Oral Surgery: Avoiding Acute Complications and Overcoming Hurdles to Future Treatment

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Definition of Surgery

"Surgery" means a procedure performed for the purpose of structurally altering the human body by incision or destruction of tissues…."

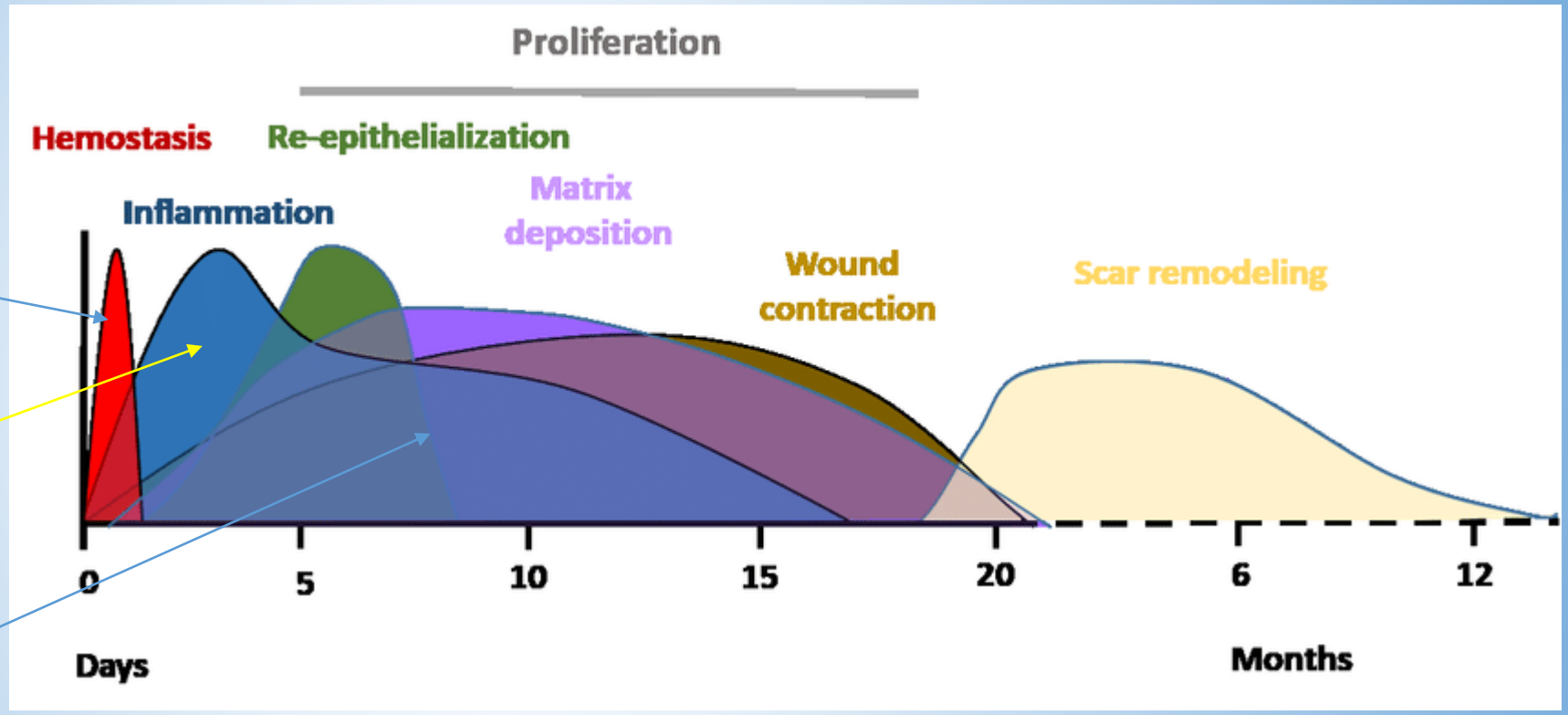
American Medical Association House of Delegates 2007

Stages of Tissue Response to Trauma

Bleeding/Clotting
12 – 24 hrs

Acute inflammation
peaks in 2 – 3 days

Granulation tissue
(ECM) deposition



Mohtadi 2021, https://www.researchgate.net/figure/Typical-timescale-and-phases-of-acute-wound-healing-stages-in-young-adult-humans_fig1_348907930

Oral Surgical Wound Healing by Intension

Primary Intension:

Clean wound with minimal tissue loss, edges can be approximated and sutured

eg. Soft tissue biopsy

Secondary Intension:

Tissue loss with contamination, wound left open to heal

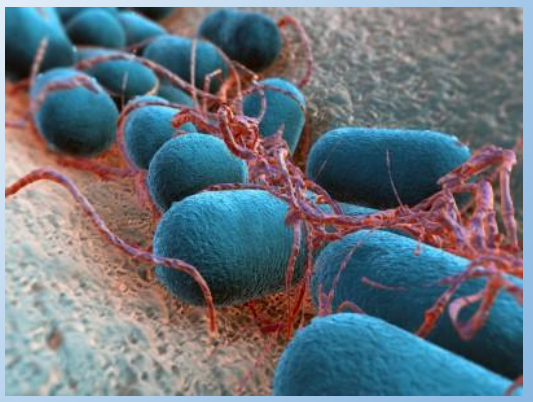
eg. Extraction without closure

Physiology of traumatic procedures: Effect on Soft Tissues

Trauma results in cellular damage – loss of integrity and function

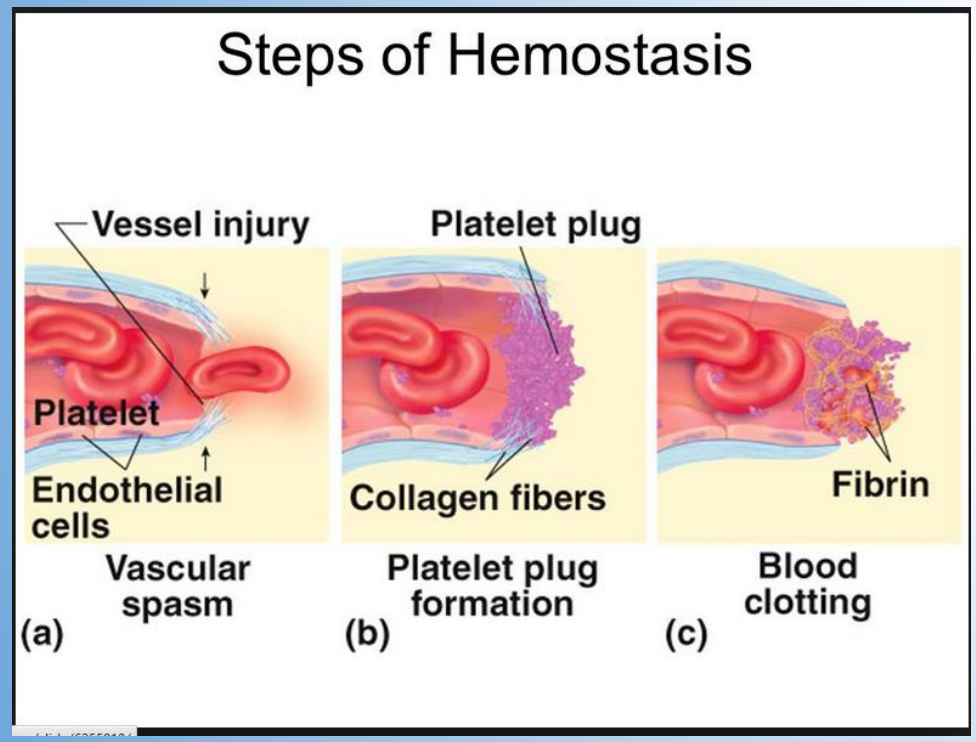
Blood vessels compromised - bleeding

Surface barrier – invasion of pathogens



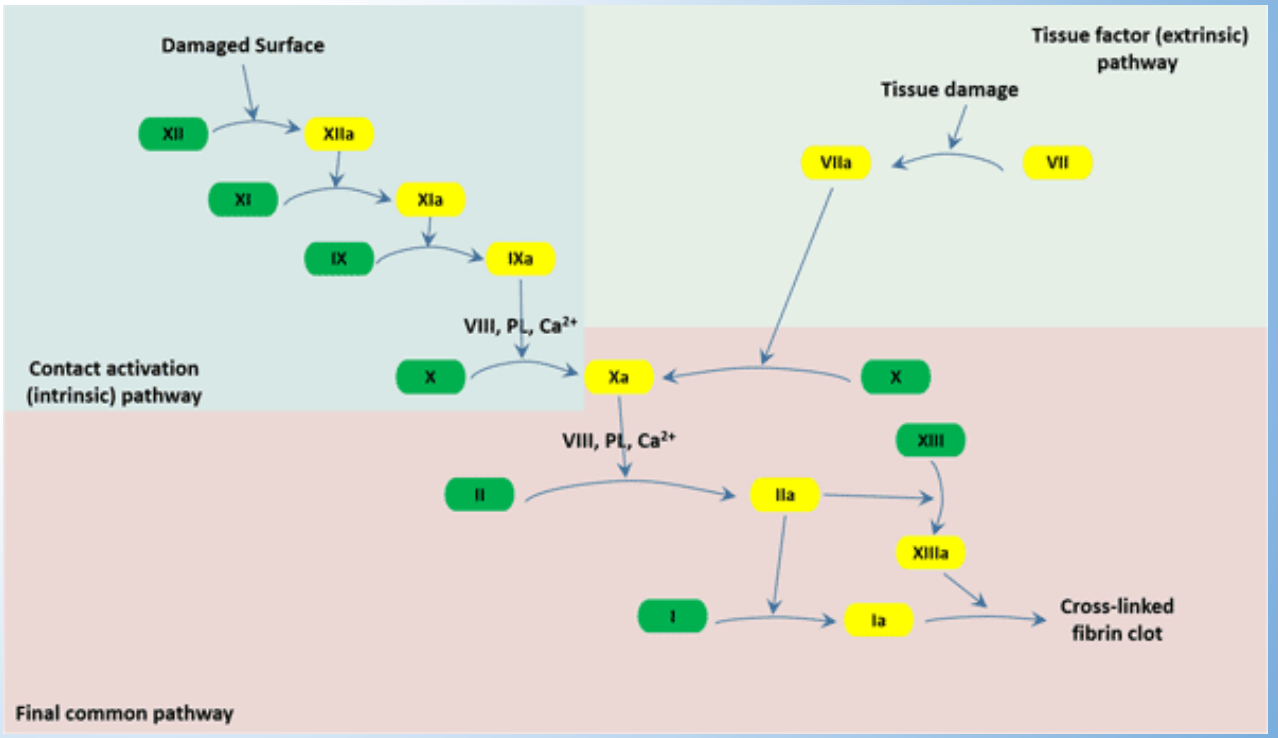
Hemostasis

Vascular Response



https://quizlet.com/268611760/hemostasis-blood-physiology-chapter-11-the-blood-diagram/

Coagulation Cascade



https://www.cusabio.com/c-16412.html

Inflammation

- Signs of Inflammation:

  (Celsus tetrad)

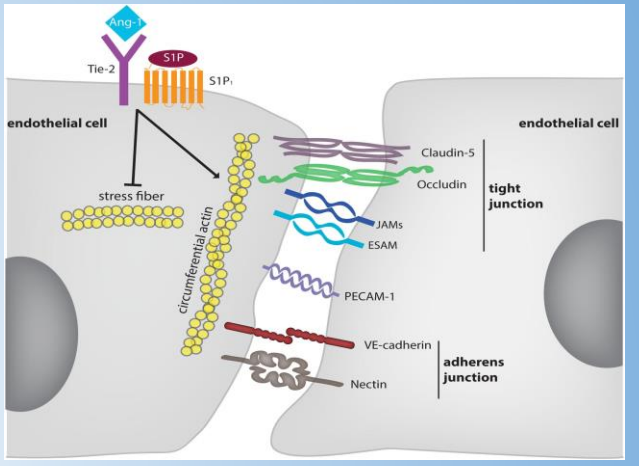
  - Rubor (redness)
  - Tumor (tissue swelling)
  - Color (warmth)
  - Dolor (pain)

Aulus Cornelius Celsus c. 25 BC – c. 50 AD

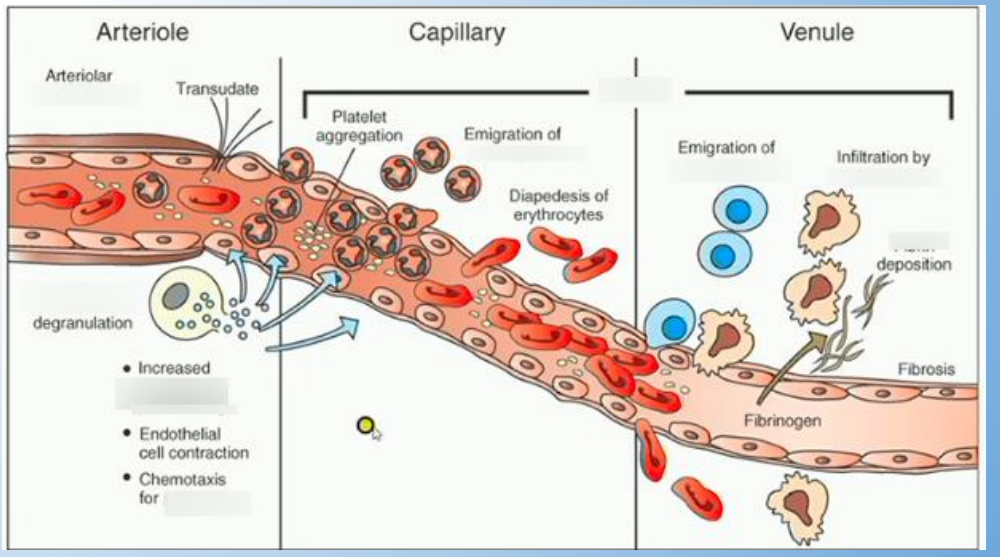
Inflammation - Vascular Phase

- Local vasodilation and endothelial leakage mediated by Histamine, Bradykinin, Complement (C3a, C5a), Leukotrienes (LTC4, LTD4), Prostaglandins (PGI2, PGE2, PGD2, PGF2)

- Exudation from vascular space to tissue – edema
  - Provides medium for immune factors such as immunoglobulins and complement to efficiently move through
  - May also improve clearance of necrotic debris and pathogenic material via lymphatics



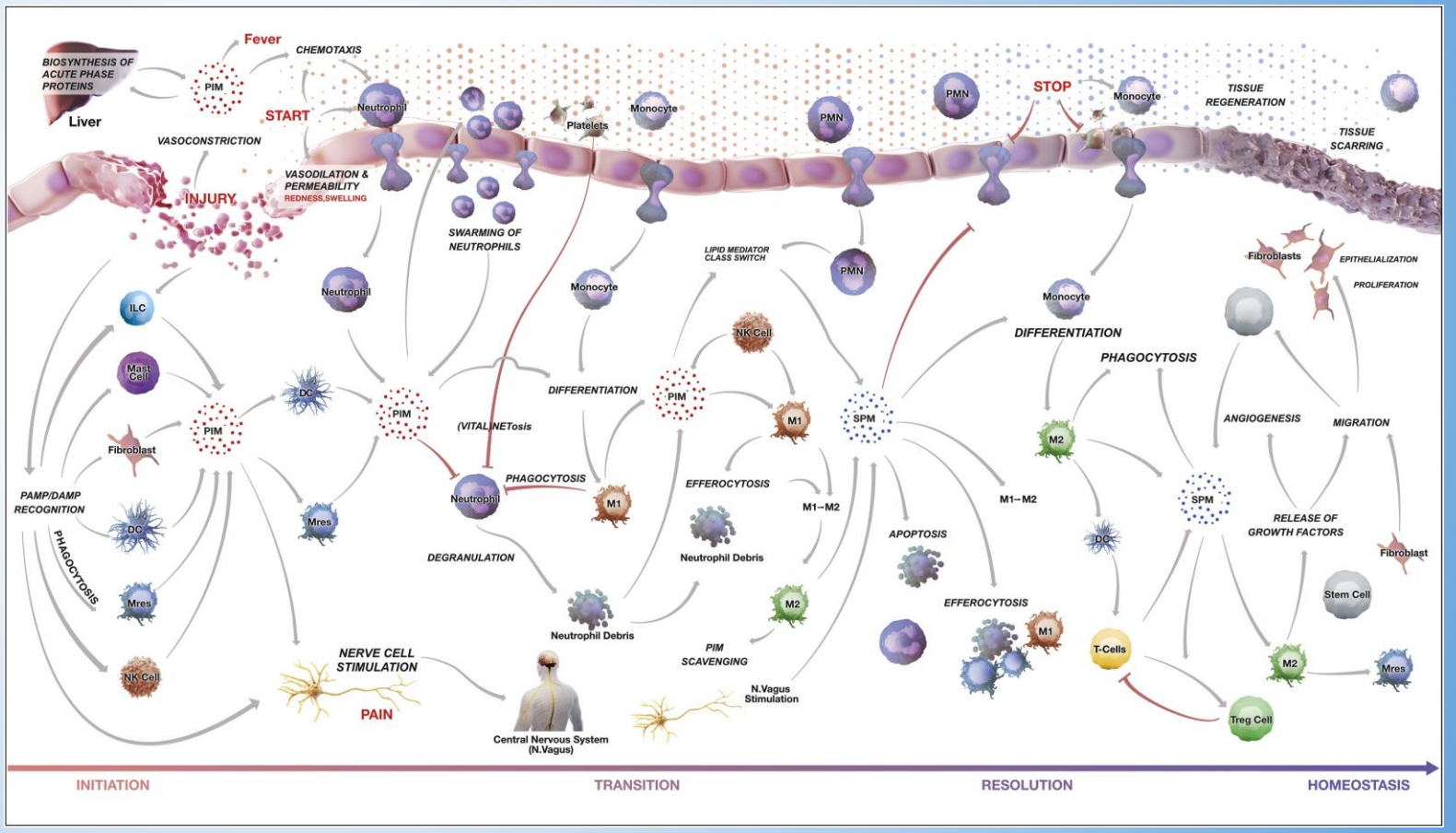
https://www.frontiersin.org/article/10.3389/fphys.2020.00519



https://quizlet.com/260281150/acute-inflammation-diagram

Inflammation – Cellular Phase

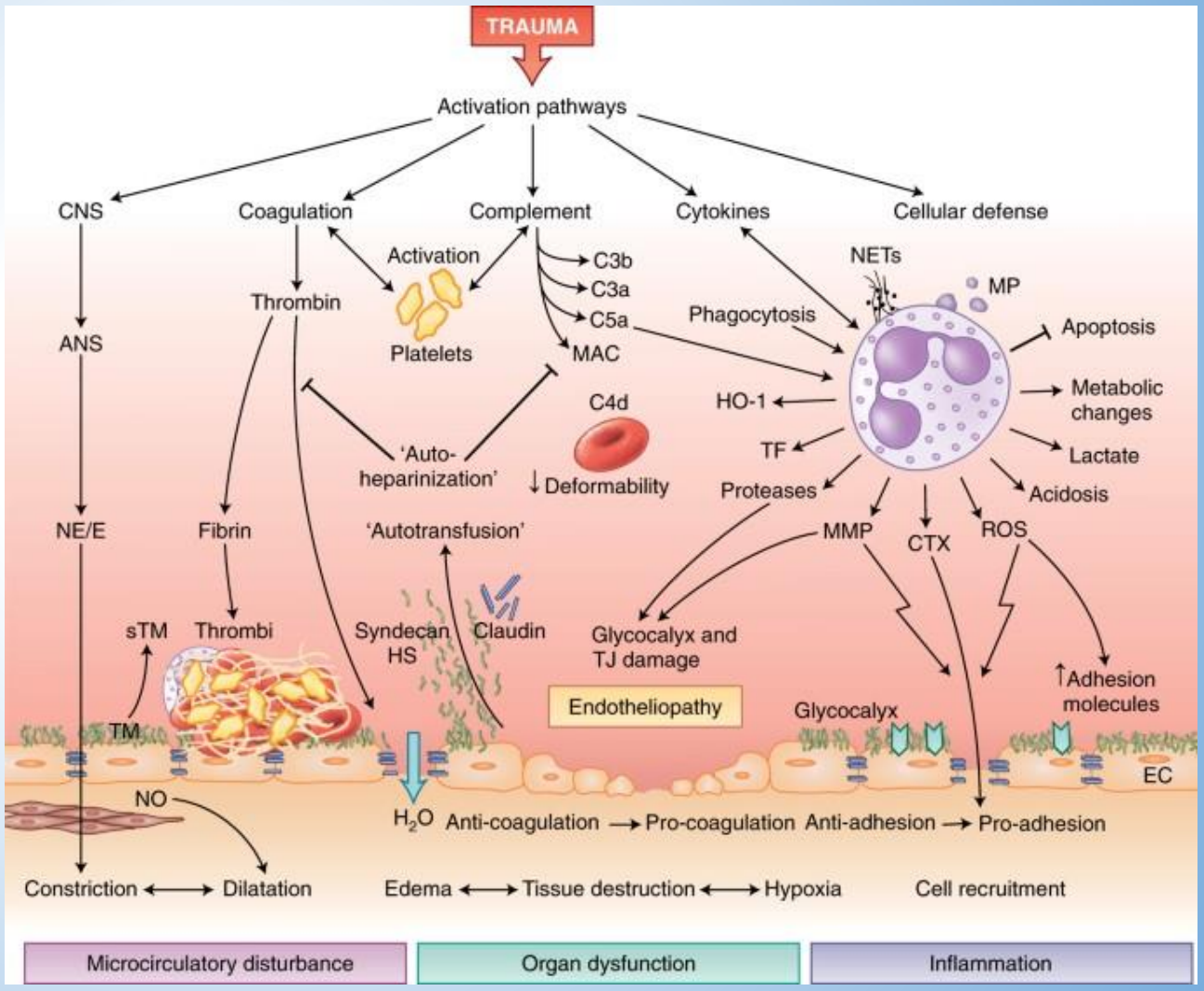
- Mast cells in damaged tissue degranulate releasing Histamine and Complement (C3a, C5a)
- Neutrophils attracted to injury by chemotaxins such as Interleukins (IL-8), PAF, Complement (C5a), Histamine
- Neutrophils phagocytose pathogens



https://www.sciencedirect.com/science/article/pii/S0098299720300960#fig1

Soft tissue Response Summary

- Response to trauma is coordinated
- Multiple parallel pathways both local and systemic
- Degree of trauma dictates intensity of response through signalling

