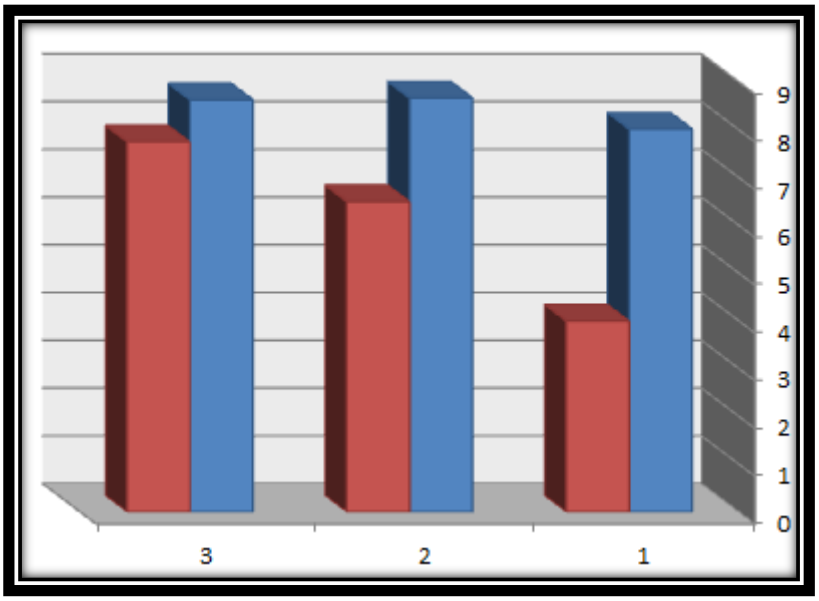


Fig.3-2 Pain VAS score at Day 0 - Before and after treatment.

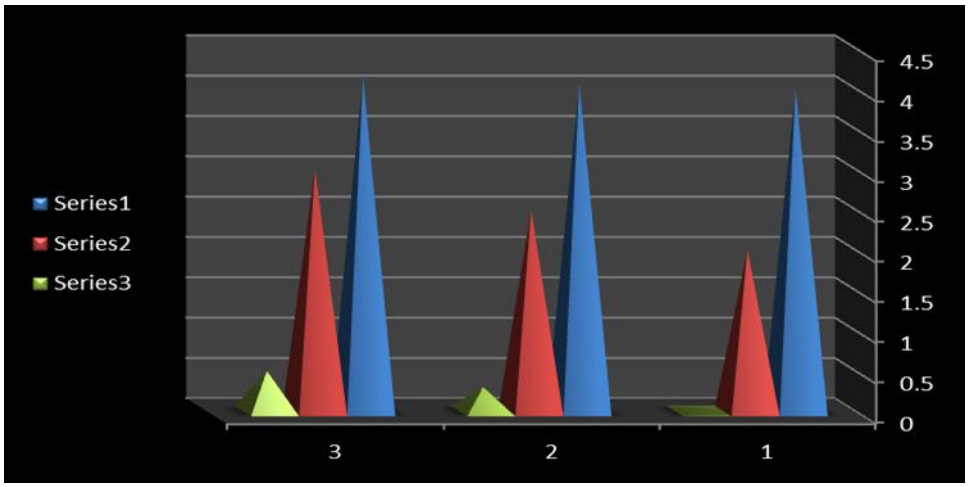


Fig.3-3 showed significant reduction of pain score and ulcer diameter with the application of LLLT in group A

3.1.2 Clinical observations

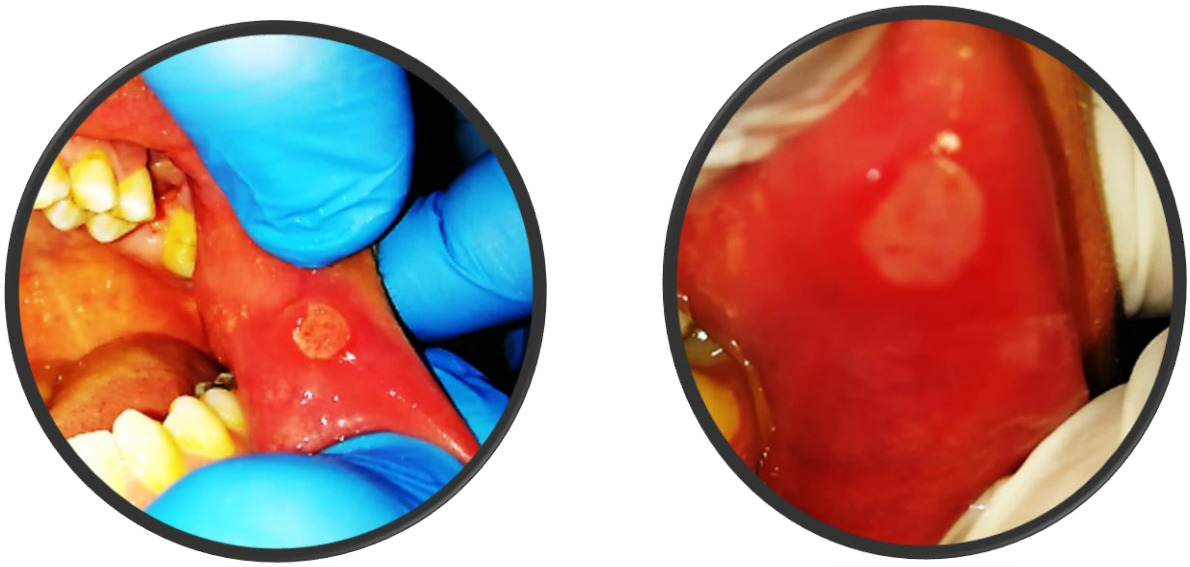
1. Immediate pain relief

2. High patient acceptance.

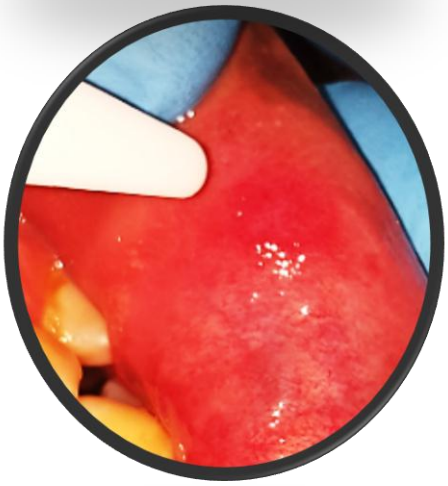
3. No harm to the surrounding tissue laser

3.1.3 Time taken:

The time taken for the treatment for the laser group ranged from 3 to 5 minutes with an average of 4 minutes where less time needed in group medication and control group.



A B



C

Fig. (3-4) patient with aphthous ulcer in the buccal mucosa left of the check

A .preoperative (laser group)

B . after 3days

.