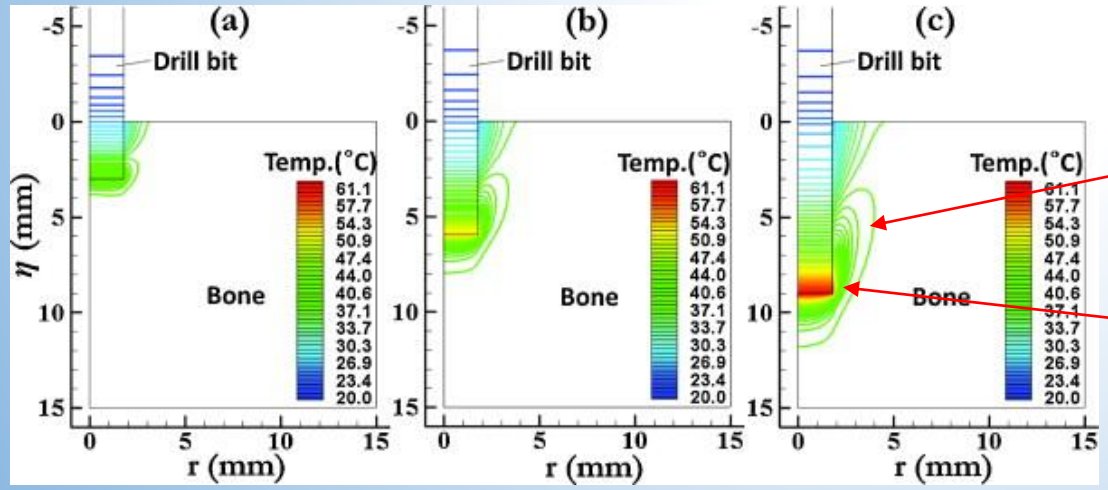


Huber-Lang 2018 https://www.nature.com/articles/s41590-018-0064-8

Physiology of traumatic procedures: Effect on Bone

Vascular Phase the same as for soft tissue – with the exception that intravascular fluid exudation creates periosteal swelling

Bone is sensitive to thermal damage – drilling or cutting



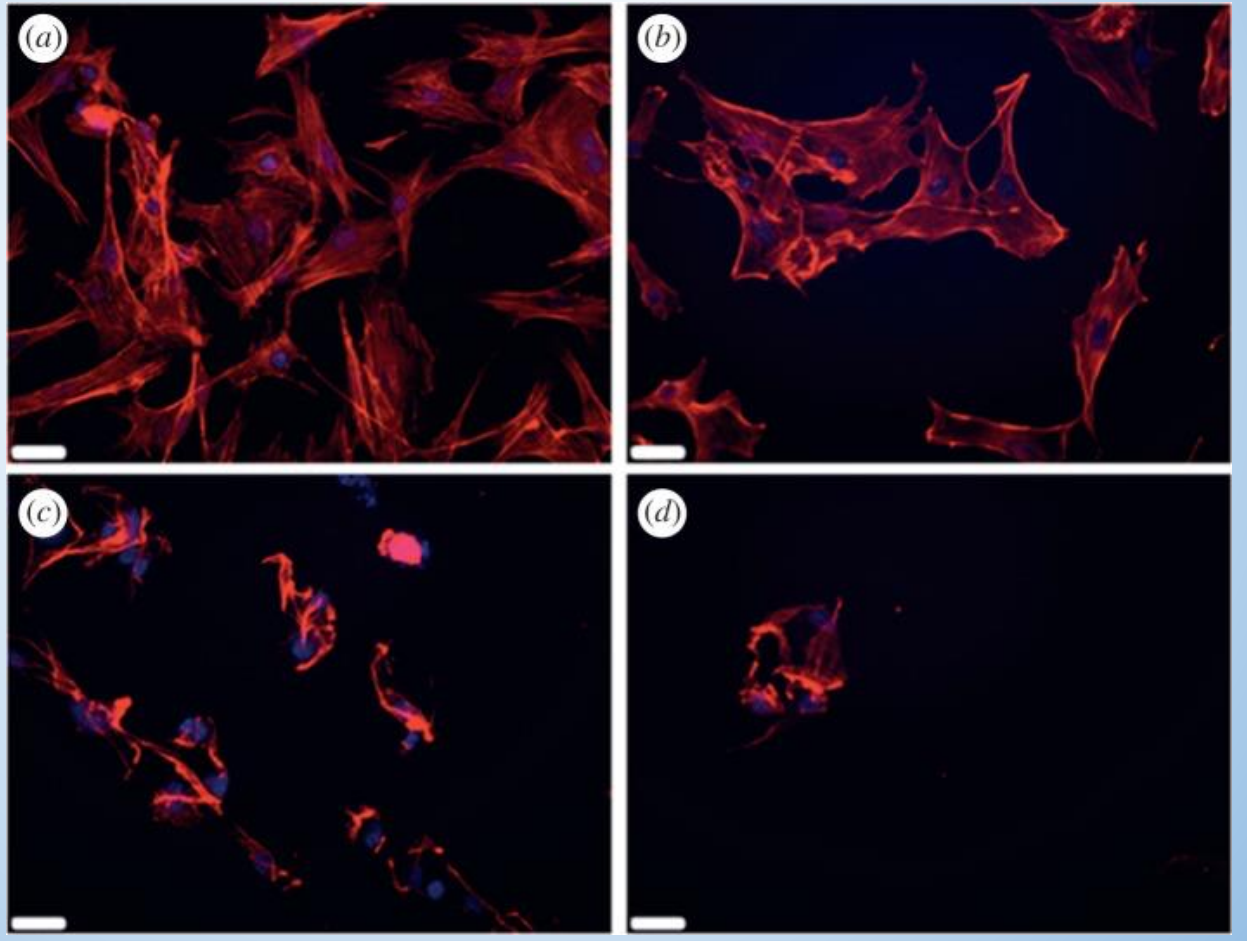
Bone does not dissipate heat well

Cutting instruments generate heat proportional to their distance from irrigant

Eriksson, A.R. and Albrektsson, T. (1983) Temperature Threshold Levels for Heat-Induced Bone Tissue Injury: A Vital Microscopic Study in the Rabbit. Journal of Prosthetic Dentistry, 50, 101-107

Thermal Trauma: 45C is deemed the critical temperature

Actin filament (phalloidin) and nucleus stained (DAPI) MC3T3-E1s following 24 h recovery after heat-treatment of (*a*) 37°C, (*b*) 45°C, (*c*) 47°C and (*d*) 60°C heat-shock for 1 min. Scale bars: (*a–d*) 32 µm.

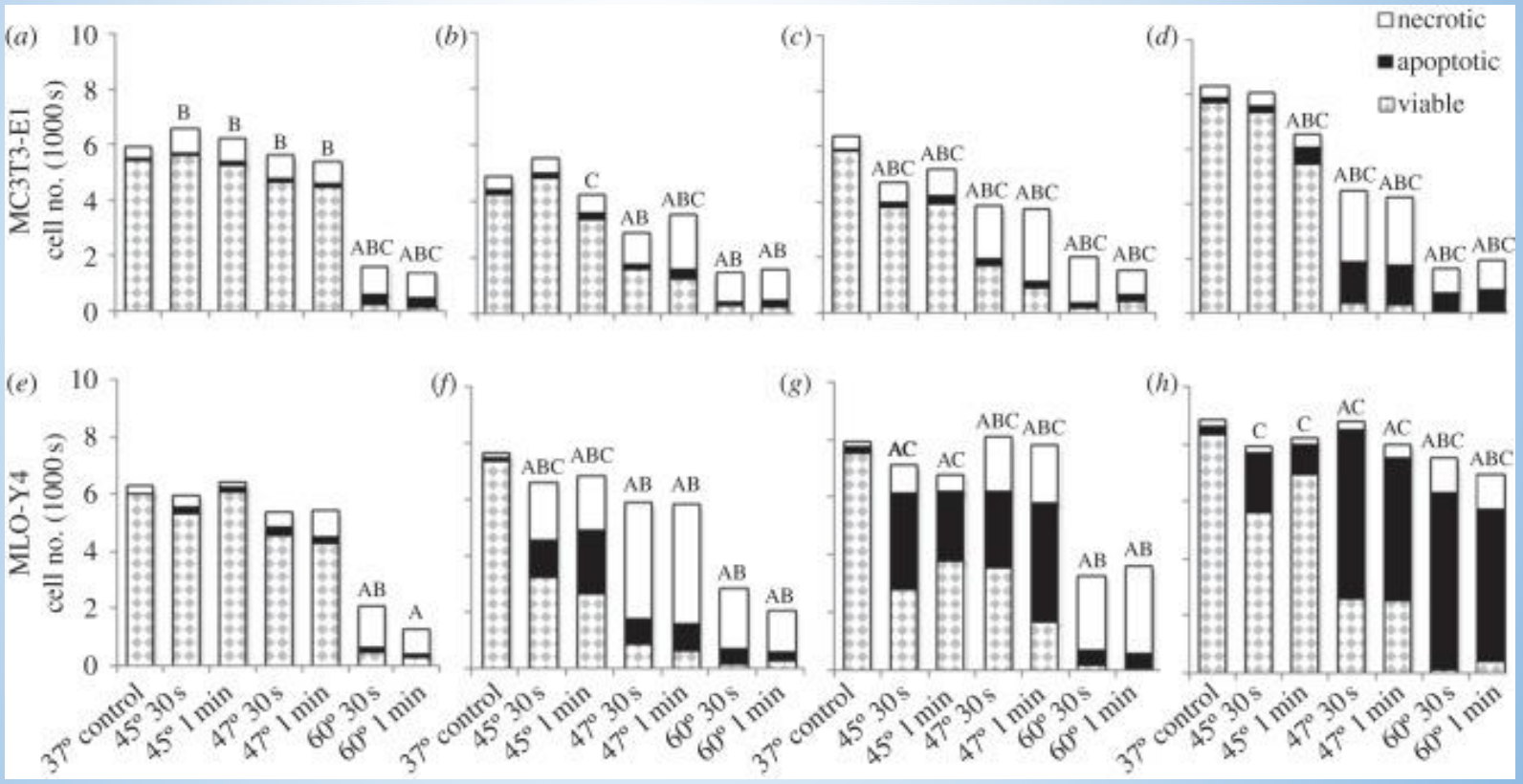


Dolan EB, Haugh MG, Tallon D, Casey C, McNamara LM. Heat-shock-induced cellular responses to temperature elevations occurring during orthopaedic cutting. *Journal of the Royal Society Interface*. 2012;9(77):3503-3513. doi:10.1098/rsif.2012.0520.

Bone cell response at 1, 12, 24hr and 4 days

Osteoblast – like cells

Osteocyte- like cells

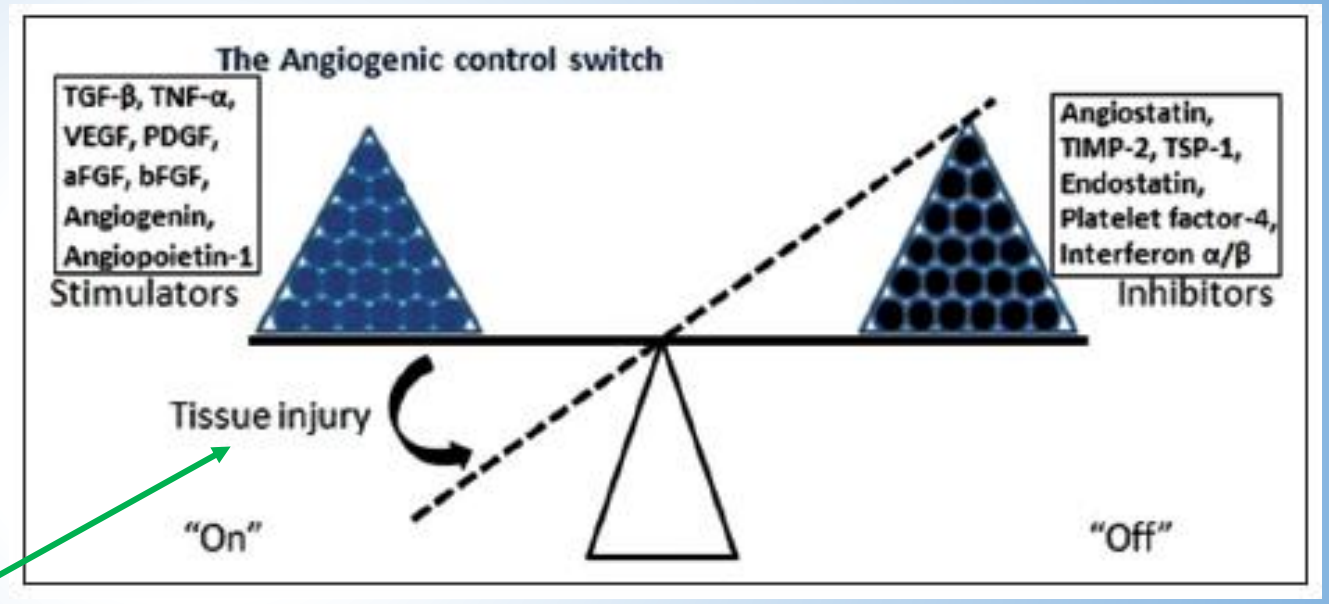


Dolan EB, Haugh MG, Tallon D, Casey C, McNamara LM. Heat-shock-induced cellular responses to temperature elevations occurring during orthopaedic cutting. Journal of the Royal Society Interface. 2012;9(77):3503-3513. doi:10.1098/rsif.2012.0520

Mechanisms of soft tissue healing: Angiogenesis

Pro and anti-angiogenic factors are present in the endothelium of the vasculature as well as in immune cells both circulating and in the extracellular matrix. In homeostasis a balance is established limiting neovascularization.

Pro-angiogenic factors can be induced by hypoxia and inflammation, specifically cyclooxygenase-2.



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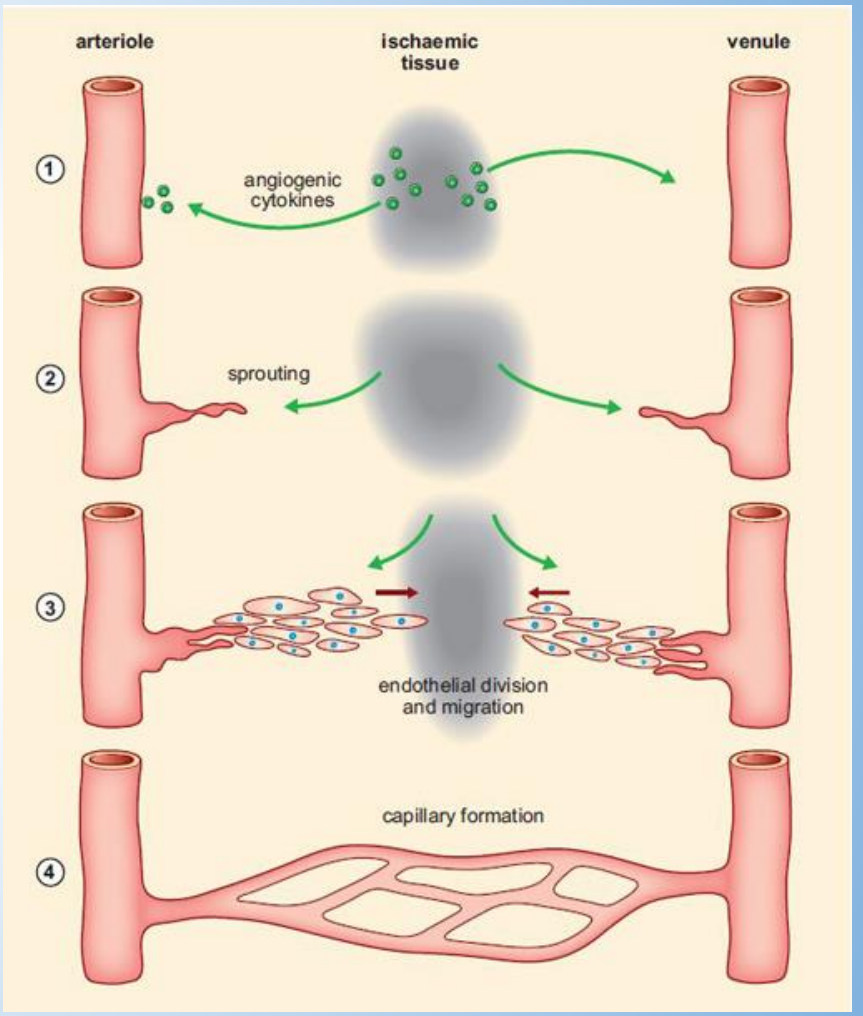
Honnegowda et al, Role of angiogenesis and angiogenic factors in acute and chronic wound healing, Plast Aesthet Res 2015;2:243

Mechanisms of soft tissue healing: Angiogenesis

Steps in re-vascularizing injured tissue:

A. Growth factor receptors on endothelial cells are stimulated
B. Endothelial cells produce and release enzymes that dissolve the wall of the parent vessel
C. Endothelial cells proliferate and sprout into the ECM following a chemotactic gradient and cell surface surface adhesion molecules such as integrins (αvβ3, αvβ5 and αvβ1)
D. Metalloproteases dissolve the matrix ahead of the sprouts
E. Sprouts form tubes and vascular loops
F. Loops differentiate into arterioles and venules

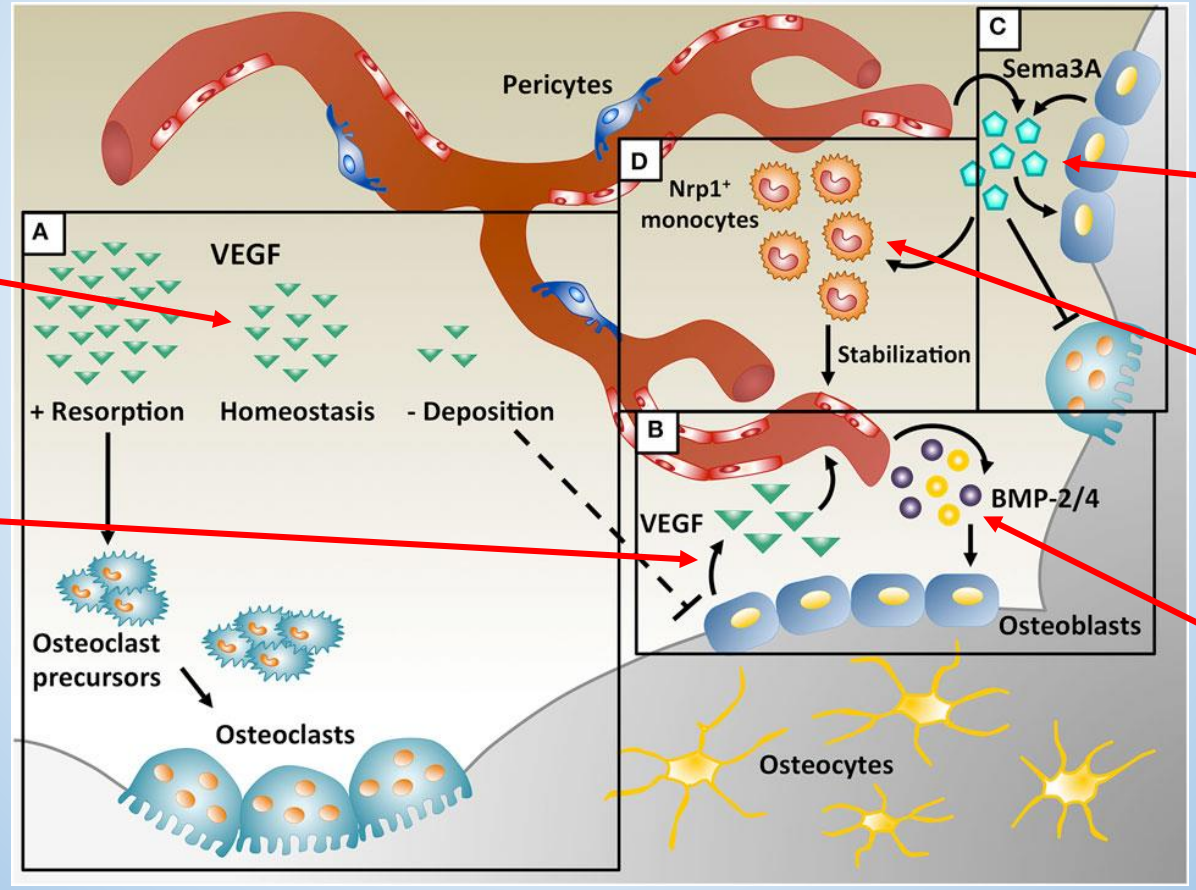


https://www.open.edu/openlearn/science-maths-technology/biology/introduction-histopathology/content-section-1.7

Mechanisms of hard tissue healing: Angiogenesis

Vascular Endothelial Growth Factor levels regulate bone homeostasis

During bone repair osteoblasts produce VEGF in response to hypoxia which stimulates angiogenesis



Expression of Sema3A is regulated by VEGF which supresses osteoclast differentiation

Sema3A also attracts monocytes which express neuropilin 1 which stabilizes new vessels

Vascular endothelial cells secrete BMP which stimulates osteoblast differentiation

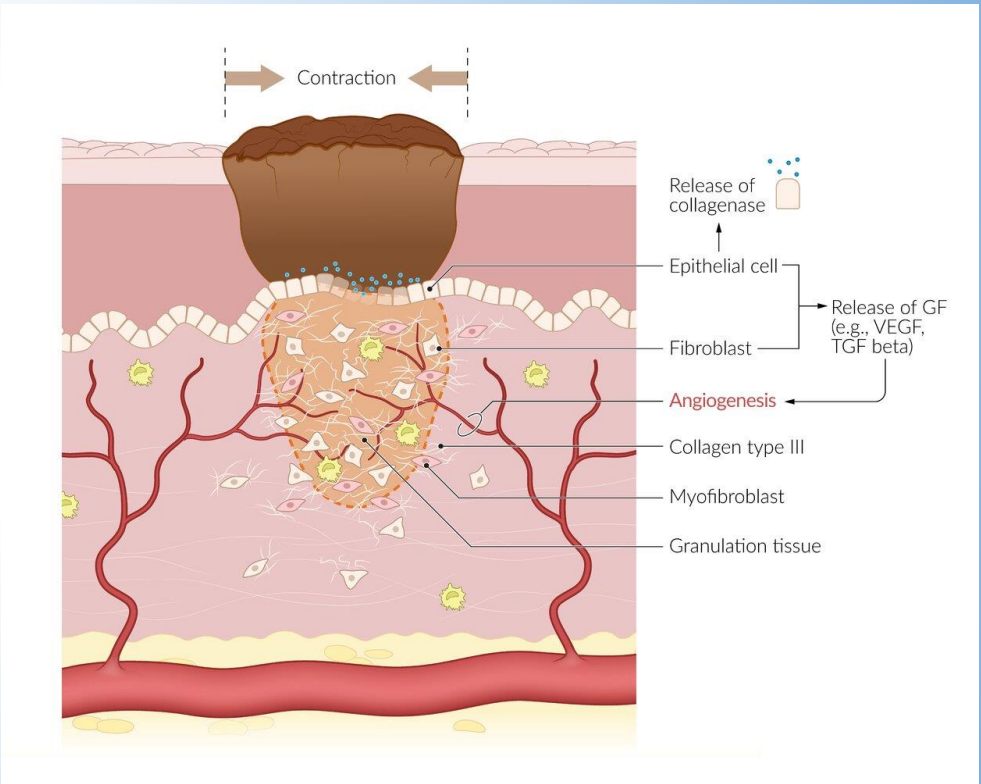
Grosso 2017, https://www.frontiersin.org/articles/10.3389/fbioe.2017.00068/full

Mechanisms of soft and hard tissue healing
Soft tissue proliferation

1. The proliferative phase of wound healing is characterized by granulation tissue and overlaps with the inflammatory and neovascularization phase
2. Fibroblasts lay down a collagen and glycosaminoglycan matrix which give the wound stability

3. Concurrently, re-epithelialization begins at the wound edges and migrates over the ECM

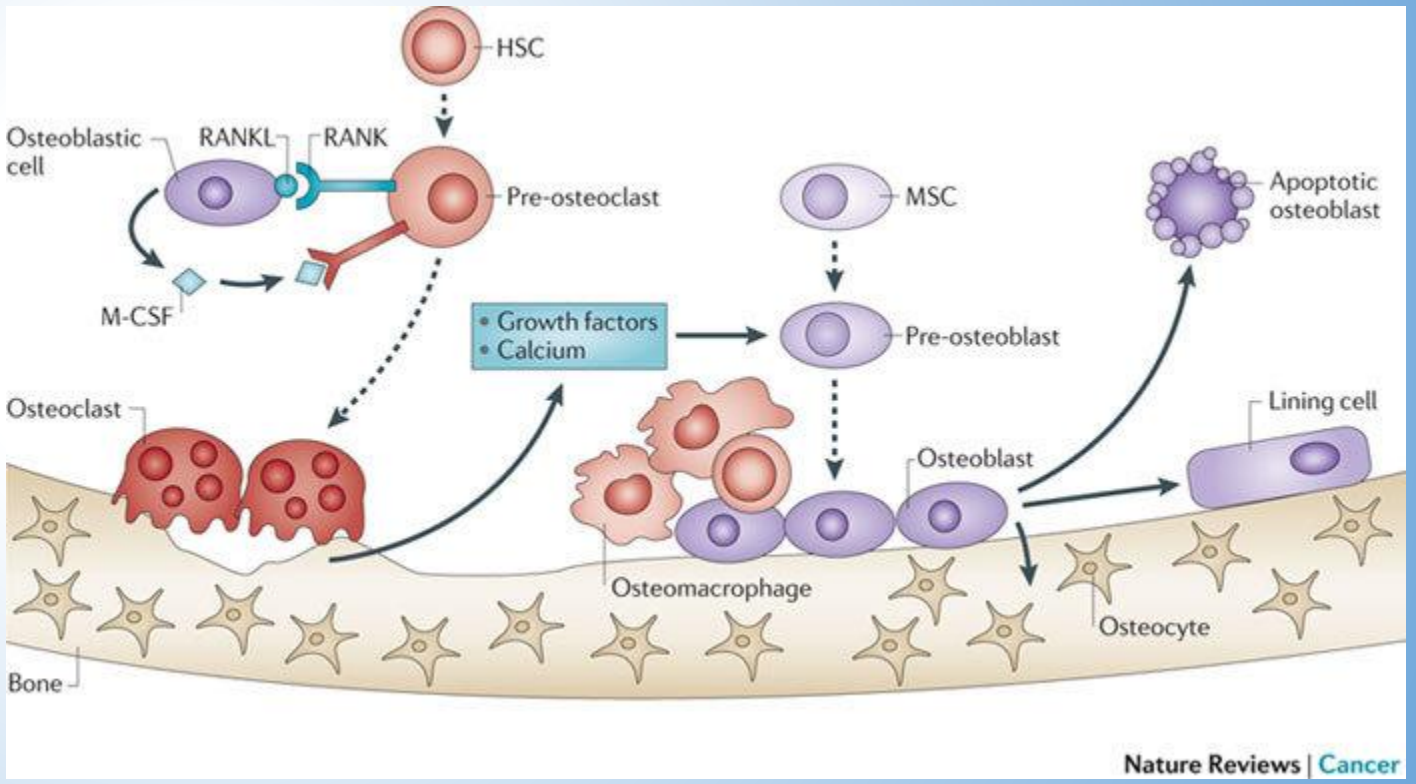
4. Myofibroblasts facilitate wound contraction which occurs as collagen synthesis increases and pulls the wound edges together.



https://www.amboss.com/us/knowledge/Wound_healing

Mechanisms of soft and hard tissue healing
Hard tissue proliferation

1. Tissue Necrosis Factors (TNF) are secreted as part of the acute inflammatory phase cytokine response.
2. Osteoclasts and osteoblasts have TNF receptors (TNFR1 and TNFR2) which when activated in conjunction with Interlukins and BMPs stimulate the recruitment of mesenchymal stem cells (MSC)
3. In conjunction with angiogenesis direct remodeling of lamellar bone and the Haversian system can occur.



https://www.researchgate.net/figure/Bone-remodellingThe-bone-is-a-dynamic-hard-tissue-that-undergoes-a-continuous_fig5_51147804

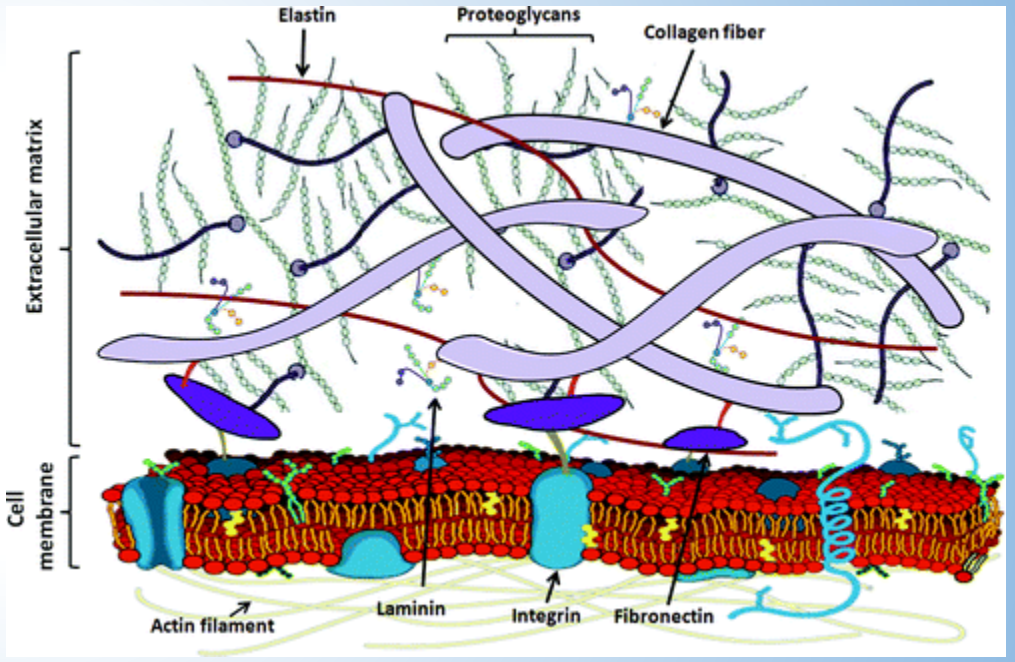
Remodelling Phase of Healing: Soft Tissue

Myofibroblasts continue to lay down structural proteins such as collagen, elastins, fibronectins and laminins in the ECM.

Integrins help regulate cell adhesion and cell to ECM signalling

Hyaluronan and other proteoglycans stabilize the migration of growth factors and provide 3 dimensional structure by binding water

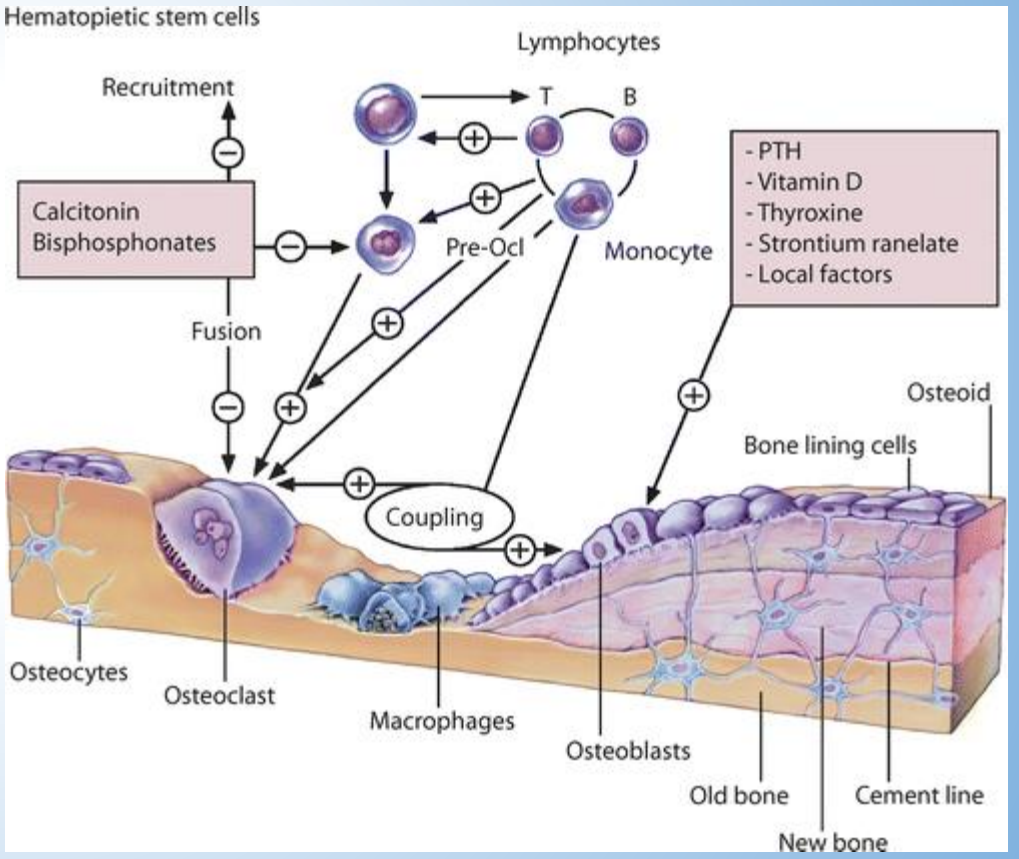
Matrix metalloproteases break down ECM in later stages promoting fibroblast mediated wound contraction



https://www.liebertpub.com/doi/10.1089/wound.2013.0485

Remodeling Phase of Healing: Bone

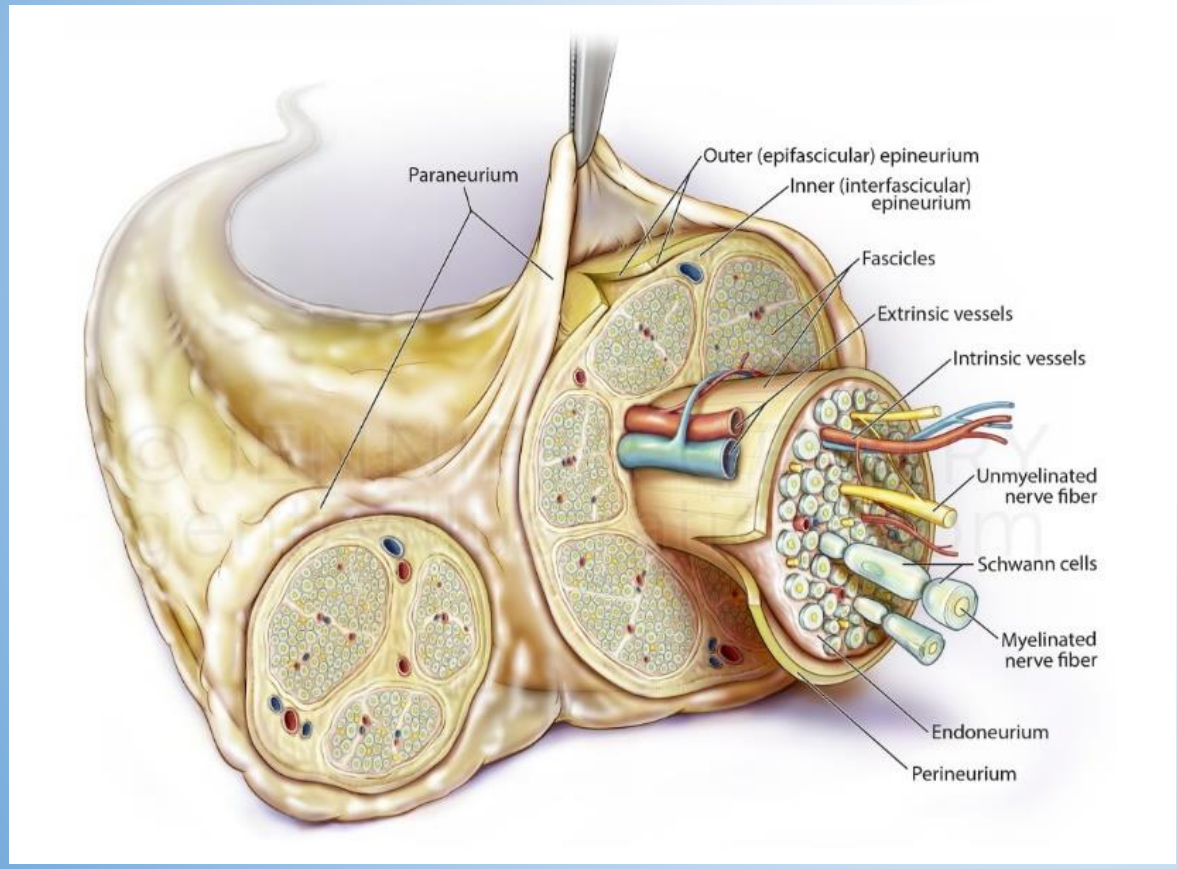
The physiological mechanisms of bone remodeling are generally the same in all bones. However, the factors that stimulate surface remodelling in the jaws vary by anatomical location, function (eg. loading) and temporally.



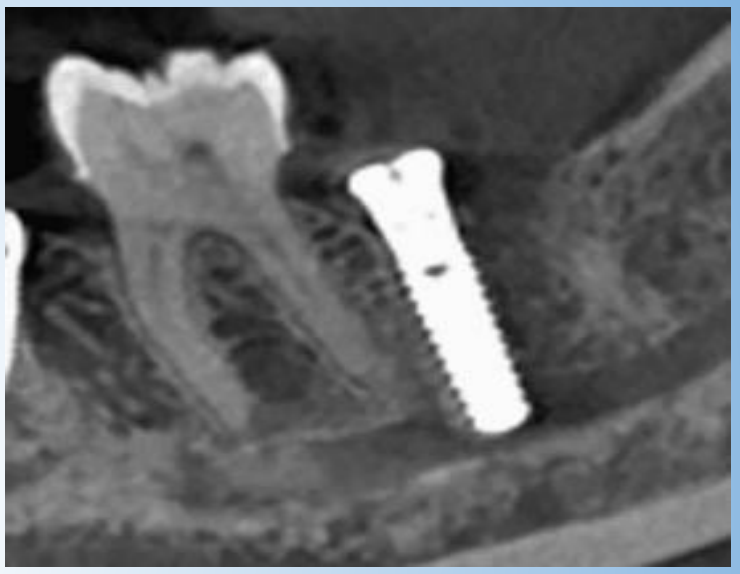
Reiner Bart, Control and Regulation of Bone Remodeling Bone Disorders pp 31-38, 2016

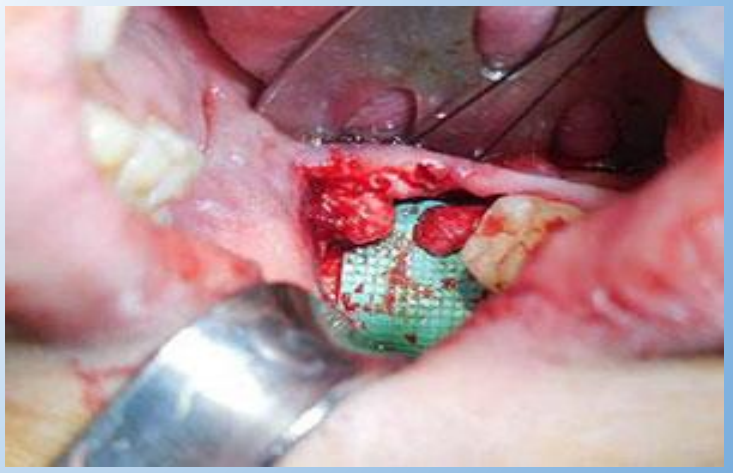
Nerve Injury and Healing: Nerve Anatomy

Most peripheral nerves are part of a ‘neurovascular bundle’ which makes injuries complex and outcomes difficult to predict



https://www.gentryvisualization.com/peripheral-nerve-anatomy/

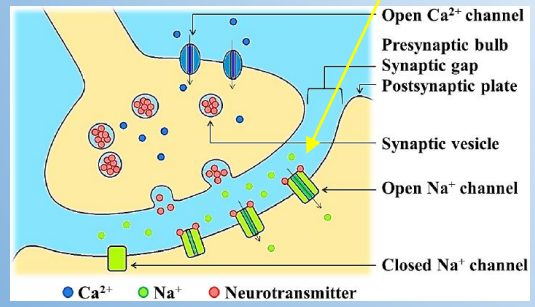


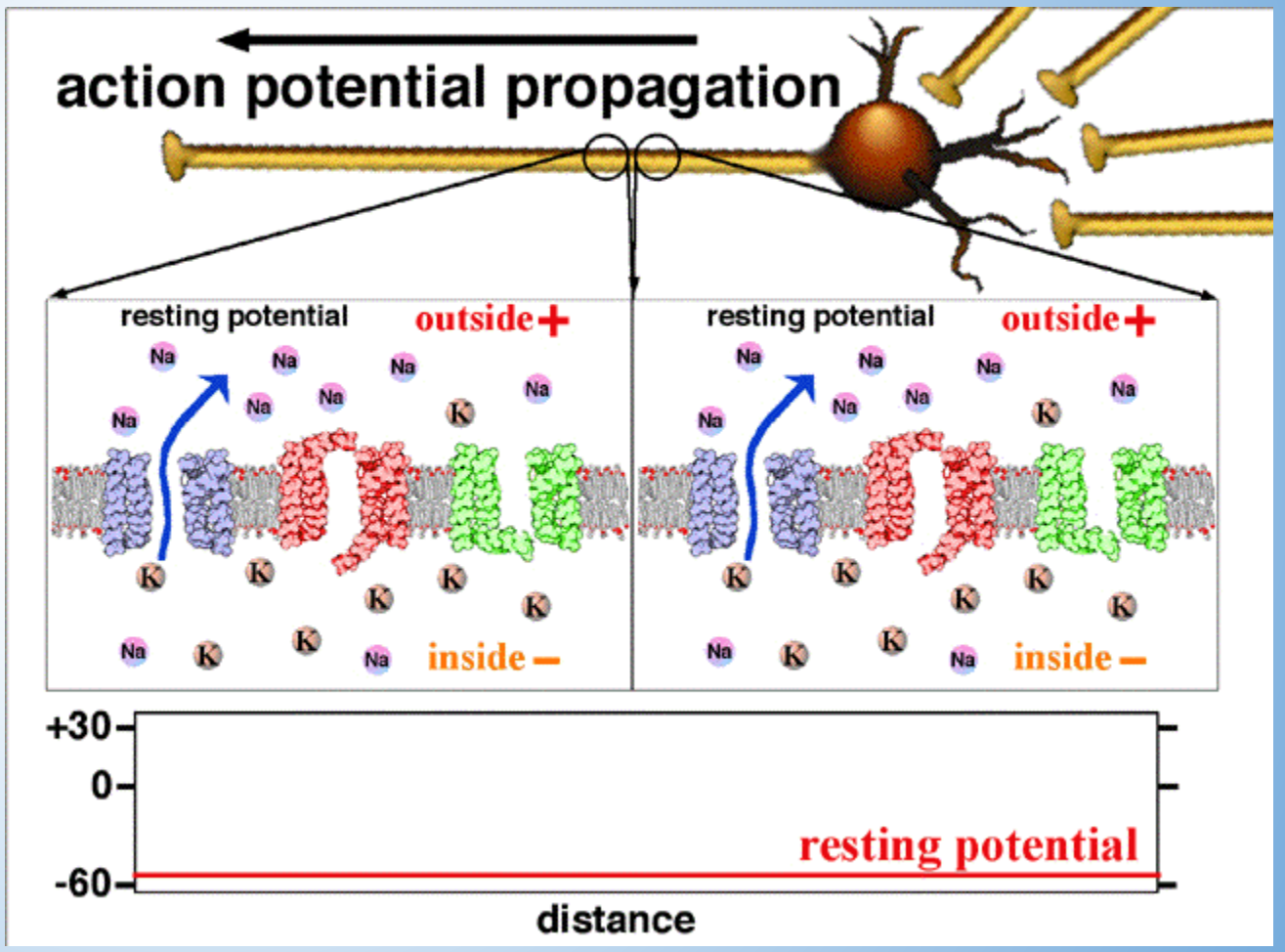


https://www.dentistrytoday.com/how-to-manage-trigeminal-nerve-injuries-in-dentistry/

Nerve Injury and Healing: Nerve Conduction

- Nerve function requires a difference in electrical potential between the inside and outside of the membrane
- Membrane has many sodium and potassium channels and ion pumps
- When stimulated by an action potential (electrical spike) the channels open allowing ions through creating a wave-like propagation
- At the synapse neurotransmitters open ion channels





https://commons.wikimedia.org/wiki/File:Action_potential_propagation_animation.gif

Nerve Injury and Healing: Classification of Injuries

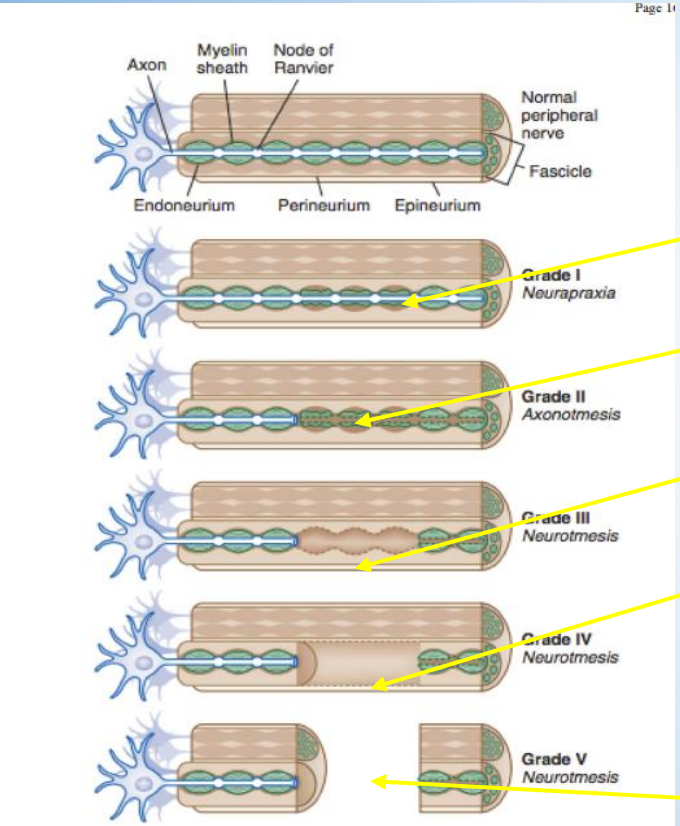


Fig. 1.
Classification of nerve trauma
From: Tsao B, Boulis N, Bethoux F, Murray B. Trauma of the Nervous System, Peripheral Nerve Trauma. In: Daroff: Bradley's Neurology in Clinical Practice, 6th ed. 2012 p 984-1001. (Image courtesy Cleveland Clinic, 2006. Illustrator, David Schumick, BS, CMI.)