AB **C**

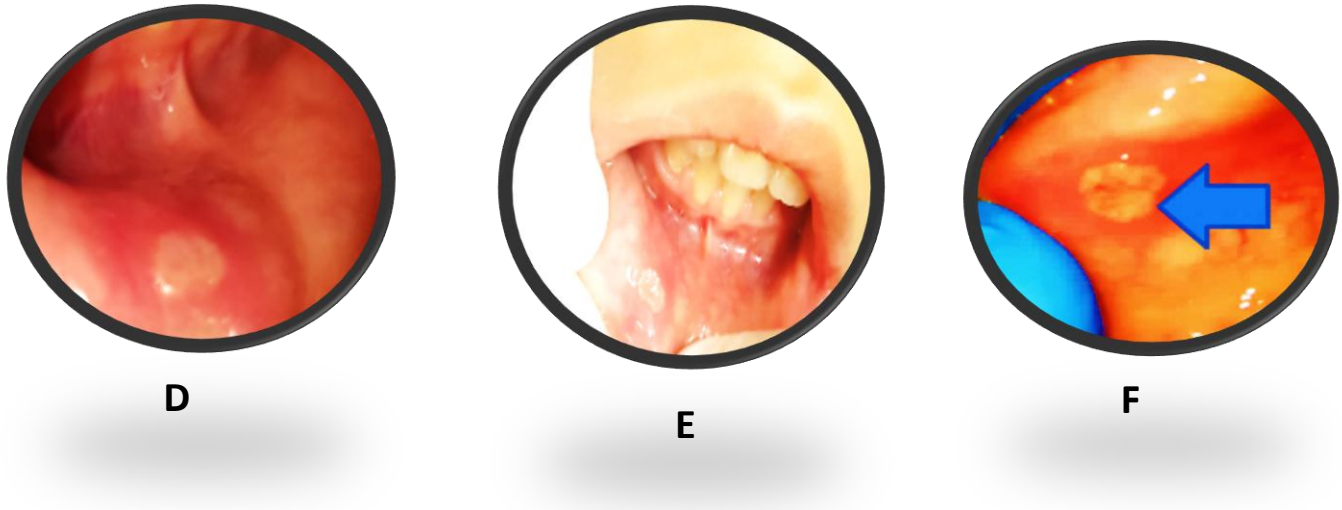


Fig. (3-5) aphthous ulcer

A. preoperative(laser group

B. intraoperative ulcer with LLLT.

C. laser dose parameter for recurrent aphthous ulcer.

D. aphthous ulcer after 3days.
E. after 6days with LLLT
F. after 6days with LLLT

3.2 Discussion

RAS is a common oral disorder affecting 5%-66% of examined adult patient groups. Although many exacerbating factors have been identified, the cause as yet remains unknown. The difficulty in establishing the exact nature of aphthous stomatitis is in part because of the nonspecific histopathologic features of the ulcers, and the lack of any reproducibly identifiable cause, endogenous or exogenous. Although the trigger of an episode of RAU is unknown, [17]

3.2.1 Sign & symptoms &discomfort for the patient with RAU

Although patients in most of the cases have spontaneous healing within 14 days, treatment is often indicated to mainly control pain and to reduce the duration and severity of symptomatic outbreaks, especially during the periods of quiescence and exacerbation (period of increased pain and sensitivity) of RAS lesions. Pain usually reduces after 4–5 days, but during this period it can cause discomfort to a patient during eating, swallowing, speaking and wearing dental prostheses. Pain control is also very important in order to maintain patient physical and mental condition, further improving effectiveness of the therapy. To date, it is widely accepted that the first-line therapy for patients with RAS are topical corticosteroids, even though the evidence of their efficiency is not overwhelming. Recently, laser as a new treatment modality has been introduced.[15].

3.2.2 Laser group

Reduction in the size of the ulcer on the subsequent visits. This is in accordance with **Muhannad A. Kashmoola** (2005) and **Hadeel Salman** et al (2008) who had observed significant decrease in size of lesion. The current study provides evidence that a single session of LLLT is effective in

management of RAS than conventional medical treatment, as the results showed significant reduction of pain score and ulcer diameter with the application of LLLT in group A than group B, C. these findings look similar to those of De Souza et al As the result, a reduction of pain (75% of the patients) in the same session after laser treatment was demonstrated. Further, a total regression of the lesion was achieved 4 days following laser irradiation (40% of the patients) compared to prolonged time (5–7 days) required to obtain the same results in the corticosteroid group. The authors concluded that under the conditions administered in the study, In GaAlP laser therapy can be safely used as the advanced RAS treatment technique in order to achieve immediate analgesia and faster healing of RAS lesions.[15]

On the other hand healing was uneventful and all the patients experienced spontaneous reduction in pain recorded on VAS immediately after treatment. The lesion healed completely within 3-4 days A follow‑up for 1 year showed no recurrence in these patients.[8]