Seddon & Sunderland Classification

Neuropraxia (Grade I) – focal demyelination

Axonotmesis (Grade II) – axonal damage, intact endoneurium

Axonotmesis (Grade III) – axonal & endoneurium damage, intact perineurium

Axonotmesis (Grade IV) – axonal, endoneurium & perineurium damage with intact epineurium

(Grades II – IV: increasing degree of connective tissue damage)

Neurotmesis (Grade V) – Nerve transection

Peripheral Nerve Trauma: Mechanisms of Injury and Recovery, Ron M. G. Menorca, BS, Theron S. Fussell, BA, and John C. Elfar, MD, Hand Clin. 2013 August ; 29(3): 317–330.

Nerve Injury Resolution

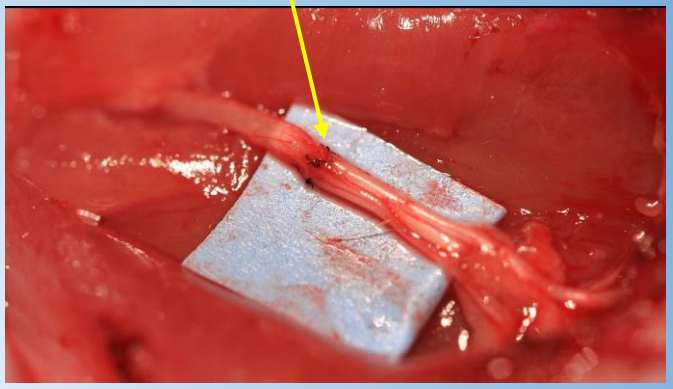
Recovery after Injury:

Neuropraxia – good prognosis, temporary loss of sensation due to ischemia and secondary inflammatory changes within the neurovascular bundle, return of function within ~12 weeks

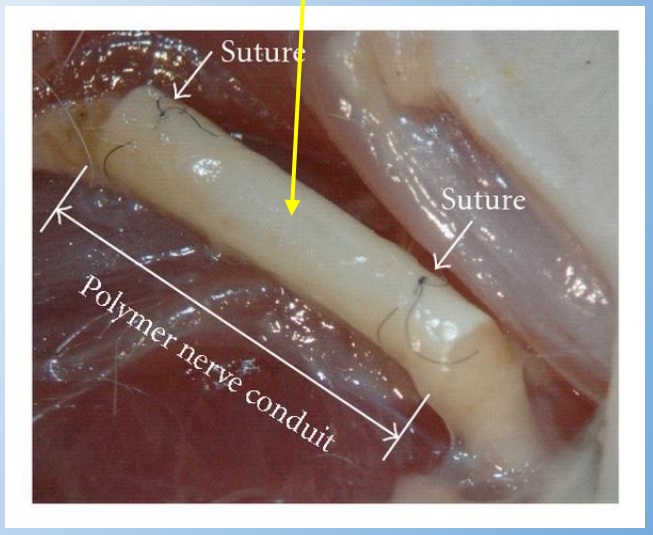
Axonotmesis – crush damage to axon, connective tissue intact, Wallerian degeneration distal to injury site, recovery depends on distance to end organ, recovery by regeneration 1 mm/day (may be partial or complete)

Neurotmesis – axon and connective tissue damaged or separated, can regenerate or re-innervate through neural sprouting, surgical repair may be indicated and improve outcome although NGF induced neuromas and neuropathic pain possible

Repair with suture



Repair using conduit



https://www.hindawi.com/journals/ijps/2010/138686/

Acute Oral Surgical Complications:

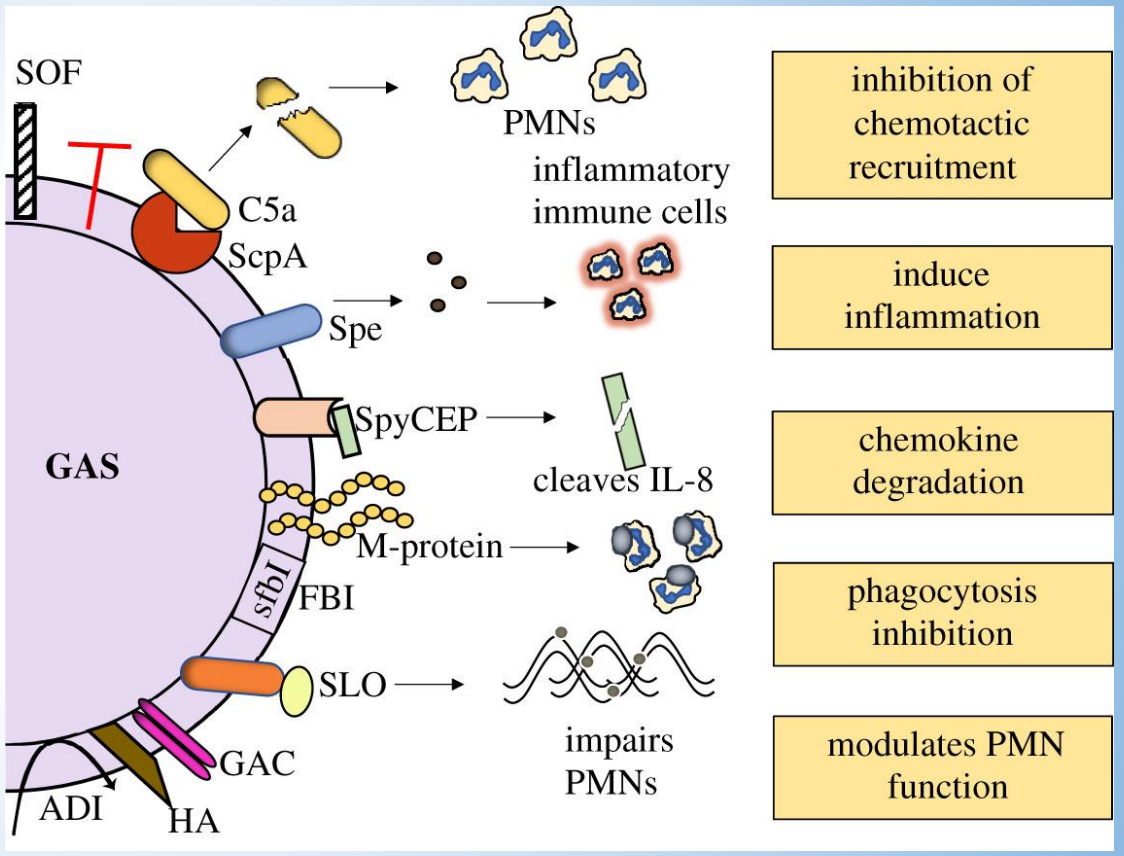
Infection
Bleeding
Sinus Perforation
Nerve Injury
Damage to Adjacent Teeth
Dry Socket

John Collier (1708-1786). 1773 Print, British Museum, London

Signs of Infection – same as for acute phase inflammation

- Pain
- Redness
- Swelling
- Warmth

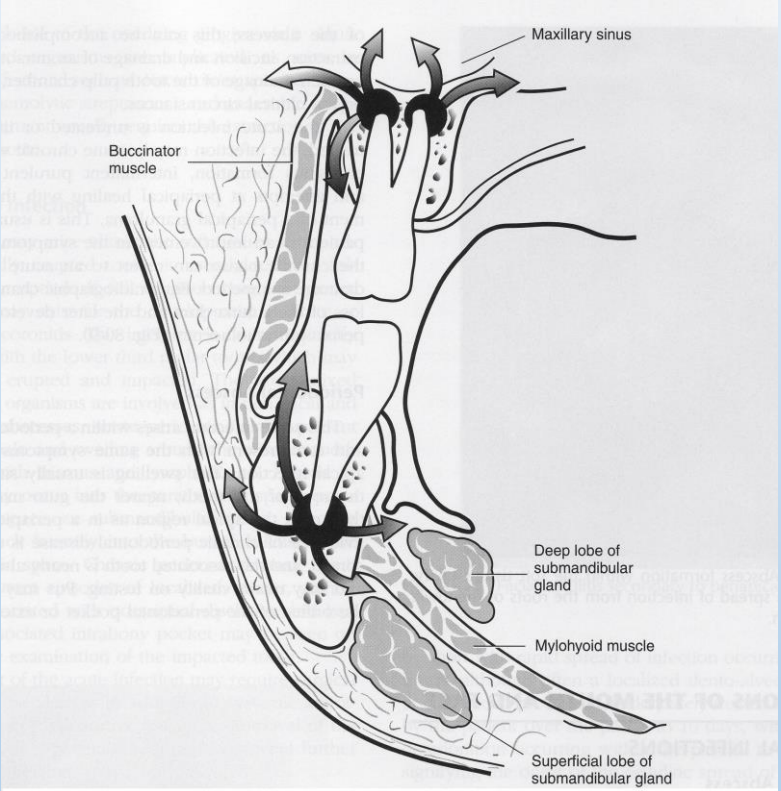
Through signaling of their own, bacteria modify or inhibit the inflammatory response which impacts tissue healing and regeneration



A brief review on Group A Streptococcus pathogenesis and vaccine development, Sowmya Ajay Castro and Helge C. Dorfmueller,Published:10 March 2021https://doi.org/10.1098/rsos.201991

Infection: Oro-facial Spread

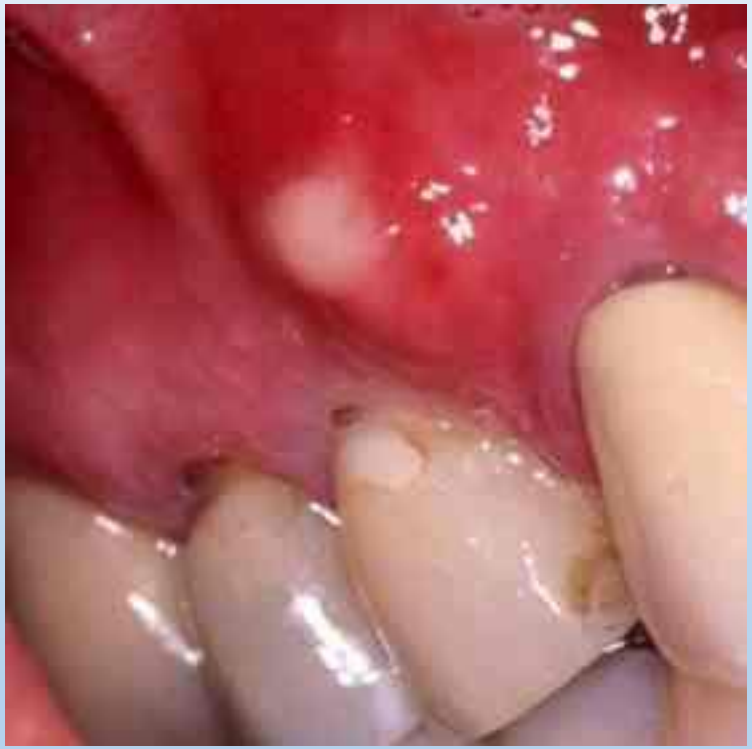
- Most but not all infections try to point to the surface to drain
- Route of spread depends on density of tissues
- Infections will travel along fascial planes



Possible pathways of spread of infection from the upper and lower jaw molar teeth

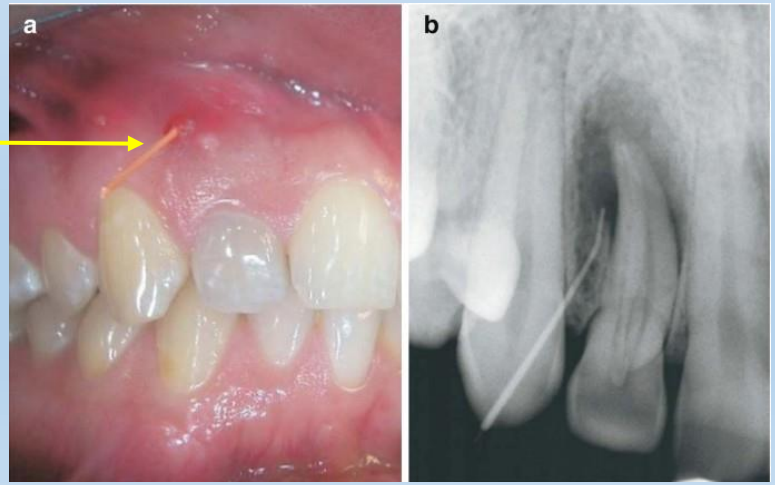
http://www.exodontia.info/LudwigsAngina.html

Ondontogenic Infections



Most odontogenic infections (particularly anterior teeth) 'point' to the closest buccal surface

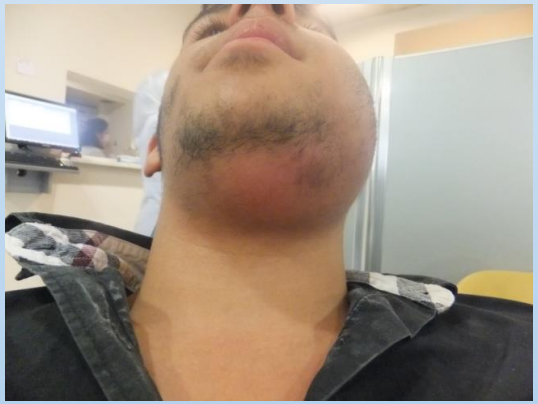
GP points can be used effectively to localize source of infection



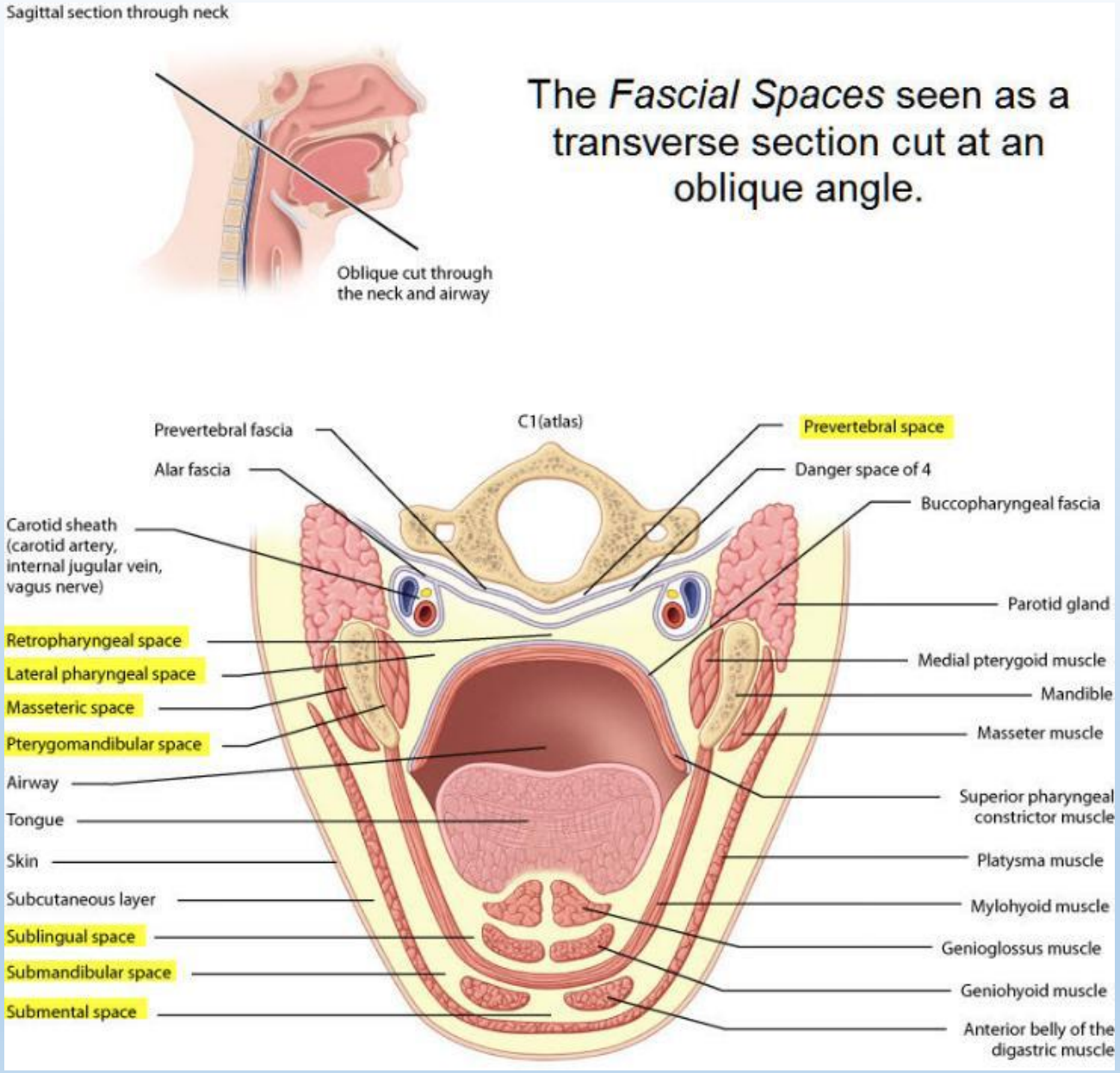
https://link.springer.com/chapter/10.1007/978-3-030-10725-3_3#citeas

Space Infections

Infections that do not point to the surface may track along fascial planes



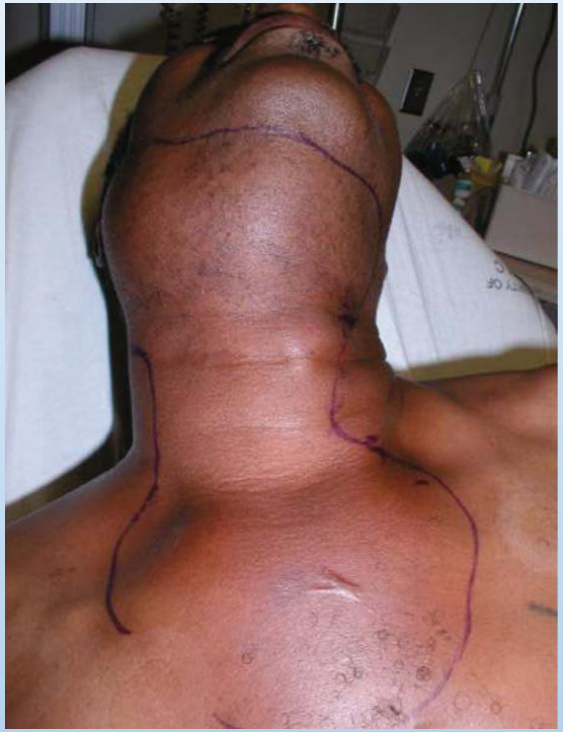
http://www.intechopen.com/books/a-textbook-of-advanced-oral-and-maxillofacial-surgery/odontogenic-infections

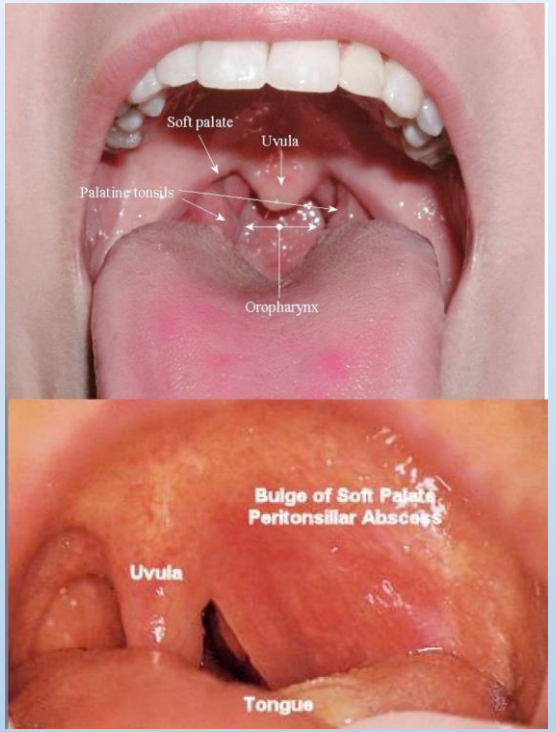


http://www.exodontia.info/LudwigsAngina.html

Warning Signs of Potentially Serious Infections

- Fever
- Trismus
- Difficulty swallowing
- Difficulty breathing
- Drooling
- Systemically unwell
- On Antibiotics with no resolution
- Very old/immunocompromised





https://www.studyblue.com/notes/note/n/pediatrics/deck/12619579

Infections: Treatment

Options depend on severity of infection:

- Drain
- Extract
- Antibiotics

Minimum treatment would be AB +/- referral

Odontogenic Infections

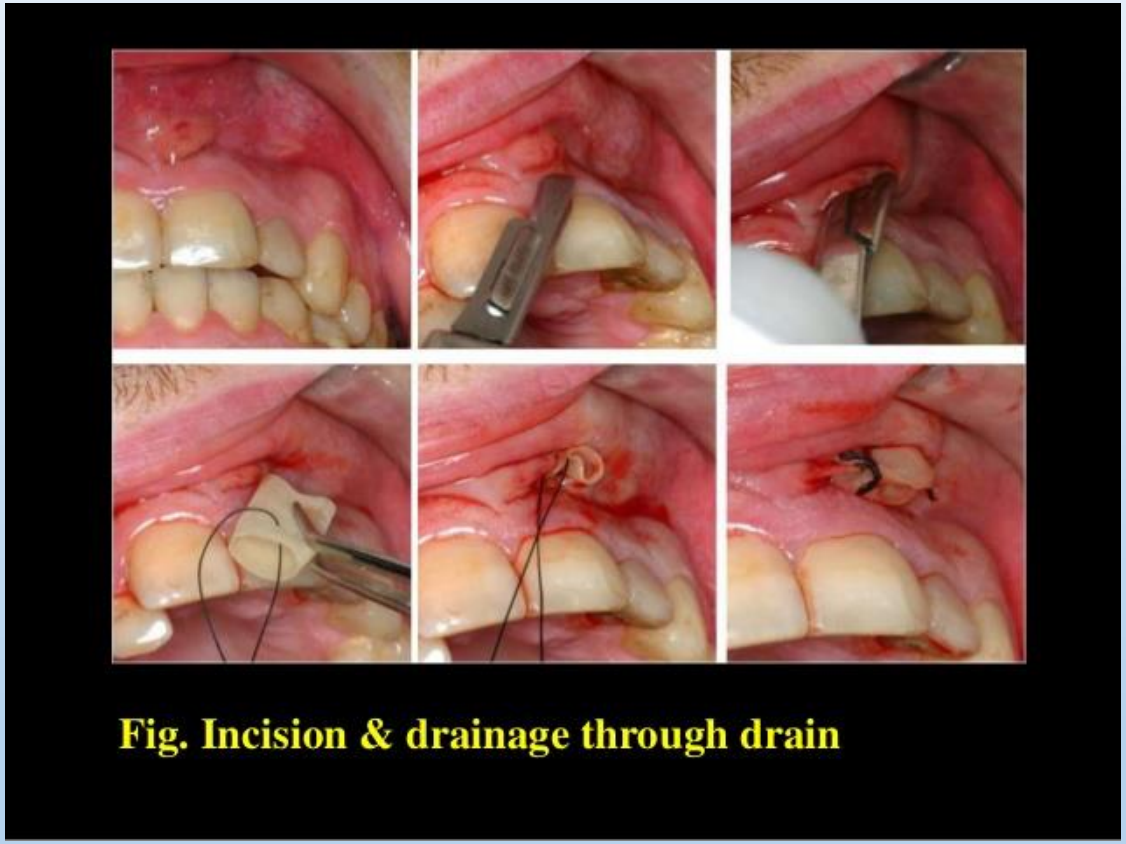
Table 1 Characteristics of the 3 stages of infection

Characteristic	Inoculation	Cellulitis	Abscess
Duration (days)	0–3	2–5	4–10
Discomfort	Mild	Severe, diffuse	Mild, localized
Palpation	Soft, doughy	Firm, indurated	Fluctuant, tender
Pus	None	None	Present
Skin	Normal	Red	Red periphery
Severity	Minimal	Greater	Less
Bacterial species	Aerobic	Mixed	Anaerobic

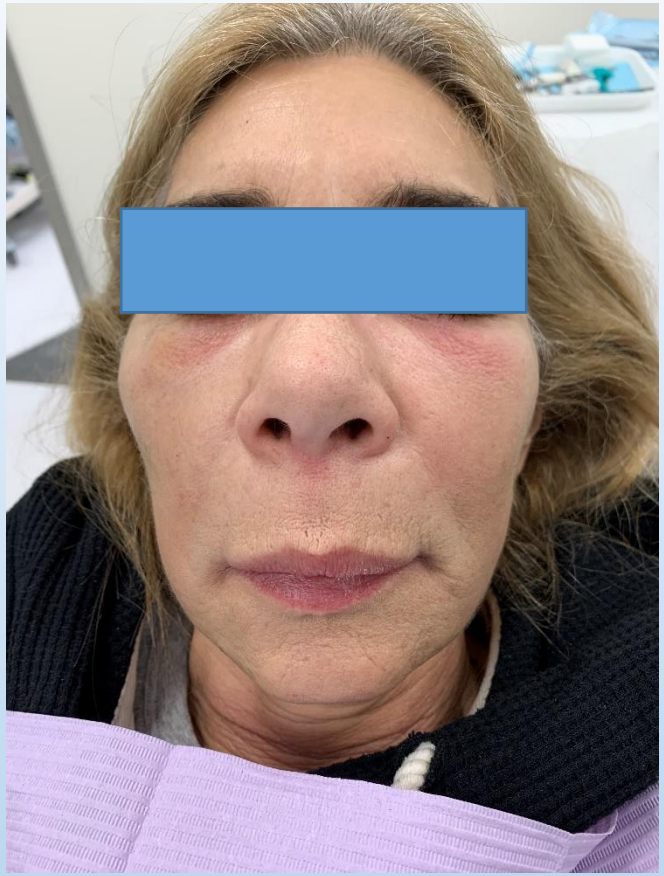
JCDA • www.jcda.ca • 2010 • Vol. 76, No. 2 •

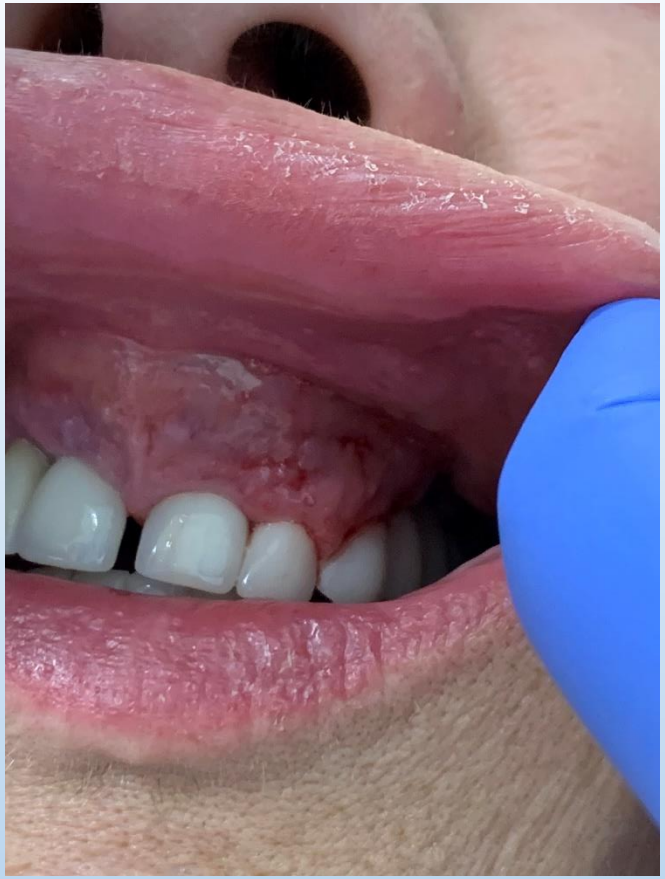
Drainage

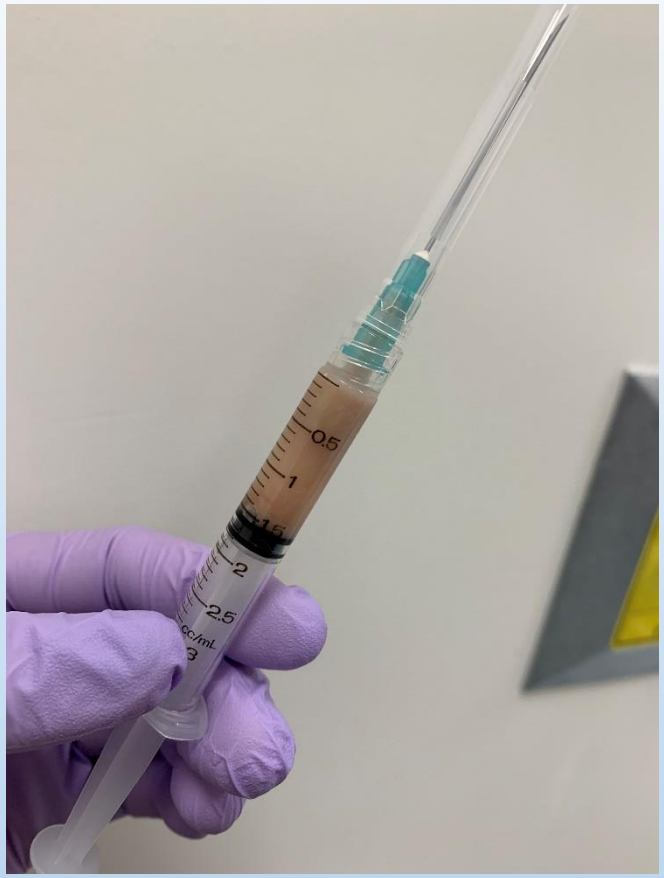
- Referred to as “I & D”
- May include placement of a drain or just incision
- Allows pus to escape (reduces risk of tracking along a ‘space’)
- Alters environment (pathogens are usually anaerobes and facultative anaerobes)



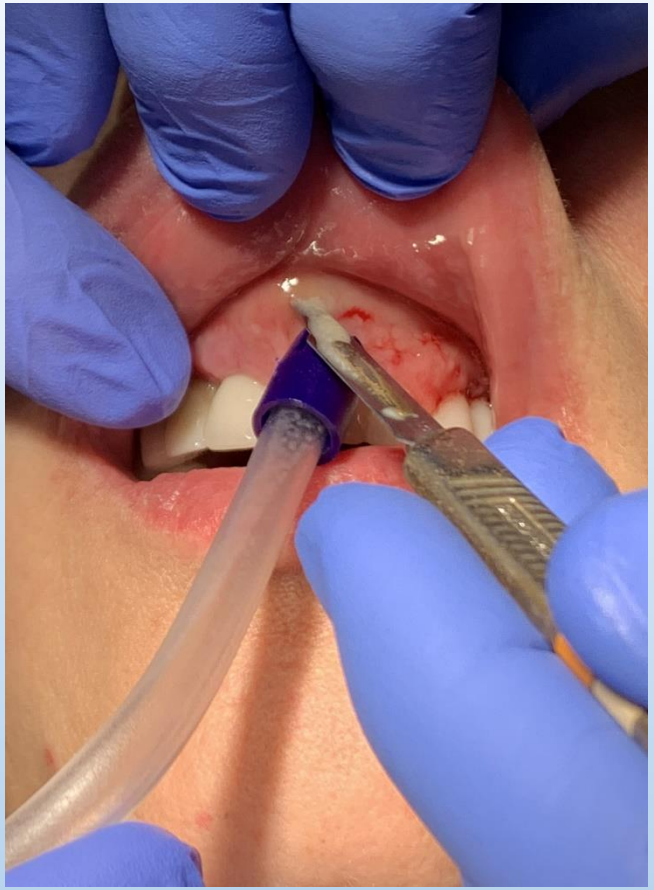
https://www.slideshare.net/Ashu9405/endodontic-surgery-43131725

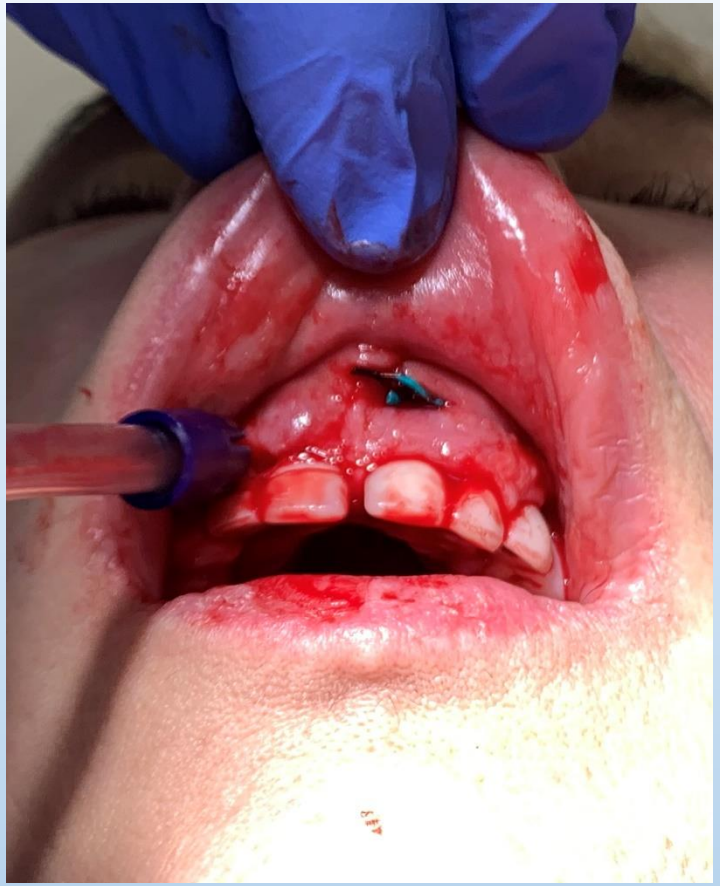


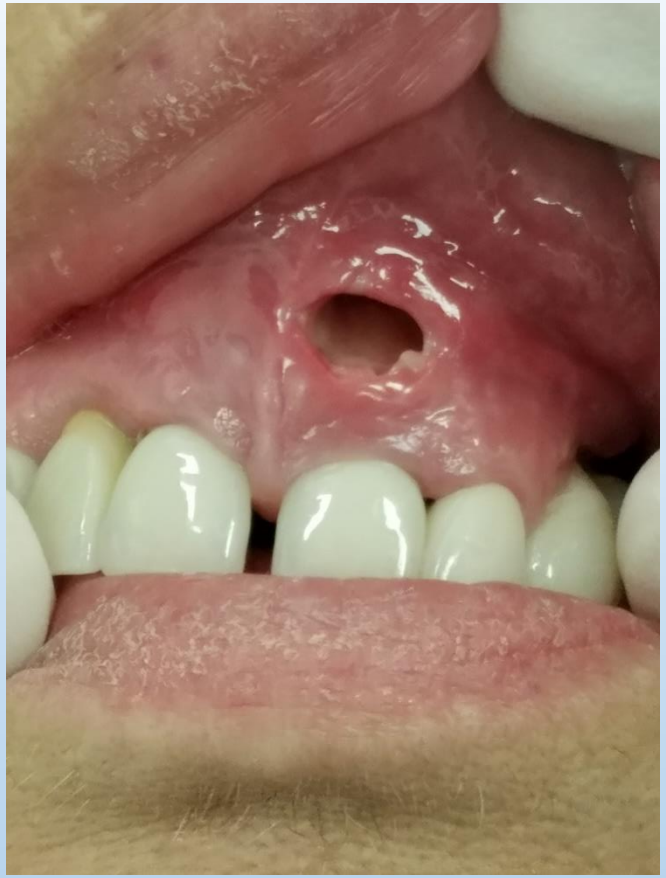




If pus is present it can be aspirated and sent for culture.







Once drain is removed the residual incision site rapidly heals.

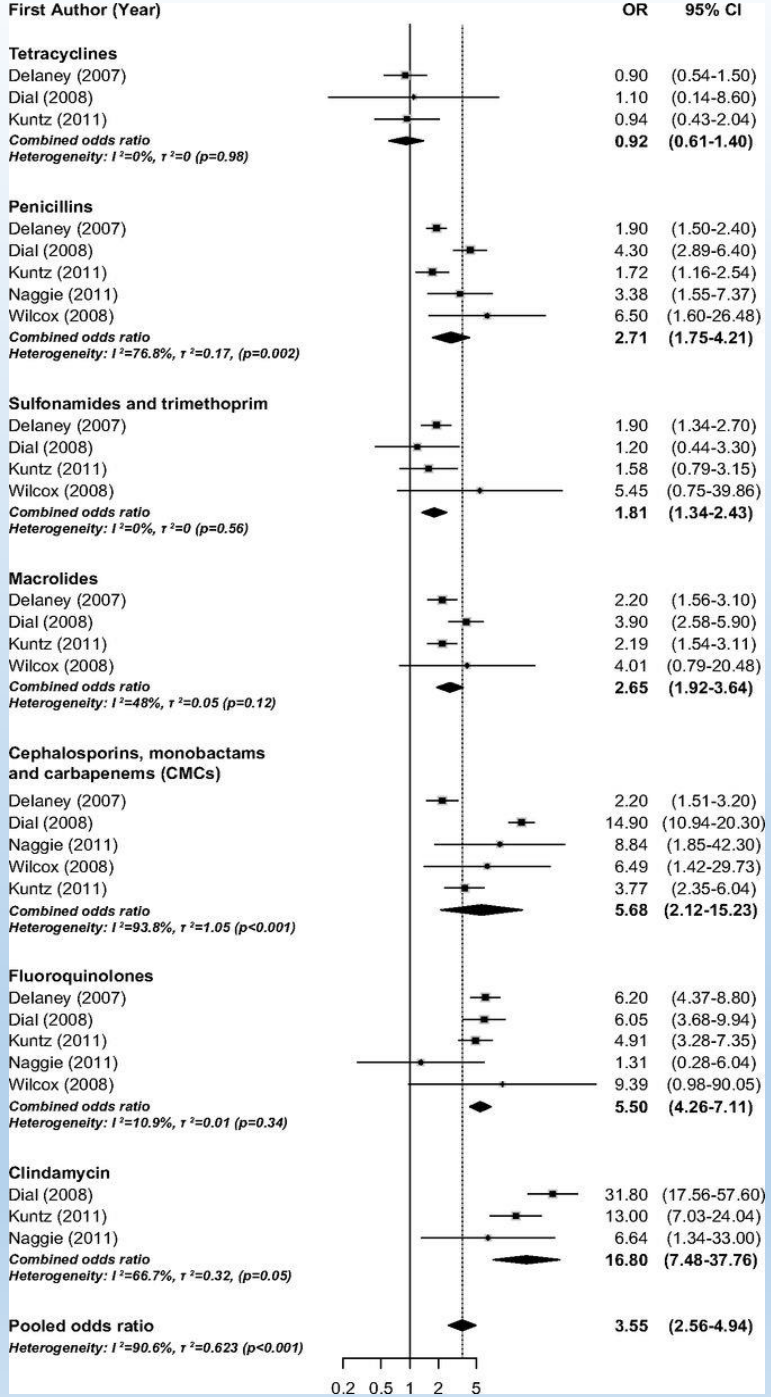
Antibiotics for Odontogenic Infections

Table 2 Antibiotics commonly prescribed for odontogenic infections[5]

Antibiotic	Usual adult dosage	Usual pediatric dosage
Penicillin V	600 mg every 6 h	25–50 mg/kg/day divided into 4 doses
Amoxicillin	500 mg every 8 h	25–50 mg/kg/day divided into 4 doses
Cephalexin	500 mg every 6 h 2 g 1 h pre-op (joint prophylaxis)	25–50 mg/kg/day divided into 4 doses
Metronidazole	500 mg twice daily	15–30 mg/kg/day divided into 3 doses
Clindamycin	300–450 mg every 6 h	10–30 mg/kg/day divided into 3 or 4 doses
Moxifloxacin	400 mg daily	Not established
Erythromycin	500 mg enteric coated every 8 h 333 mg enteric coated every 6 h 250 mg (base) every 6 h	30–50 mg/kg/day divided into 2–4 doses

Clostridium Difficile Infection (Antibiotic Associated

- 15% of CDI associated with dental AB Rx
- previous ADD increases risk of CDI
- CDI in dental practice tend to be older (>55 yrs)
- Majority of all CDI associated with in-patient
- CDI: 9.1% clindamycin, 4.8% penicillin
- Almost any antibiotic can cause a pseudomembranous colitis – not the same as CDI



Brown et al https://aac.asm.org/content/57/5/2326

http://www.cidrap.umn.edu/news-perspective/2017/10/study-links-dental-antibiotics-c-diff-cases

Antibiotics Summary

Acute Infections (< 1 week)

-Amoxixillin 500mg 1 po TID x 7 days

or

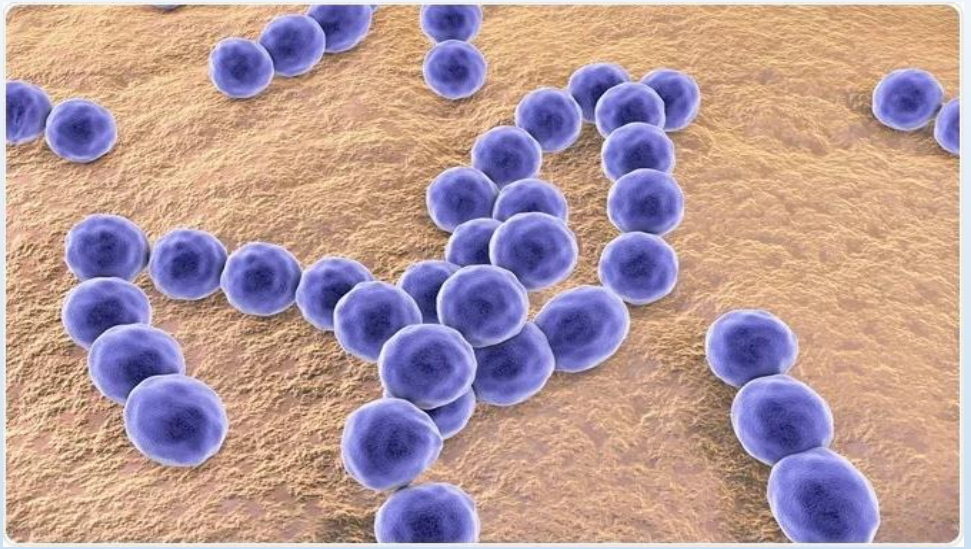
-Clindamycin 300mg 1 po TID x 7 days

Acute/Chronic infections (> 1 week)

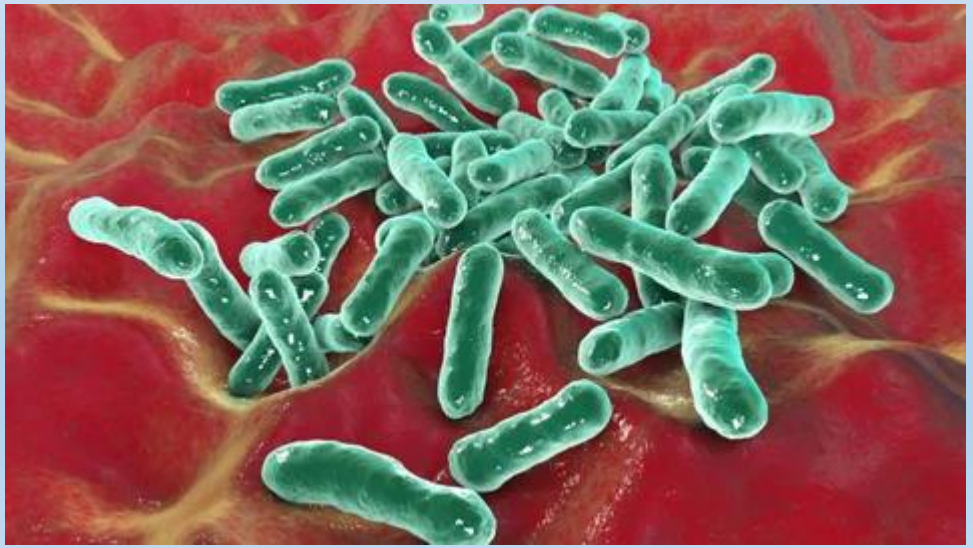
-Amoxicillin 500mg 1 po TID x 7 days + Metronidazole 500 mg po BID

or

-Clindamycin 300mg 1 po TID x 7 days



https://www.news-medical.net/life-sciences/Gram-Positive-Bacteria.aspx



https://www.shutterstock.com/video/search/anaerobic-bacteria

Acute Oral Surgical Complications:

Infection
Bleeding
Sinus Perforation
Nerve Injury
Damage to Adjacent Teeth
Dry Socket

John Collier (1708-1786). 1773 Print, British Museum, London

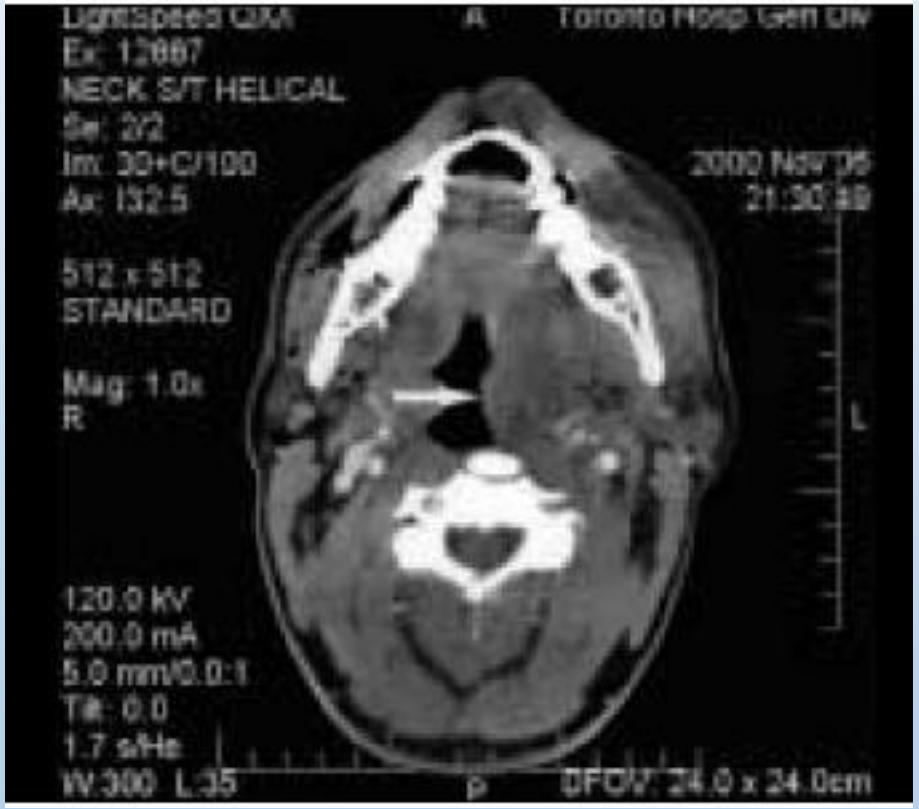
Acute complications: Bleeding

- Bleeding is considered a complication when it is either excessive in volume or time – ask about a history of bleeding
- Although not directly applicable both ‘bleeding time’ can be used as a guide in surgery
- Bleeding time (a specific laboratory test) ranges from 1 - 9 minutes dependent on vascular constriction and platelet function
- From 9 – 15 minutes indicates platelet dysfunction or low platelet count
- Factors that affect bleeding: hemophilia, CT diseases, medications (aspirin, nonsteroidal anti-inflammatory drugs [NSAIDs], antibiotics [penicillin, cephalosporins], anticoagulants, tricyclic antidepressants, antipsychotics, theophylline) as well as Vitamin C deficiency, alcohol intoxication, uremia and liver failure

Ritu Adhana, Comparison of bleeding time and clotting time between males and females, National J of Phys and Pharm, 2018(8)10, 1388.