The result agreement with recently study, which stated LLLT, was suggested to be one of the important treatment modalities for wound repair processes and pain control. [16]

the result was also in agreement with **De Souza TO et al (2010)** [51] reported that LLLT InGaA1P diode laser can cause reduction in pain and a total regression of the lesion after days and it was reported that low level laser can decrease the healing time, pain intensity and also decrease the time of pain relief in patients with aphtae. [45]

The patients reported significantly less pain as well as less functional complications after LLLT therapy. Furthermore, they stated that they experienced faster healing compared with the usual medication therapy. [46]

☒ REDUCTION IN SIZE OF ULCER

There was significant reduction in the size of the ulcer on the subsequent visits 3 and 6days. This is in accordance with **Muhannad A. Kashmoola (2005)** and**Hadeel Salman** who had observed significant decrease in size of lesion**.**[16]**.**Thus, the results of present study suggest that there was decrease in size of ulcer on subsequent visits more in Group 1 followed by Group 2 and last by Group 3.

☒ HEALING TIME

Although aphthous heals itself in 10-14 days, but still the ulcer is treated to reduce morbidity and healing time. On the other hand, clinically studies explained different mechanisms through which LLLT can accelerate wound healing. These mechanisms includes: local vasodilatation and increased of blood flow, cellular bio-stimulation, in addition to analgesic and anti-inflammatory effects. [16]

On the other hand differences between low level laser therapy and triamcinolone acetonidekenalog on healing of recurrent aphthous ulceration is that the laser light shows activation of suppressor T-lymphocyte which inhibits B-lymphocytes from antibody production and then decreased production of histamine and kinins that are responsible for inflammation. [6]

Further, a potential biostimulation of underlying and surrounding cells, increased collagen organization and promoting of growth factors and cytokines in response to laser irradiation have been demonstrated. [15]

☒ REDUCTION IN PAIN INTENSITY

In The present study, reduction in the pain intensity, VAS score was evaluated in all the Groups before and after treatment at day 0 and 3days

and 6days. Moreover, researchers claimed that LLLT is effective in pain reduction and they provided some explanations such as: the role of LLLT in increasing the production of opioid peptides, decreasing the histamine release, reducing the prostaglandin and bradykinin production, increasing local circulation and oxygen supply, as well as blocking of the action potential generation in the primary afferent neuron.[16]

The results are in accordance with study conducted by Muhannad A. Kashmoola(2005), HadeelSamanet al (2008), Khademi H et al (2009)[54], De Souza TO et al(2010)[51] who have concluded that 75% of the patients reported a reduction in pain in the same session after LASER treatment**.** [16]

It is well-known that LLLT causes immediate analgesia in various painful oral lesions. To date, there are several suggested mechanisms for pain reduction following LLLT application, such as effect in modulating key factors of inflammation, reduction of the prostaglandin E2 level, inhibition of cyclo-oxygenase, and/or lymphocyte metabolism that could lead to reducing of edema, and further reduction of inflammatory processes. [15.]

It was shown that release of endogenous pain relievers – endorphins and enkephalins, the increase in production of serotonin and suppression of bradikinin activity . It has been also shown that laser therapy increases systemic micro-circulation by nitric oxide synthesis, causing the reduction in swelling and pain. Even though, there are several potential mechanisms proposed, the real underlying mechanism following laser therapy for pain reduction is yet to be determined. It is believed that not just one, but two or more coexisting mechanisms or their combination are responsible for the beneficial outcome of LLLT in achieving analgesia. Apart from documented analgesic effect, LLLT is successfully applied for tissue healing, mainly due to successful hemostasis, sterilization and anti-inflammatory effect[15].