How much blood loss is too much?

- Extremely variable – generally considered that 30 – 40% of blood volume loss leads to decompensation
- In oral surgical procedures it can be difficult to quantify as blood is mixed with saliva
- Patients often continue to bleed at home making volume of bleeding difficult to assess
- Fewer than 2% of wisdom tooth extractions result in ‘hemorrhage’
- Not all bleeding is visible



Moghadam & Caminiti, Life-Threatening Hemorrhage after Extraction of Third Molars: Case Report and Management Protocol, JCDA, December 2002, Vol. 68, No. 11

Report of a workshop on the management of patients with third molar teeth. J Oral Maxillofac Surg 1994; 52(11):1102–12

Mechanical Hemostasis

- Most peri-operative bleeding is from traumatized blood vessels at the operative site – small blood vessels ooze, larger vessels spurt
- Promote vessel spasm and occlusion

Burnish bone around bleeder

Plug bleeder

Occlude bleeder – direct pressure

Mechanical Hemostasis

Create and maintain backpressure, enhance clot stability – consider in the presence of anticoagulants

Also marketed as ‘Gelfoam’ made of methyl cellulose – absorbable scaffold for clot

Collagen plugs (bovine)
Stimulates platelet adherence

Oxidized methyl cellulose - low pH percipitates fibrin

All products stabilize blood clots - most effective when over-sewn

Thermal Hemostasis

Battery Powered Cautery – effective thermal coagulation if single vessel can be identified

Chemical Hemostasis

- AlCl3
- Ferric subsulfate (Fe4(OH)2(SO4)5)
- Fe2(SO4)3
- Silver nitrate (AgNO3)

- All act as astringents, constricting blood vessels
- Iron containing compounds are kinder to tissues
- 1:50,000 epinephrine – cardiovascular risk

How to manage the ‘spurter’ after extraction

Locate the vessel

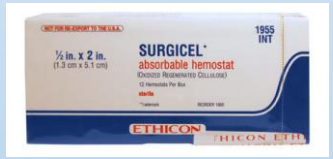
In bone try to burnish or place bone wax

In soft tissue ligate with suture or cauterize (chemical or thermal)

How to manage the ‘oozer’ after extraction

Locate the area of bleeding

In bone occlude & suture



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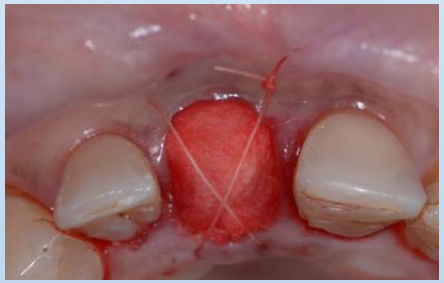
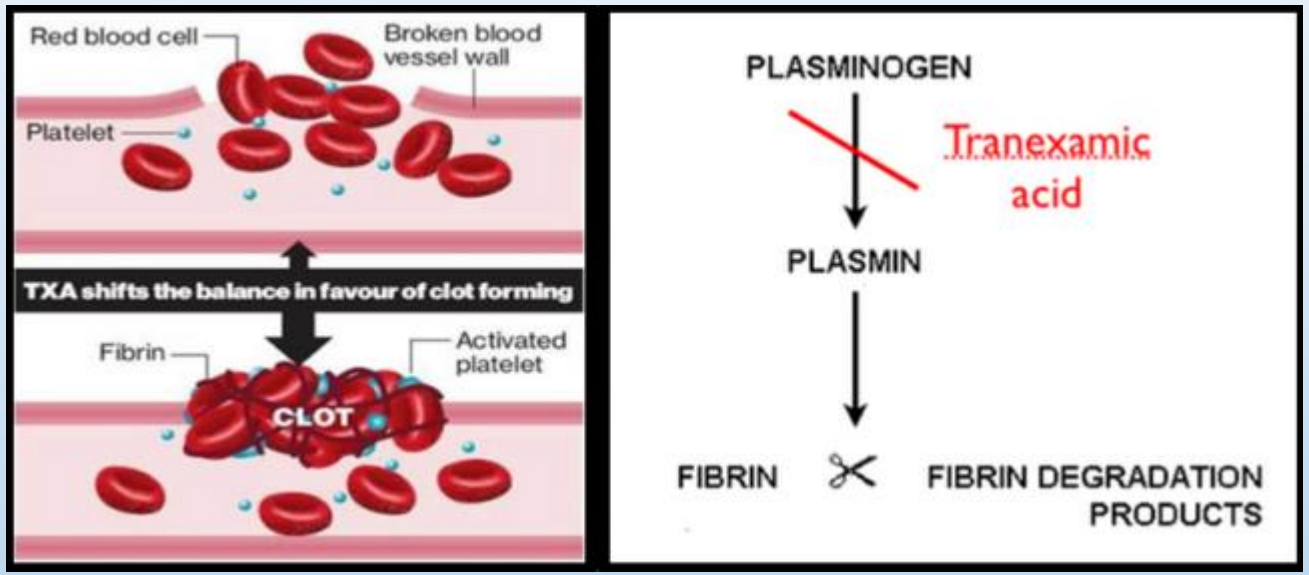


In soft tissue suture closed tightly apply pressure to the area

Tranexamic Acid (Cyklokapron)

- Tranexamic acid binds plasminogen preventing conversion to plasmin which degrades fibrin
- Clot remains stable longer
- Useful in patients with hemophilia or on anticoagulants
- Use topically as a paste or rinse for TID for2 -3 days post-op



500 or 650 mg tablet can be crushed and mixed with 20 ml saline or can be ordered from compounding pharmacy as 5% rinse

Table 3 Composition of active 5% tranexamic acid mouthwash

Tranexamic acid	500 g
Methyl hydroxybenzote (Nipagin M)*	15 g
Propyl hydroxybenzoate (Nipasol M)*	1.5 g
Distilled water (cold)	10 L

* Preservatives.

Eric Boccio, Topical Tranexamic Acid for Hemostasis of an Oral Bleed in a Patient on a Direct Oral Anticoagulant, Clin Pract Cases Emerg Med. 2020 May; 4(2): 146–149.

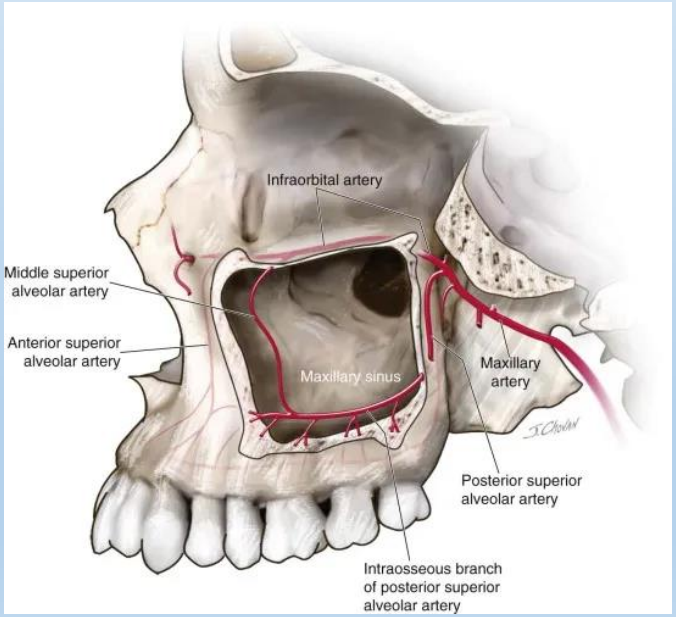
Acute Oral Surgical Complications:

Infection
Bleeding
Nerve Injury
Sinus Perforation
Damage to Adjacent Teeth
Dry Socket

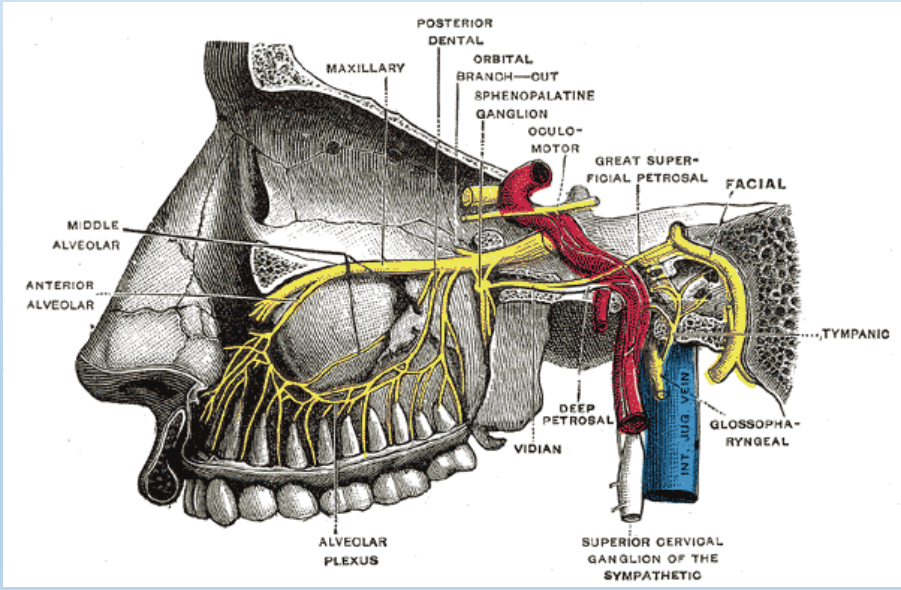
John Collier (1708-1786). 1773 Print, British Museum, London

Acute complications: Sinus perforation

Maxillary antrum - ventilated space lined by thin layer of secretory mucosa (Schneiderian membrane)
Blood supply – maxillary artery
Nerve supply – V2



https://pocketdentistry.com/the-maxillary-sinus-lift/



https://en.wikipedia.org/wiki/Maxillary_nerve

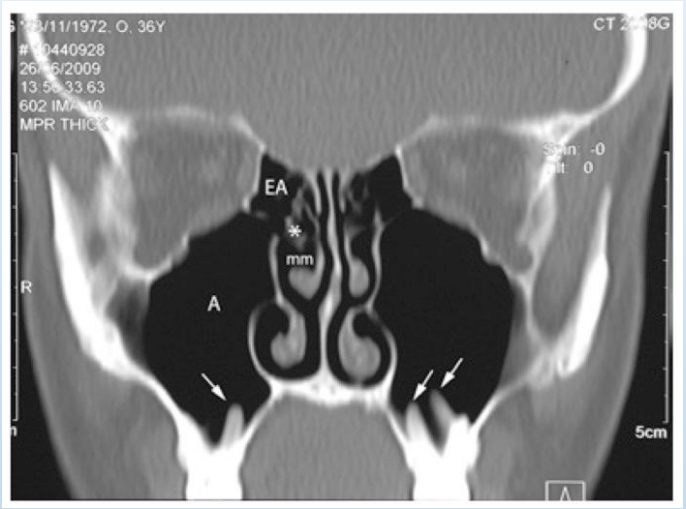
Acute complications: Sinus perforation

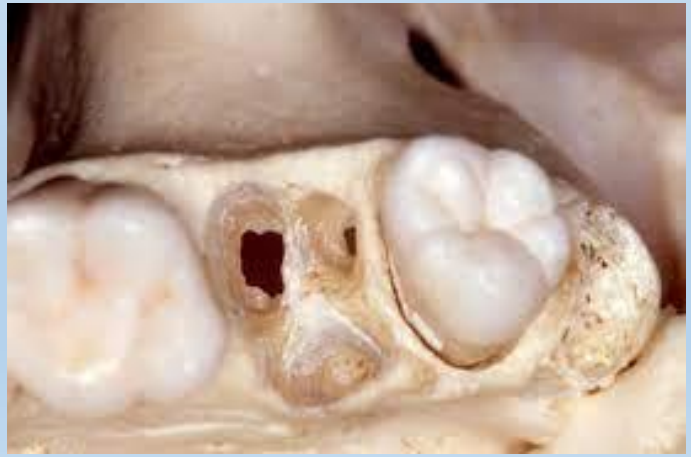
Sinus perforation most commonly associated with:

- Maxillary molar extraction
- Implant placement
- Maxillary wisdom tooth removal

Most common Sequelae:

- Oral antral fistula
- Foreign body



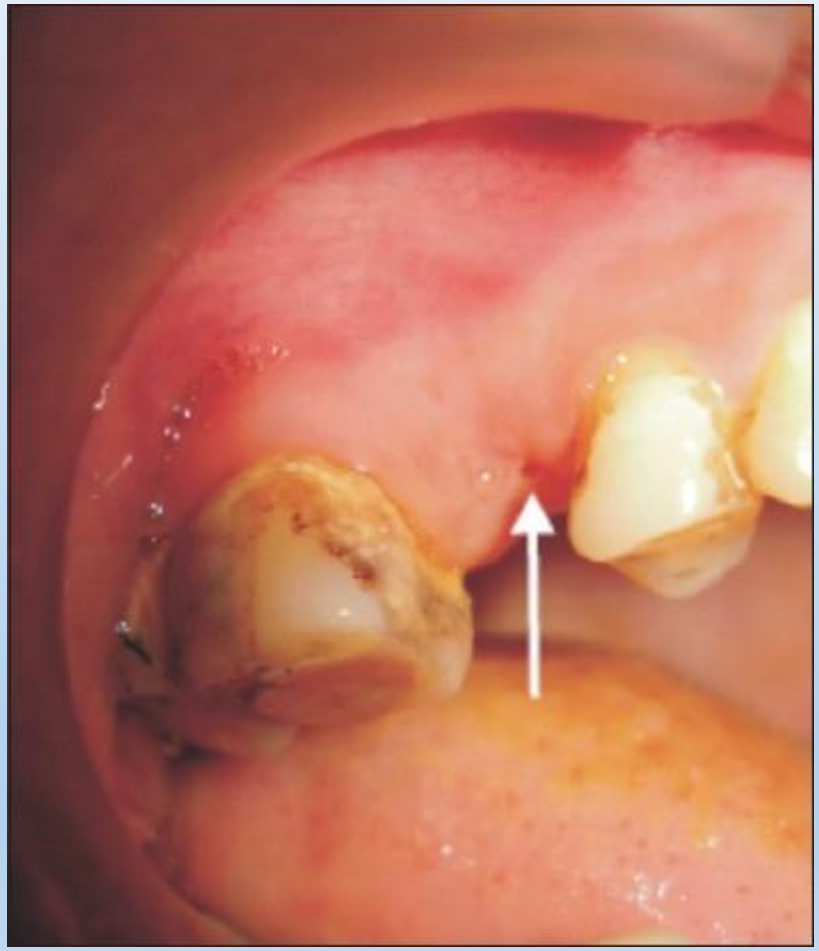


https://www.researchgate.net/figure/CT-scan-coronal-plane-of-the-maxillary-and-anterior-ethmoid-area-corresponding-to-a_fig1_260645343

Acute complications: Sinus perforation

Sinus perforation can lead to an ‘oro-antral communication’ or ‘oro-antral fistula’ (OAF)

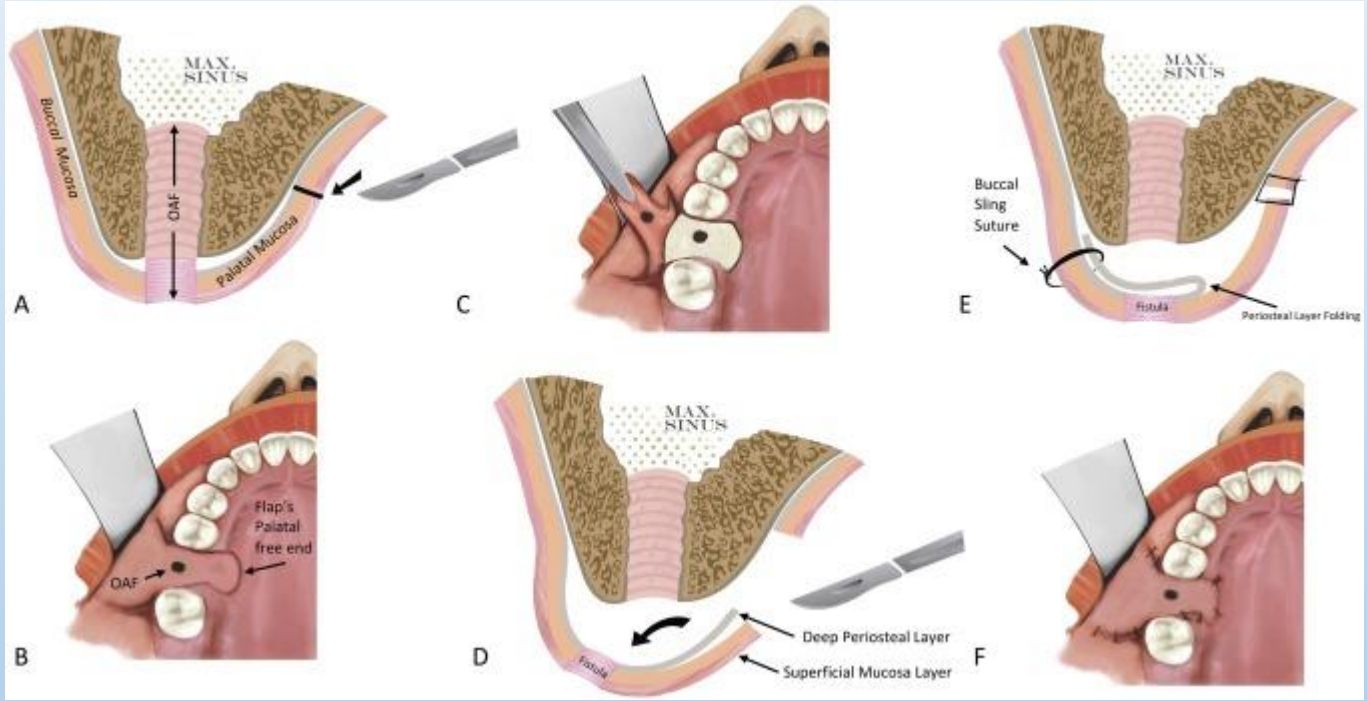
- Most perforations or communications heal spontaneously if small
- Ongoing movement of air or fluid (saliva) can cause epithelialization of tract
- Sinusitis may develop with chronic OAF



https://www.researchgate.net/figure/Intraoral-view-of-oro-antral-fistula-group-II_fig11_221971302

Acute complications: Sinus perforation

- Acute treatment: closure with or without socket grafting
- OAF treatment: de-epithelialize tract and close with or without reinforcing materials



BLAL, K., CLINICAL PAPER ORAL SURGERY| VOLUME 49, ISSUE 8, P1087-1091, AUGUST 01, 2020

Acute Oral Surgical Complications:

Infection
Bleeding
Sinus Perforation
Nerve Injury
Damage to Adjacent Teeth
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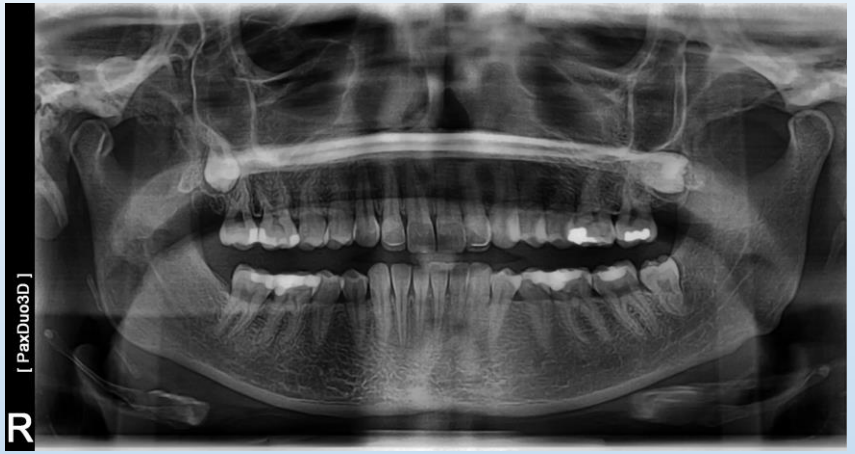
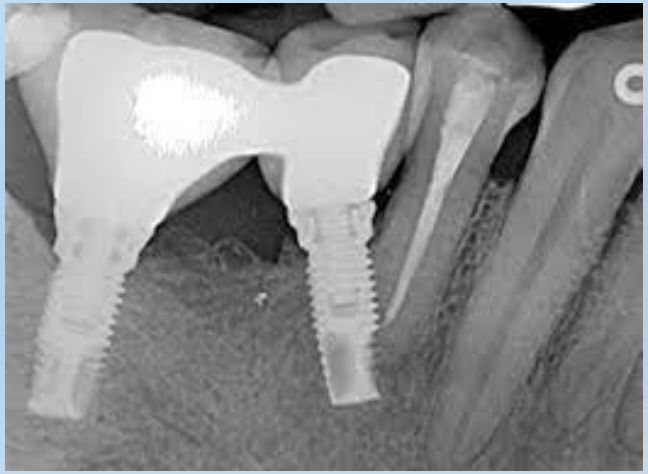
John Collier (1708-1786). 1773 Print, British Museum, London

Acute complications: Damage to adjacent teeth

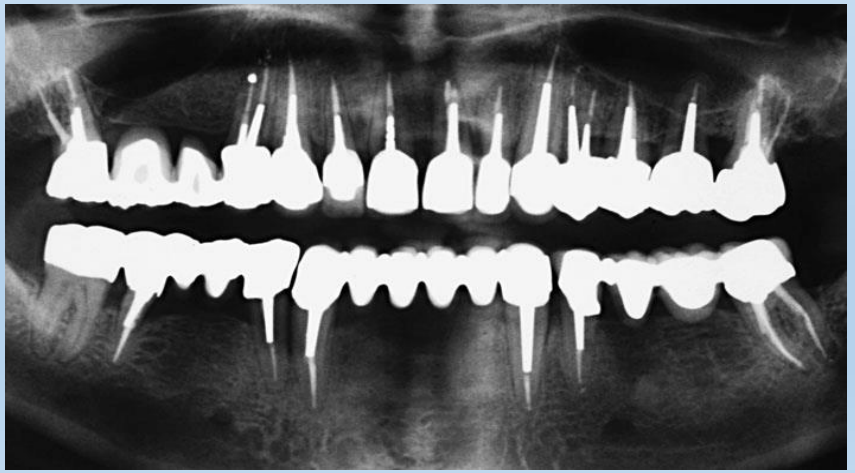
Damage to adjacent tooth roots or coronal structure is commonly due to poor planning, poor visibility, poor access or lack of awareness
Highest risk: adjacent restorations, roots next to implants, upper maxillary second molars next to impact upper wisdom teeth



https://www.hokholdinc.com/procedures/case-presentations

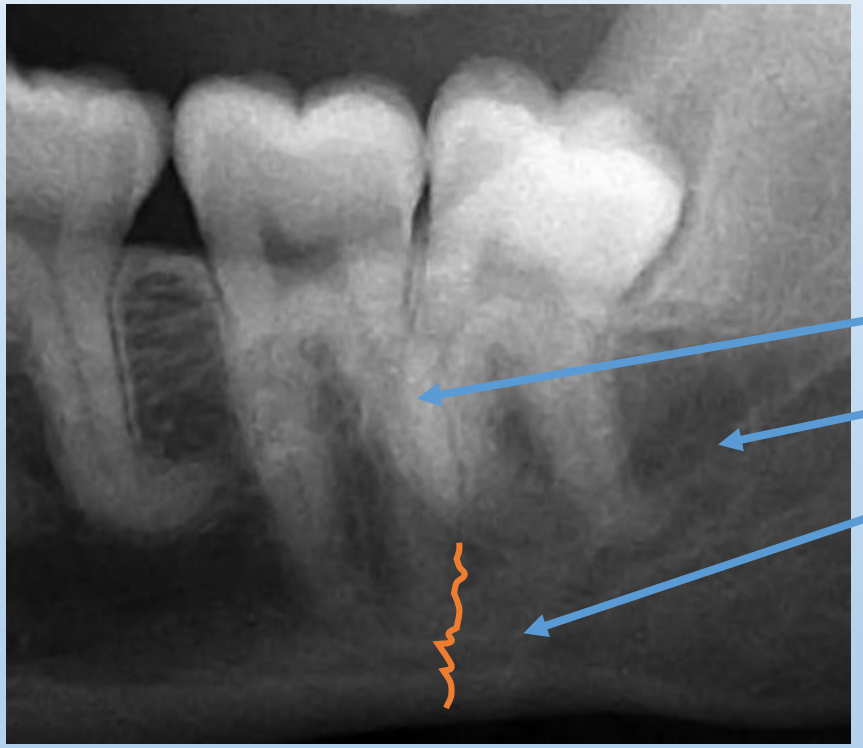


http://www.quintpub.com/userhome/prd/prd_39_2_Nohra_p239.pdf



https://www.researchgate.net/figure/Panoramic-radiograph-of-a-70-year-old-patient-with-a-heavily-restored-dentition-The_fig8_26717730

Teeth to be very cautious with: disto-angular lower wisdom tooth



Risks:

- Damage to roots of second molar
- Potential for IDN injury
- Jaw fracture

Acute Oral Surgical Complications:

Infection
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Damage to Adjacent Teeth
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John Collier (1708-1786). 1773 Print, British Museum, London

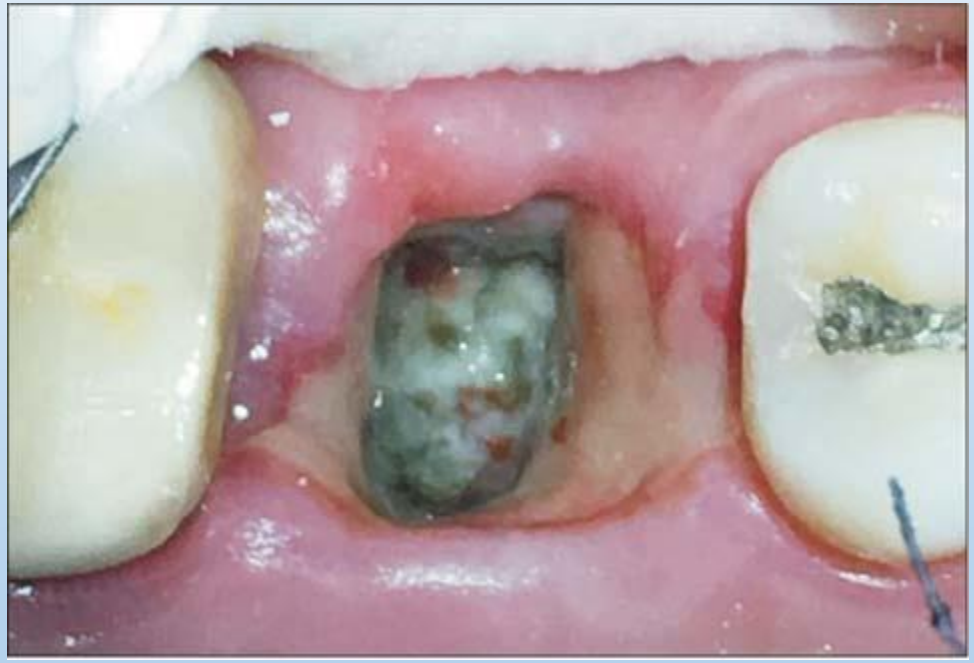
Acute complications: Dry Socket (alveolar osteitis)

- Prevalence: 1 – 4% of all extractions, up to 40% of lower third molars in some studies
- Prophylactic extractions associated with 7% DS while therapeutic extractions result in 21% DS
- Typically happens 3 – 4 days after extraction
- Etiology not well defined – premature fibrinolysis where clot is replaced with fibrinous exudate
- Proposed mechanism – kinins formed from increased presence of plasmin which stimulates sensory nerves previously sensitized through inflammatory mediators
- Interaction of bacteria and trauma leads to plasmin release and fibrinolysis, bacteria may also contribute through pyrogens
- Blood clots contain antiplasmin which may explain delayed fibrinolysis

Cardoso et al, Clinical Concepts of Dry Socket, J Oral Maxillofac Surg 68:1922-1932, 2010

Dry socket: risk factors

- Peak age 5th decade – increasing age increases risk
- Oral contraceptives associated with increased risk (11% vs 4%)
- Smoking 10 cigarettes per day 11% vs 2%, additional 40% increase for smokers who smoked on day of surgery or first post op day
- EtOH aslo a minor risk factor



https://www.dentalnotebook.com/dry-socket-diagnosis-and-management/

Dry Socket: Prophylaxis

Preventive strategies:

- pre and post extraction antibiotics – inconclusive results, some studies showed benefit from anaerobe targeting antibiotics
- Antibiotic impregnated socket dressings – some studies show significant protection
- Pre extraction Chlorhexidine rinse - inconclusive
- Post extraction irrigation with NS or Chlorhexidine mouth wash – inconclusive results

Cardoso et al, Clinical Concepts of Dry Socket, J Oral Maxillofac Surg 68:1922-1932, 2010

Dry Socket: Treatment

- Treatment focuses on inhibiting bacterial proliferation and protecting alveolar wall
- Iodine containing compounds or irrigation inhibit bacterial growth
- Peroxide releases free oxygen radicals supressing anaerobes
- Eugenol or topical local anesthetics are sedative
- No single product has been shown to be consistently superior

Cardoso et al, Clinical Concepts of Dry Socket, J Oral Maxillofac Surg 68:1922-1932, 2010

Oral Surgical Sequelae

Nerve Injury
Osteonecrosis
Osrteomyelitis

“The Dentist” Jan Miense Molenaer 1629.

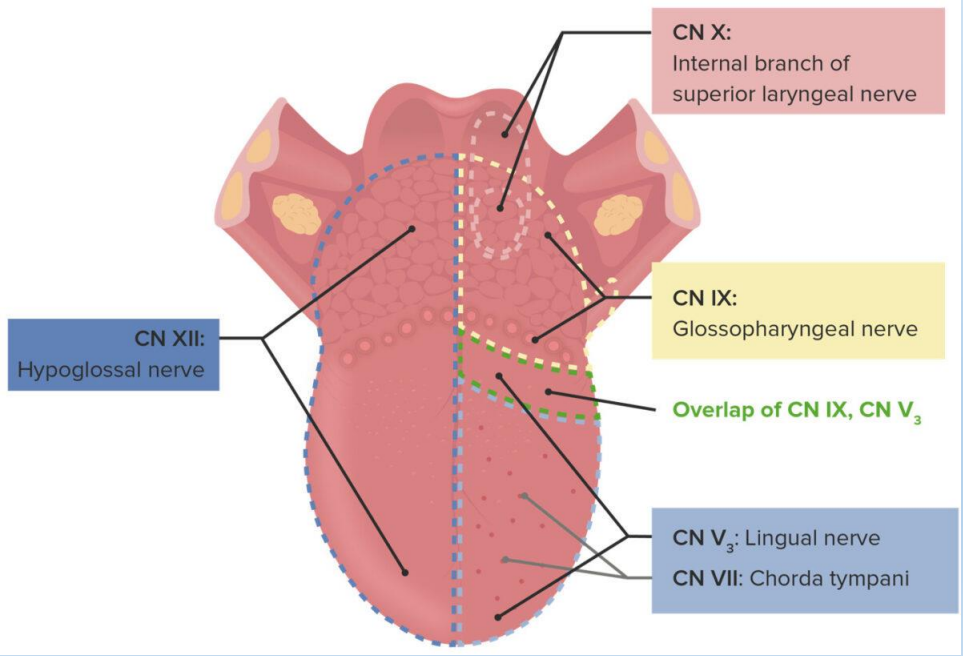
Acute complications: Nerve Injury

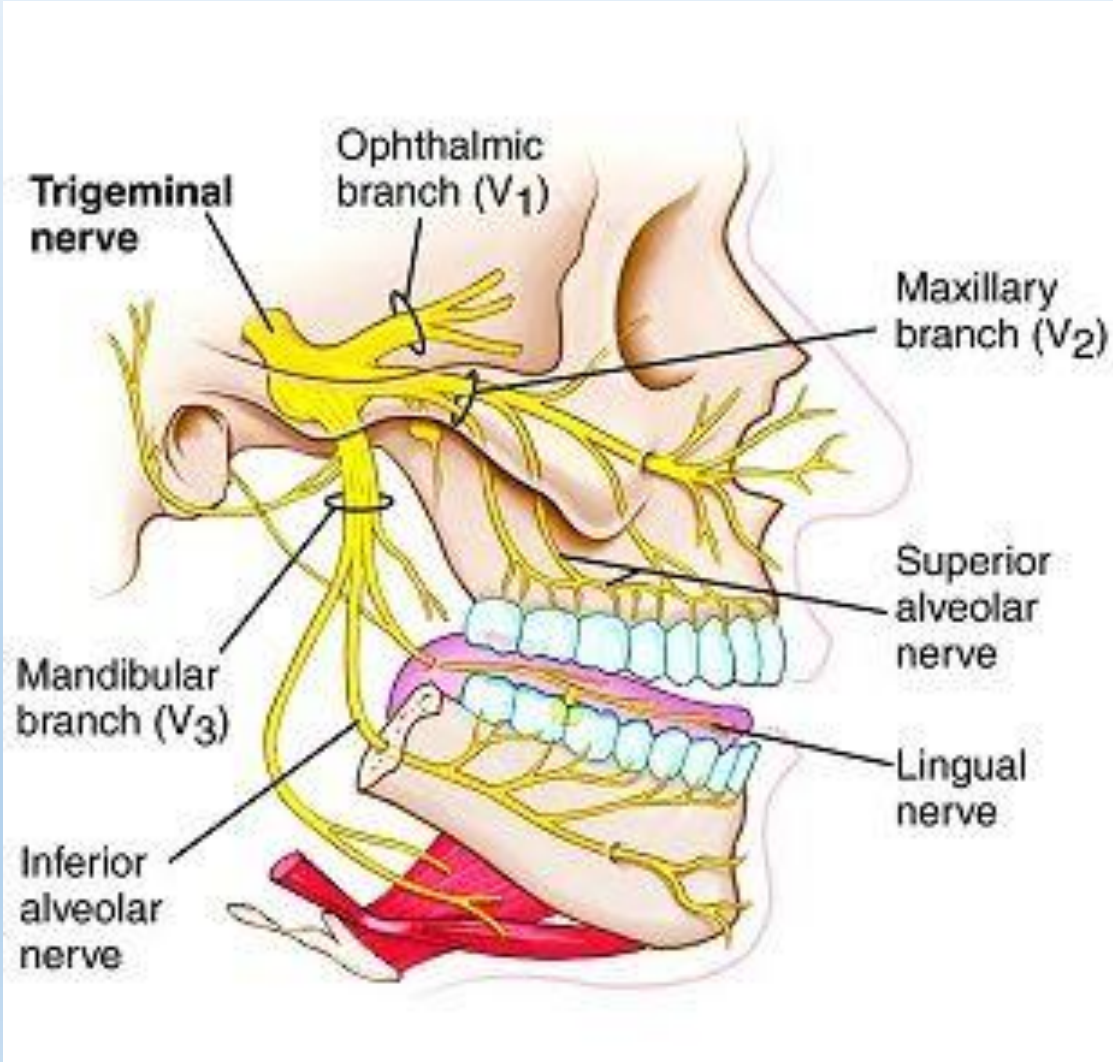
- 91% of damage claims for nerve injuries are secondary to surgical extractions
- 78% are GPs, 15% OMFS
- >50% of dentists had less than 10 yrs experience
- Compensation paid in 67% of cases

Ventä 1, C Lindqvist, P Ylipaavalniemi, Acta Odontol Scand. 1998 Aug;56(4):193-6 Malpractice claims for permanent nerve injuries related to third molar removals

Trigeminal Nerve

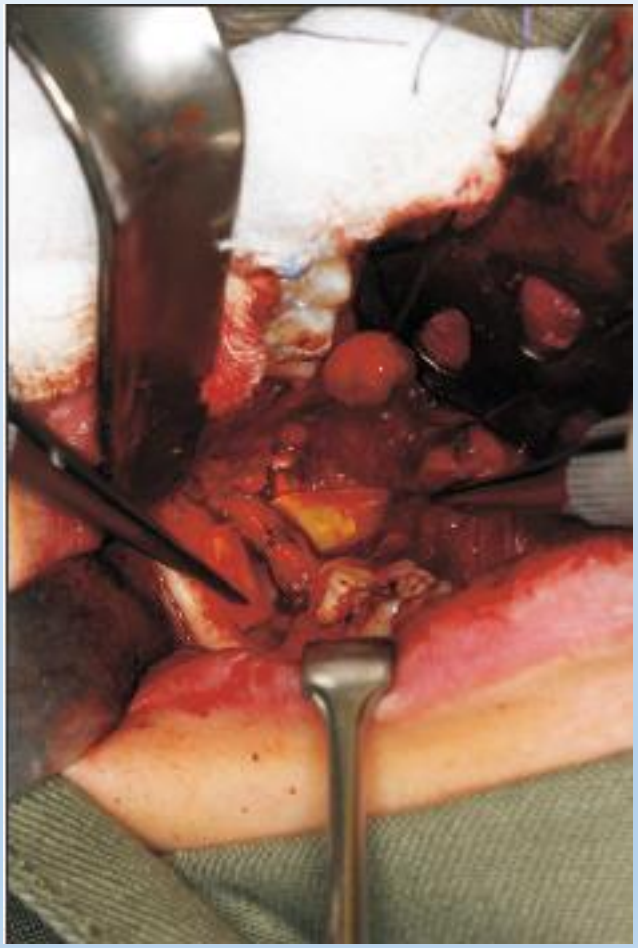
V3 (IDN) sensation to lower lip and teeth
V3 (LN) sensation and taste to anterolateral tongue





Nerve Injury: Wisdom Tooth Removal

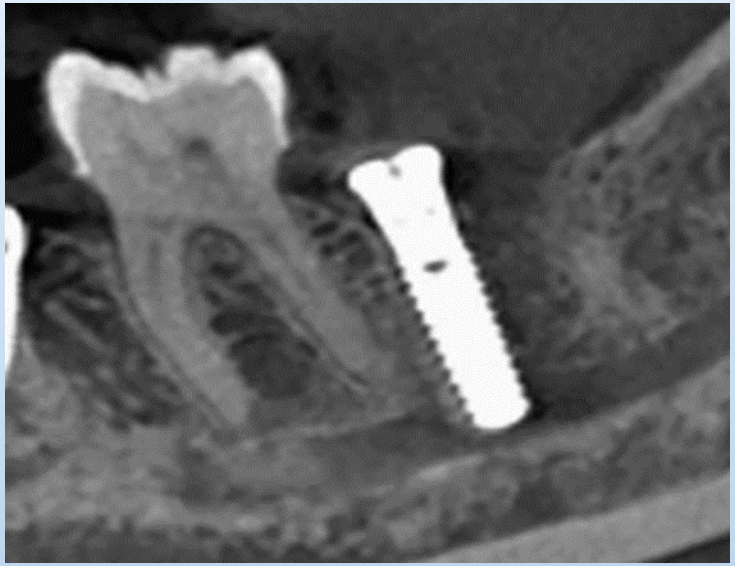
- Most common nerve injury in Oral Surgery is secondary to wisdom tooth extraction involving IDN or LN
- Estimated prevalence 1%
- Most common mechanism – compression, laceration
- Risk increases with age and systemic disease such as diabetes
- Preventive measures include coronectomy, LN protection controversial
- Healing more common in IDN where regrowth is guided by canal
- Treatment: severe injury repaired through suturing, grafting or conduit



Yiu Yan Leung, Management and prevention of third molar surgery-related trigeminal nerve injury: time for a rethink. J Korean Assoc Oral Maxillofac Surg 2019;45:233-240

Nerve Injury: Dental Implant Placement

- Most common nerve injury in Implantology involves IDN
- Prevalence ranges up to 24% with 11% being permanent
- Most injuries are crush type from implant placement and a minority are lacerations from rotary instruments
- Treatment – most successful treatment is removal of implant, steroid may be helpful



Shavit, I., & Juodzbalys, G. (2014). Inferior alveolar nerve injuries following implant placement - importance of early diagnosis and treatment: a systematic review. Journal of oral & maxillofacial research, 5(4), e2. https://doi.org/10.5037/jomr.2014.5402

Oral Surgical Sequelae

Nerve Injury
Osteonecrosis
Osteomyelitis

“The Dentist” Jan Miense Molenaer 1629.

Sequelae: Osteonecrosis

Osteonecrosis of the Jaws (ORN) is fundamentally an avascular necrosis of bone

Caused by:

- radiation (osteoradionecrosis)
- high dose steroids
- medications that alter bone blood supply or bone turnover
- infections (Staph osteomyelitis)

First similar condition reported in 1860s as “phossy jaw” believed due to phosphorous in matches. Yellow phosphorus was added to match heads was converted to a bisphosphonate during manufacturing exposing factory worker.

Wan, J.T., Sheeley, D.M., Somerman, M.J. et al. Mitigating osteonecrosis of the jaw (ONJ) through preventive dental care and understanding of risk factors. Bone Res 8, 14 (2020).

Sequelae: Osteonecrosis

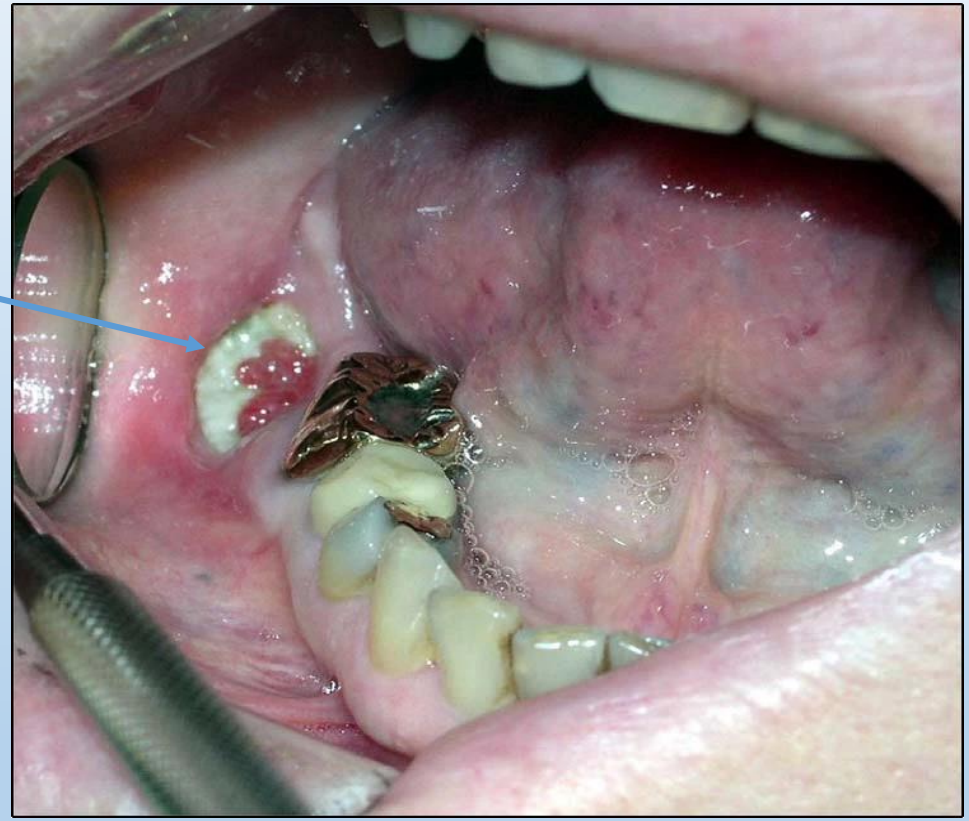
Case description:

Early stages

- pain (not always)
- radiographic changes and exposed bone
- soft tissue inflammation

Later Stages

- pathologic fractures
- extra-oral fistula



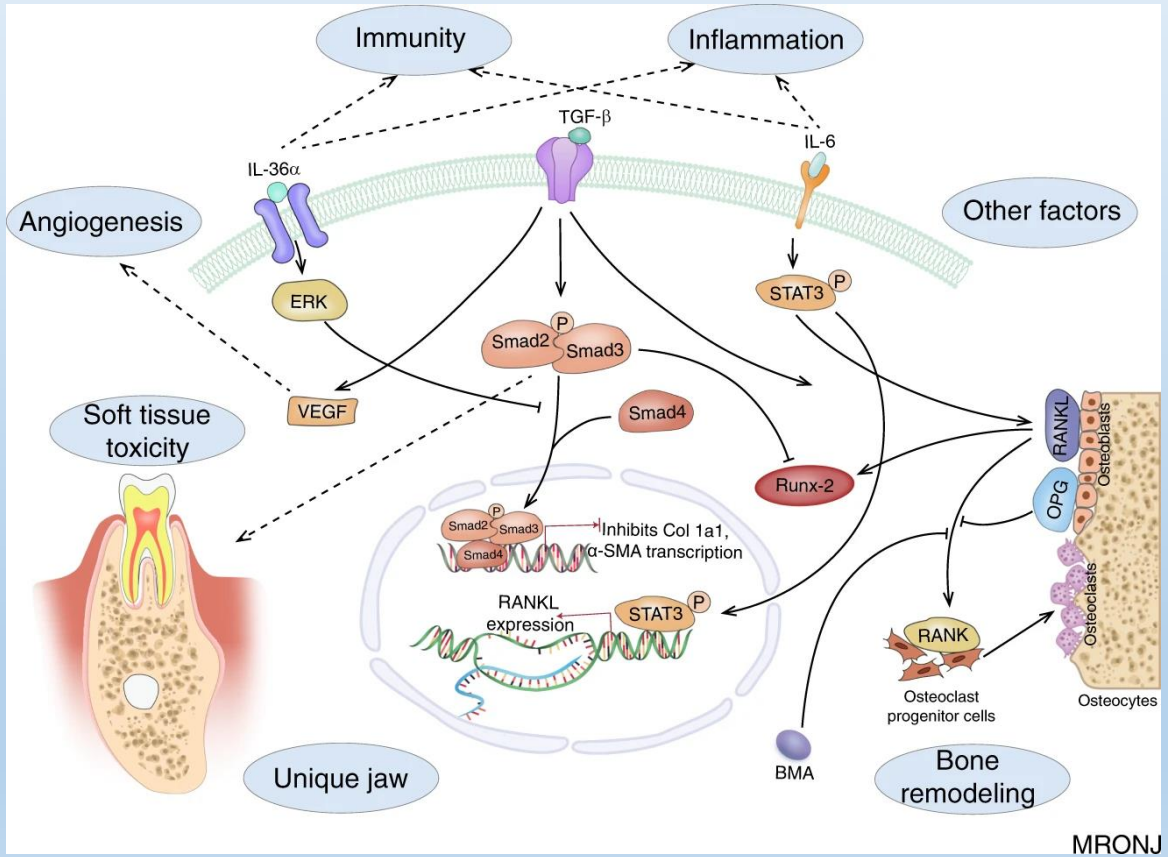
Wan, J.T., Sheeley, D.M., Somerman, M.J. et al. Mitigating osteonecrosis of the jaw (ONJ) through preventive dental care and understanding of risk factors. Bone Res 8, 14 (2020).