According to the results of our study, the clinical parameter of pain was reported by patients to be less at the sites treated with laser therapy than at the other control sites. This effect is in agreement with results of another study in which 10 patients treated with 940 nm GaAs laser.[3]

The results are in accordance with study conducted by Sana Mirzaa[45] we reported some preliminary data about LLLT for patients in which most of the patients reported an immediate pain relief after the first sitting, and all of them reported a complete resolution of symptoms at the end of the laser sessions, even if some lesions had only a partial clinical response.[44]

3.2.3 Group 2 with medication

Pain intensity was less as compared to the intensity before treatment In addition, Topical corticosteroids such as hydrocortisone in the anaginovag spray are effective and have two modes of action;

- anti-inflammatory action and specific blocking effect of T-lymphocyte epithelial cell interaction. On the other hand, the mechanism of action ofTopical corticosteroids results partly from vasoconstriction; the vasoconstrictions may be a direct or indirect effect exerted by the reduction of catecholamine, prostaglandin, or histamine levels at a target cell sites.
- The anti-inflammatory effects ofTopical corticosteroids also may result from interference with the migration of polymorph nuclear leukocytes through the capillary walls and from decreased and adherence of WBCs to the capillary endothelium. This drug also exerts anti-inflammatory effects by interfering with the function of lymphocytes and macrophages and by decreasing the action of lymphokines. TheTopical glucocorticoids also decrease cell membrane permeability, impair the release of toxins or lysosomal enzymes, and inhibit the release or action of other Chemical mediators during the inflammatory process. These mediators normally

contribute to increase vascular permeability and subsequent changes including edema, leukocyte migration and fibrin deposition.[6]

Most steroids will provide short term pain relief, and

1. some have the problem of being prescription **medications**.
2. being **costly** and
3. having the potential for significant **side effects** and systemic implications.[6]

3.2.4 Group conservative treatment

There was only slight reduction in pain intensity after 3days and 6days also duration of pain was shortest.

3.2.5Comprisem with other studies

This is in accordance with **Muhannad A. Kashmoola**(2005) and **Hadeel Salman** et al (2008) who had observed significant decrease in size of lesion.De Souza TO et al (2010) reported that LLLT InGaA1P diode laser can cause reduction in pain and a total regression of the lesion .[45]

Table 3.3 Effects of low-level laser therapy (LLLT) treatment of recurrent aphthous stomatitis (RAS).[4 51 58 59, 60]

Table 4

Effects of low-level laser therapy (LLLT) treatment of recurrent aphthous stomatitis (RAS)

Author and the year of the publication (reference)	Laser device (wavelength, emission mode)	Laser parameters	Anaesthesia prior to irradiation	Oral gel prior to irradiation	Laser distance (between laser and RAS lesion)	Laser application	Observation period and follow-up	Treatment outcome
Zand et al. 2009. [5]	CO_2 laser (10.600 nm) continuous emission mode	Power: 1W Irradiation time: 5-10 s	No	Yes	5–6 mm (circular motion)	Single	Before Immediately after, and 4h, 8h, 12h, 24h, 48h, 72h and 96h after irradiation	Immediate pain relief
de Souza et al. 2010. [6]	InGaAlP diode laser (670 nm) continuous emission mode	Power: 50 mW Energy density: 3 J/cm^2 Irradition time: 60 s	No	No	Touching the surface of RAS	Daily (once *per* day) on consecutive days	Before Immediately after irradiation and every day up to 10 days	Immediate pain relief Enhanced healing
Zand et al. 2012. [28]	CO_2 laser (10.600 nm) continuous emission mode	Power: 1W Irradiation time: 5-10 s	No	Yes	5–6 mm (circular motion)	Single	Before Immediately after irradiation and every day until the resolution of signs	Enhanced healing
Prasad et al. 2013. [29]	CO_2 laser (10.600 nm) continuous emission mode	Power: 0.7 W Irradiation time: 5-8 s	No	Yes	5–7 mm (spiral motion)	Single	Pain: Before Immediately after and 24h after irradaition Healing: Before-3-4 days after irradiation and up to 14 days	Immediate pain relief Enhanced healing

3.2.6 Parameter with same laser

The clinical parameter of pain was reported by patients to be less at the sites treated with laser therapy than at the other control sites. This effect is in agreement with results of another study in which 10 patients treated with 940 nm GaAs laser.[3]

3.2.7 Using of other laser

In the literature, four types of lasers have been used to treat aphthous ulcers: **CO2**, **Nd:YAG**, **diode** and **GaAlAs**. Although all of them have succeeded in providing immediate pain relief to patients. Although all of them have succeeded in providing immediate pain relief to patients،**CO2** lasers have the unique advantage of requiring a very short exposure time (5–10 s). [1]

Diode laser wavelength λ=810-980nm approximate the absorption coefficient of soft tissue pigmentation (melanin, hemoglobin an doxyhemoglobin). Therefore, the light energy from the diode is highly absorbed by the soft tissues and poorly absorbed by teeth and bone. A 940 nm laser can be used to coagulate, cut or ablate soft tissue, in a contact mode for enhanced surgical precision and tactile feedback, or in a non-contact mode.[18]

Other studies in the literature used different ranges of power in their treatment of minor RAUs (60mW and0.5W). Furthermore، the studies differed in other respects as well: the authors used very similar wavelengths in their treatments: 809 nm and 810nm.In their meta-analysis, **Enwemeka et al. (2004)** studied the effect of low-power lasers (<500mW) on conditions such as sores and ulcer wounds and concluded that laser therapy is effective at repairing tissue and controlling pain, although the outcomes may be influenced by the wavelength of the laser.[47]

Some studies concerning acute pain also revealed that lasers operating at infrared wavelengths led to more effective pain reduction. Other studies in the literature that were not selected for this review once were not controlled clinical trials used other laser wavelengths, including 633nm670nm, and 904nm. These studies did not find significant differences in their results. Strong evidence that wavelength plays an important role in the final results of RAU treatment. Future studies are encouraged to test the influence of different wavelengths on pain control and reducing the sizes of RAUs. The laser parameters described by the authors were GaAlAs semiconductor laser with a wavelength of 809 nm, 60mW,‹1800Hz, a duration of 80 seconds per treatment, and a dose of 6.3 J/cm2. [47]

Other studies in the literature duration of action was noted, both after diode laser at 0.5w in ncc mode application and benzocaine 20% gel application. It was observed that diode laser at 0.5w in ncc mode application had rapid onset of 1-2 minutes and duration of pain free period after diode laser at 0.5w in ncc mode application was 40-50 minutes. [48]

In comparism with our study laser unit was set at an output power of 0.5W, wavelength of 810 nm, applied in Non-Contact, Continuous (NCC) mode with a distance of 2-3mm between the LASER tip and ulcer surface. The LASER beam was applied in a continuous sweeping motion so as to cover the entire ulcer surface.[48]

In addition to, Different kinds of laser were successfully used in studies for treatment of RAS. The **GaAlAs** diode laser‹**He-Ne** laser, **argon** laser, **InGaAlP** laser, **Nd:YAG** laser, **diode** 830 nm GaAs (904 nm), CO2, diode laser were used in case reports and studies. For cases with aphthous like lesion in Behçet syndrome, CO2 laser and GaAs (904 nm) were used successfully. For cases with aphthous-like ulcer in AIDS (Acquired Immune Deficiency Syndrome) cases, diode 660 nm laserwere used with good result .[49]

Although the assessed literature demonstrated significant analgesia and enhanced RAS tissue healing following laser therapy without any reported side effects .areduction in the sensation of pain associated with aphthous ulcers using an Nd:YAG laser (2 W, 25 Hz, non-contact 50–60 seconds) is described by **Blandowski et al (2014)**. the result here was an almost immediate analgesic effect (24 h).Similar results were obtained by **Brader (2008**) in the application of an Nd:YAG laser،with comparable parameters. It can be assumed that the basic differences in the parameters of pulsed Nd:YAG and diode lasers with regard to wavelength،pulse output power and duration are not relevant for treatment success as long as the average values for irradiance, average output power and treatment duration concur (Tab4-2). Thus treatment with the infrared diode laser at 970 nm and similar average parameters produce similarly successful results [50]

In other study ,the laser was started using tip in a defocussed mode 5-8 mm from the lesion and advanced slowly toward the area end in up 2-3 mm away from the lesion, moving continuously from the periphery of the lesion to the center, The setting was initially put at 0.6 W CW for 30-45 seconds. A refractory period of 15-20 seconds between laser" was given to allow the tissue to cool down. A second and third pass with the laser was further applied to decrease the pain of the area on palpation.A second pass was done with the setting of 0.7 W CW W pulsed) for 30-45 seconds, and a third and final pass was completed with 0.8 W CW for a similar period of time.[8]

Although various types of lasers have succeeded in providing immediate pain relief to patients, carbon dioxide (CO2) lasers have the unique advantage of requiring a short exposure time (5–10 s).[1]

Table 3.4 studies included in this review[1]

dies included in this review.

Number of patients (n)	Female (n or %)	Age (mean years)	Cause of aphthous	Laser used	Control	Blinding	Frequency (Hz)/wavelength (nm/μ)	Power (W)	Energy	Duration of exposure to laser	Dose (J/cm^2)	Follow-up	Pain relief
2	$n=1$	57.5	Stress and radiation therapy	CO_2	N/A	N/A	10,600 nm	1.0–1.5 W	N/A	5 s	Not stated	1 week	Immediate pain relief more in test group
28	11	30.6 ± 4.1	Behcet's disease	Nd:YAG	Corticosteroids, Orabase	None	F = 20 Hz	2 W	2 mJ	2–3 min	Not stated	1 month	Pain relief more in te group ($p < 0.001$)
20	13	Not stated	RAS	Nd:YAG	Topical steroid	None	F = 20 Hz, 1.064 nm	2 W	100 mJ	2–3 min	Not stated	7 days	Pain relief more in te group ($p < 0.05$)
15	13	37.9 ± 10.9	RAS	CO_2	Placebo	Single	10,600 nm	1 W	Not stated	5–10 s	Not stated	96 h	Pain relief more in te group ($p < 0.001$)
10	Not stated	35.6	RAS	CO_2	Placebo	Single	10,600 nm	1 W	Not stated	5–10 s	Not stated	Until healing completed	Pain relief more in te group ($p < 0.001$)
1	0	25	RAS	Diode	N/A	N/A	940 nm	0.1 W	Not stated	1 min	3	2 months	Pain relief more in te group
25	Not stated	Male = 28.20 ± 6.11, female = 26.40 ± 7.99	RAS	CO_2	Placebo	Single	Not stated	0.7 W	Not stated	5–8 s	Not stated	2 weeks	Pain relief more in te group ($p < 0.001$)
40	Not stated	22.5	RAS	GaAlAs	Placebo	Single	809 nm	60 mW	Not stated	80 s	6.3	3 days	Pain relief more in te group ($p < 0.001$)
180	82.8%	43.01 ± 1.25	RAS	Diode	Placebo	Single	658 nm	27 mW	Not stated	1.14 min	[illegible]	5 days	Pain relied more in t test group ($p < 0.001$)

3.3 Limitations

Although the results of the study are encouraging, there were a few limitations worth considering .

A. The current study may be limited by the small sample size, which limits generalization. Therefore, large sample size is recommended.
B. The application of the laser & medicament to the posterior regions of the oral cavity was relatively difficult because of access.
C. Pain data were derived from subjective assessment, so there could be interindividual variations in the perception of pain. As the pain scale sheet was given to the patient for marking the post treatment percentage of pain each day until the ulcer healed, subjects who were illiterate faced problem and had to seek help from other literate individuals in the family.

3.4 Conclusions

☒ LLLT is more effective in producing great reduction in pain, ulcer size and duration of the apthous ulcer when compared with symptomatic treatment.
☒ In view of the discoveries of the present study, it can be presume that LLLT is a successful methodology for the treatment of aphthous ulcers. LLLT gives immediate pain relief and patient become more comfortable in swallowing and eating.

3.5 Suggestions for future studies:

☒ Further study on larger sample is needed in this field.
☒ A combination therapy of LLLT with medication is to be tried for controlling postoperative complaints which containing reducing of pain and decrease edema.
☒ Evaluation of other types of LLLT machine with different dose of laser exposures Therefore, future studies need to observe the efficacy of LLLT

on ulcers in patients who are smokers and those with systemic conditions which may lead to manifestation of oral ulceration

- ☒ Application of the same study design with different types of oral ulcer like lichen planus.
- ☒ Further studies are needed to evaluate the influence of LLLT with different wavelength, output powers and energy density.
- ☒ Used for patient with immunosuppression and chemotherapy, as those patient reliable for oral developing of such type of ulcer.

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وزارة التعليم العالي والبحث العلمي

جامعة بغداد

معهد الليزر للدراسات العليا

علاج التهاب الفم القلاعي البسيط المتكرر بأستخدام ليزر الدايود (٩٤٠نانومتر)

(دراسة سريرية)

دراسة مقدمة إلى جامعة بغداد-معهد الليزر للدراسات العليا

كاستكمال لمتطلبات الحصول على درجة الدبلوم العالى في

الليزرفي الطب /جراحة الوجه والفكين

الباحث

حسين غالب غالي

اختصاص جراحة الفم والوجه والفكين

باشراف

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١٤٤٠ هجري

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الخلاصة

الخلفية – المسببات الدقيقة للقرحة القلاعية المتكررة غيرمعروفة،إدارةالقرحةالقلاعيةالمتكررة ليست دائما مستقيمةللأمام،التهاب الفم القلاعي المتكررة شائعةجدا وقدتختلف في الحجم من صغيرة جدا الى كبيرةجدا.

الهدف- تقييم انخفاض شدة الألم ومدة تخفيف الألم ، وانخفاض حجم القرحة ، ومدة التئام القرحة(وقت الشفاء) في المرضى الذين يعانون من التهاب الفم القلاعي المتكرر بعد تطبيق تضخيم الضوء منخفض المستوى بواسطة انبعاث الإشعاع المحفز العلاج مقارنة معالموضعية انجينوا فيك رذاذ الدواء ومجموعة التحكم.

المواد والطرق - تم تقسيم إجمالي ٢١ فرد تم تشخيصهم على أنهم التهاب الفم القلاعي المتكرر إلى ثلاث مجموعات متساوية كما يلي:

المجموعة الاولى: تم علاج القرحة القلاعية البسيطة من خلال إعطاء تضخيم الضوء منخفض المستوى بواسطة انبعاث الإشعاع المحفزباستخدام شبه الموصلات .

المجموعة الثانية: تم علاج القرحة القلاعية البسيطة بواسطة دواءانجينوا فيك الموضعي.
المجموعة الثالثة : تم علاج القرحة القلاعية الصغرى بواسطة العلاج التحفظي .

النتائج- في هذه الدراسة التجريبية العشوائية المتحكم بهاتضخيم الضوء منخفض المستوى بواسطة انبعاث الإشعاع المحفزباستخدام شبه الموصلاتيسبب انخفاضًا كبيرًا في شدة الألم الناتجة عن القرحة القلاعية البسيطة وبالتالي تقليل المراضة ، هناك أيضًا تحسن كبير في انخفاض حجم ووقت الشفاء من القرحة بالمقارنة مع دواء رذاذ انجينوا فيك ومجموعة التحكم.

الخلاصة - على الرغم من استخدام طرق العلاج المختلفة ، ولا يستخدم تضخيم الضوء منخفض المستوى بواسطة انبعاث الإشعاع المحفز بشكل شائع لعلاج القرح القلاعية ، إلا أن هذه الدراسة توحي بأن استخدام تضخيم الضوء منخفض المستوى بواسطة انبعاث الإشعاع المحفز سيكون طريقة علاج آمنة وفعالة لمرضىالقرحة القلاعية البسيطة.