Sequelae: Osteonecrosis

Risk factors

- Dental factors
- Oral infections and associated inflammation
- Periodontal disease
- Untreated caries
- Pulp infections
- Dentoalveolar surgery
- Trauma or injury
- Tooth extractions or removal of failed implants
- Ill-fitting dentures
- Medical factors
- Systemic infections
- Rheumatoid arthritis
- Diabetes
- Vascular disease
- Sjögren's Syndrome

Proposed Pathogenesis



He, L., Sun, X., Liu, Z. et al. Pathogenesis and multidisciplinary management of medication-related osteonecrosis of the jaw. Int J Oral Sci 12, 30 (2020).

Sequelae: Osteonecrosis

Treatment relative to stage

	Stage 1	Stage 2	Stage 3
Staging criteria	• Exposed bone • Asymptomatic	• Exposed bone • Associated pain • Adjacent/regional soft-tissue inflammatory swelling or infection	As Stage 2 + at least one of: • pathological fracture • extra-oral fistula • oroantral fistula • radiographic evidence of osteolysis extending to inferior border of mandible or floor of maxillary sinus
Treatment	• Conservative therapy – improve oral hygiene • Consider surgical treatment to remove necrotic bone • Treat active dental and periodontal disease • Topical antibiotic mouth rinses	As Stage 1, also: • surgical treatment to remove necrotic bone • systemic antibiotics to treat any infection • treat symptoms if patient does not want surgery or cannot be treated surgically	As Stage 1, also: • surgical treatment to remove necrotic bone • in extended cases, consider resection including jaw reconstruction • systemic antibiotics to treat any infection

Sven Ottoa, Medication-related osteonecrosis of the jaw: Prevention, diagnosis and management in patients with cancer and bone metastases, Cancer Treatment Reviews 69 (2018) 177–187

Oral Surgical Sequelae

Nerve Injury
Osteonecrosis
Osteomyelitis

“The Dentist” Jan Miense Molenaer 1629.

Sequelae: Osteomyelitis

Osteomyelitis has been identified in 2 forms:

- chronic recurrent multifocal osteomyelitis (CRMO)
- infective osteomyelitis

CRMO

- rare
- effects mostly children and adolescents
- presents with pain and fever and facial swelling
- autoimmune in nature (dysregulation of chemokine/cytokine signalling
- treated with NSAIDs, steroids, bisphosphonates, DMARDs

Kim SM, Lee SK. Chronic non-bacterial osteomyelitis in the jaw. Journal of the Korean Association of Oral and Maxillofacial Surgeons. 2019 Apr 1;45(2):68-75.

Sequelae: Osteomyelitis

Infective Osteomyelitis

suppurative, diffuse sclerosing, focal sclerosing, proliferative periostitis

Suppurative

deep infection of bone from adjacent nidus initiated by trauma or intervention (surgery)

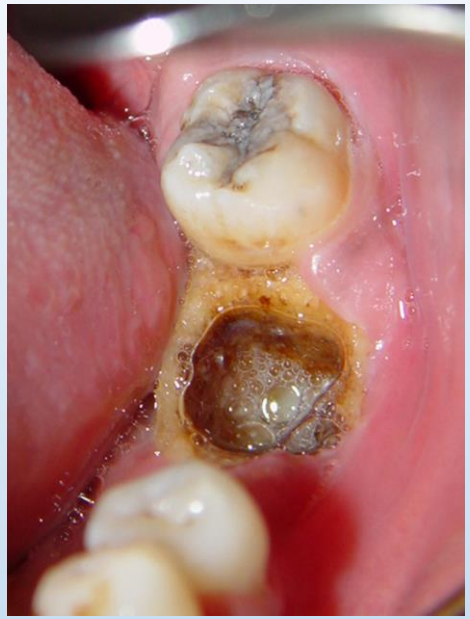
mandible most often affected

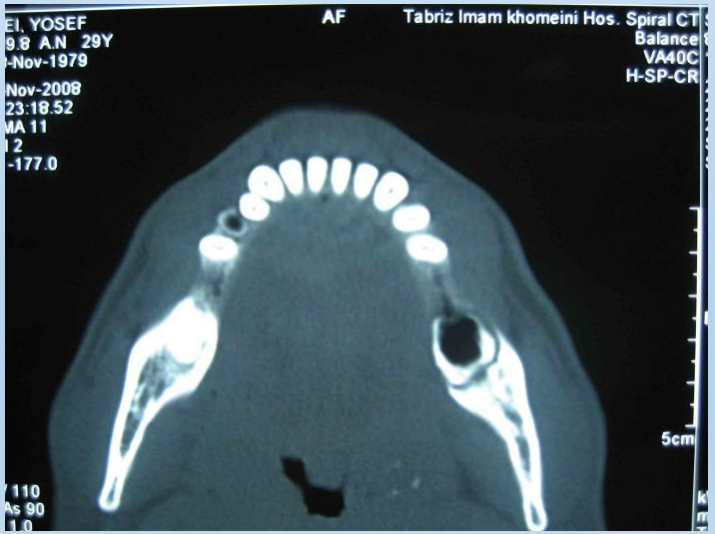
typically polymicrobial

bacteria penetrate bone causing inflammatory response compromising blood supply suppuration begins stripping periosteum, necrosing bone creating sequestrum

presents as pain and swelling may develop fistula to skin

treatment consists of surgical debridement and antibiotics



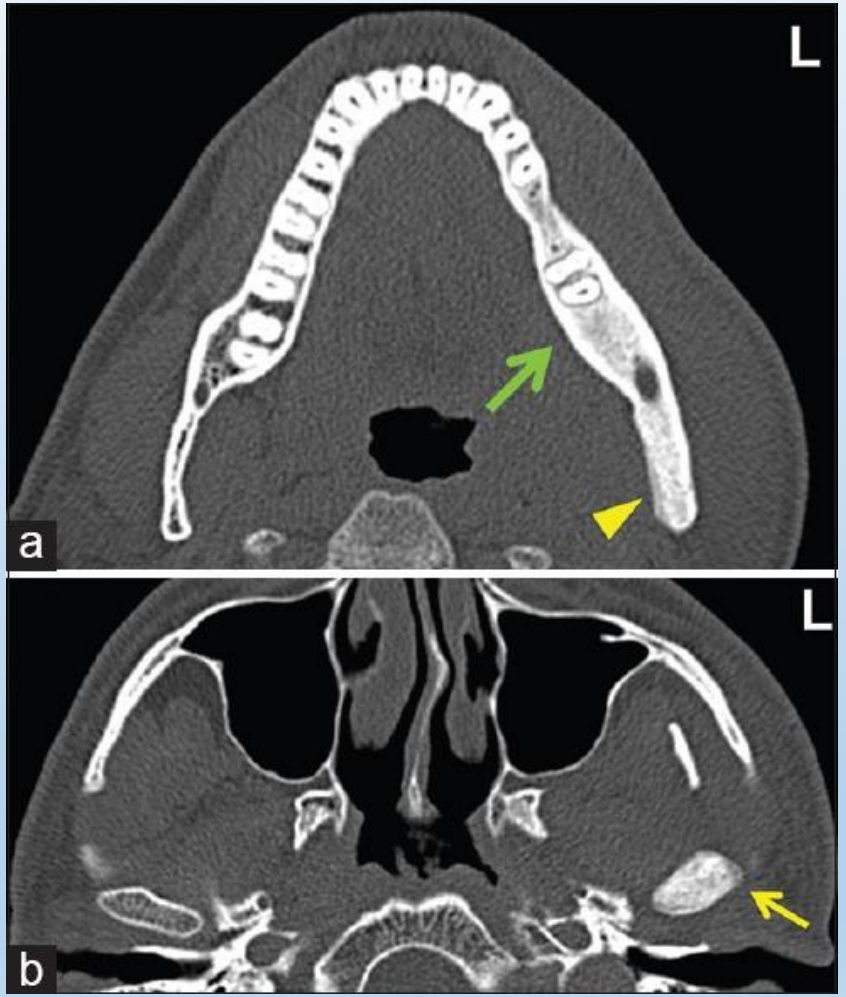


Nezafati, S., Ghavimi, M. A., & Yavari, A. S. (2009). Localized osteomyelitis of the mandible secondary to dental treatment: report of a case. Journal of dental research, dental clinics, dental prospects, 3(2), 67–69..

Sequelae: Osteomyelitis

Sclerosing (non-suppurative)

- much less common than suppurative
- proliferative reaction to low grade infection
- cyclical course
- presents as swelling with or without pain, paresthesia
- treated with antibiotics surgery depends on subtype (focal or diffuse) +/- HBO



Antao CJ, Dinkar AD, Khorate MM, Raut Dessai SS. Chronic Diffuse Sclerosing Osteomyelitis of the Mandible. Ann Maxillofac Surg. 2019 Jan-Jun;9(1):188-191.

Risk Factors in Oral Surgical Procedures

Disease States:

Diabetes
Cancer
Immunocompromised
Bleeding Disorders

Thomas Rowlandson (1757-1827). 1811 Print Wellcome Collection, London

Risk Factor: Diabetes

- Poorly controlled diabetes has been associated with impaired sodt tissue healing, graft healing, osseointegration, reduced long-term implant survival and increased marginal bone loss.
- Maintaining glycemic control improves patient outcomes.
- The degree of control should be assessed prior to initiating reconstructive or implant therapy if possible.
- There are two blood sugar tests that can be helpful:

1) A fasting blood sugar fasting blood sugar level will give a measure of glycemic control at a single time point, less than 100 mg/dL (5.6 mmol/L) is considered normal.

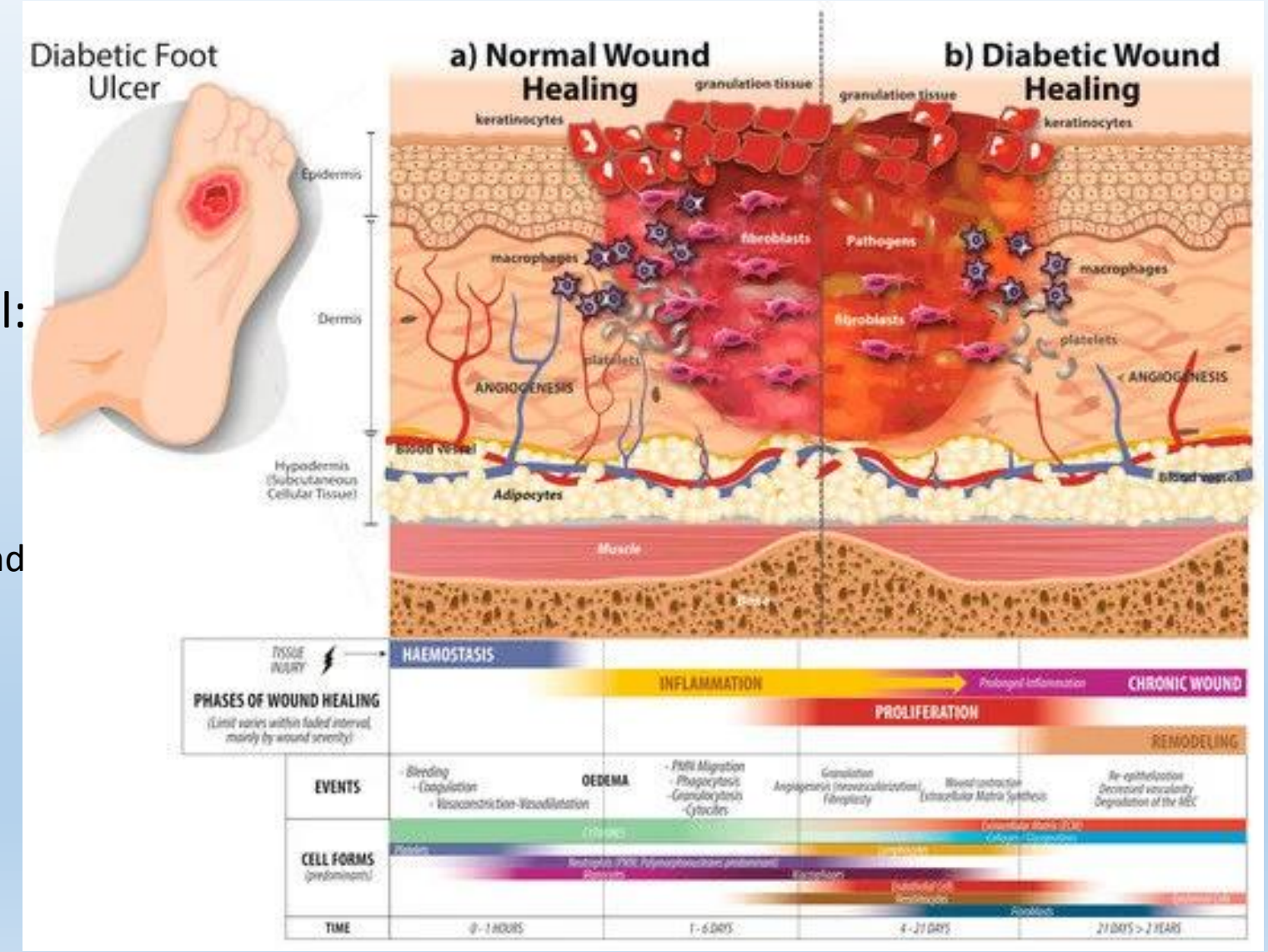
2) For the purpose of grafting or implant surgery measuring the degree of hemoglobin glycosylation, known as HbA1c gives a measure of control over a period of time. An HbA1c of less than 7% is a sign of consistently good diabetes management over the preceding 3 months and is associated with better implant success.

Fawad Javed, George E. Romanos,Impact of Diabetes Mellitus and Glycemic Controlon the Osseointegration of Dental Implants:A Systematic Literature Review, J Periodontol 2009;80:1719-1730.

Diabetes and Wound Healing

Poor chronic blood sugar control:

- Reduced fibrinolysis and cytokine imbalance results in irregular wound closure
- Hyperglycemia reduces angiogenesis and fibroblast migration
- Reduced fibroblast presence results in reduced ECM



https://www.mdpi.com/1648-9144/55/11/714/htm

Risk Factors in Oral Surgical Procedures

Disease States:

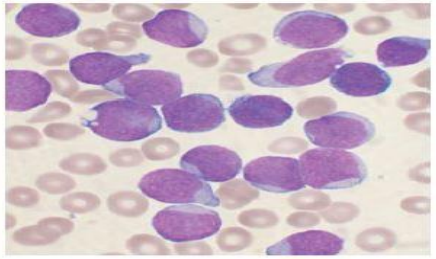
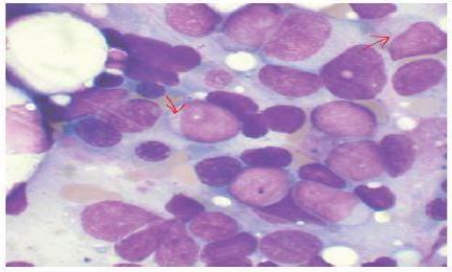
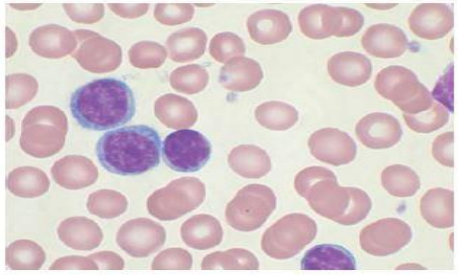
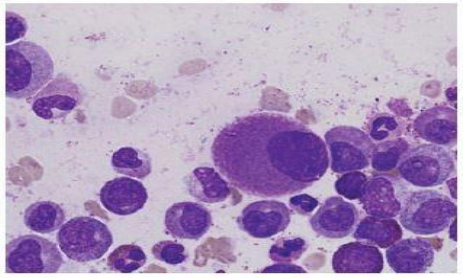
Diabetes
Cancer
Immunocompromised
Bleeding Disorders

Thomas Rowlandson (1757-1827). 1811 Print Wellcome Collection, London

Risk Factors: Cancer

- Cancer, whether solid or liquid is not generally a direct risk to Oral Surgical outcomes, it is Cancer treatment and its impact on the immune system that needs to be considered
- Hematologic cancers (such as leukemia) prior to treatment cause hematopoietic and immune suppression resulting in low platelet counts and impaired immunity, increasing the risk of bleeding and infection.
- Common forms of cancer treatment include radiation therapy and chemotherapy. Protocols and drugs differ depending on the disease.

TABLE 2. DIAGNOSTIC PERIPHERAL BLOOD SMEAR OF LEUKOCYTE[6]

ALL (B cells)	AML (Auer rods)	CLL (B cells)	CML (Ph+)
			

ALL indicates acute lymphoid leukemia; AML, acute myeloid leukemia; CLL, chronic lymphoid leukemia; CML, chronic myeloid leukemia; Ph+, Philadelphia chromosome positive.

Jerry A. Barbee, Leukemia: Causes, Symptoms, and Treatments, December 1, 2018, Health-System Edition, November 2018, Volume 7, Issue 6

Risk Factors: Radiation Soft & Hard Tissue Pathology

Ionizing radiation damage is initiated by depletion of tissue stem cells, progenitor cells and damage to vascular endothelial capillary networks.

Recovery of stromal stem cells remain chronically impaired by long-lived free radicals, reactive oxygen species, and pro-inflammatory cytokines/chemokines resulting in progressive damage after radiation exposure.

Soft tissues become fibrotic, hypo-cellular and hypo-vascular

Bone may develop ‘osteoradionecrosis’

Jae Ho Kim. Mechanisms of radiation-induced normal tissue toxicity and implications for future clinical trials, Radiat Oncol J 2014;32(3):103-115
Chunyue Ma, Radiation-Induced Soft Tissue Injuries in Patients With Advanced Mandibular Osteoradionecrosis: A Preliminary Evaluation and Management of Various Soft Tissue Problems Around Radiation-Induced Osteonecrosis Lesions, Front. Oncol., 28 April 2021 | https://doi.org/10.3389/fonc.2021.641061

Risk Factors: Radiation Soft & Hard Tissue Pathology

Soft tissues become fibrotic, hypo-cellular and hypo-vascular resulting in stiffness and poor healing

Bone may develop ‘osteoradionecrosis’ – exposed necrotic bone usually secondary to some form of trauma (eg. extraction) which does not heal

Teeth (enamel and dentin) deteriorate – altered crystalline

Xerostomia – both major glands and minor glands affected, leads to decay

Oral Surgical procedures are best done before radiation

F. J. Lieshout & C. P. Bots The effect of radiotherapy on dental hard tissue. A systematic review, Clinical Oral Investigations, January 2014

Risk Factors: Radiation Therapy-Implants & Grafting

- Guidelines suggest that placing implants or grafts in jaws irradiated with more than 50 Gy of ionizing radiation is an absolute contraindication. Current literature is less definitive arguing that newer modulated radiation treatments with doses ranging from 40 to 70 Gy still have survival rates between 75% and 95%.
- A number of studies have shown consistent trends such as a higher failure rates in the maxilla and posterior mandible, an inverse relationship between radiation dose and implant survival as well as higher rates of osteoradionecrosis with higher doses.
- Confounding factors include type of cancer being treated, site specific radiation doses, concurrent surgical ablation with grafting and patient survival.
- One study has clearly shown that immediate placement of implants prior to radiation offers the best chance of implant survival and functionality for the patient.
- The benefit of hyperbaric oxygen therapy is unproven.

Franziska Wolf, Significance of site-specific radiation dose and technique forsuccess of implant-based prosthetic rehabilitation in irradiated head and neck cancer patients—A cohort study, Clin Implant Dent Relat Res. 2021;23:444–455.

Risk Factors: Chemotherapy

- Controlled studies examining the effect of active chemotherapy on surgical interventions such as grafting and implant integration and survival are lacking. Most of the evidence is limited to retrospective case control studies with limited numbers or animal studies.
- Mechanistically it would be expected that chemotherapeutic agents would inhibit cell proliferation in bone as well as soft tissue and therefore negatively affect soft tissue, bone healing as well as implant integration and survival. However, this has yet to be shown definitively.

Bruno Ramos Chrcanovic, Dental Implants in Patients Receiving Chemotherapy: A Meta-Analysis, IMPLANT DENTISTRY, VOLUME 25, NUMBER 2 2016

Risk Factors in Oral Surgical Procedures

Disease States:

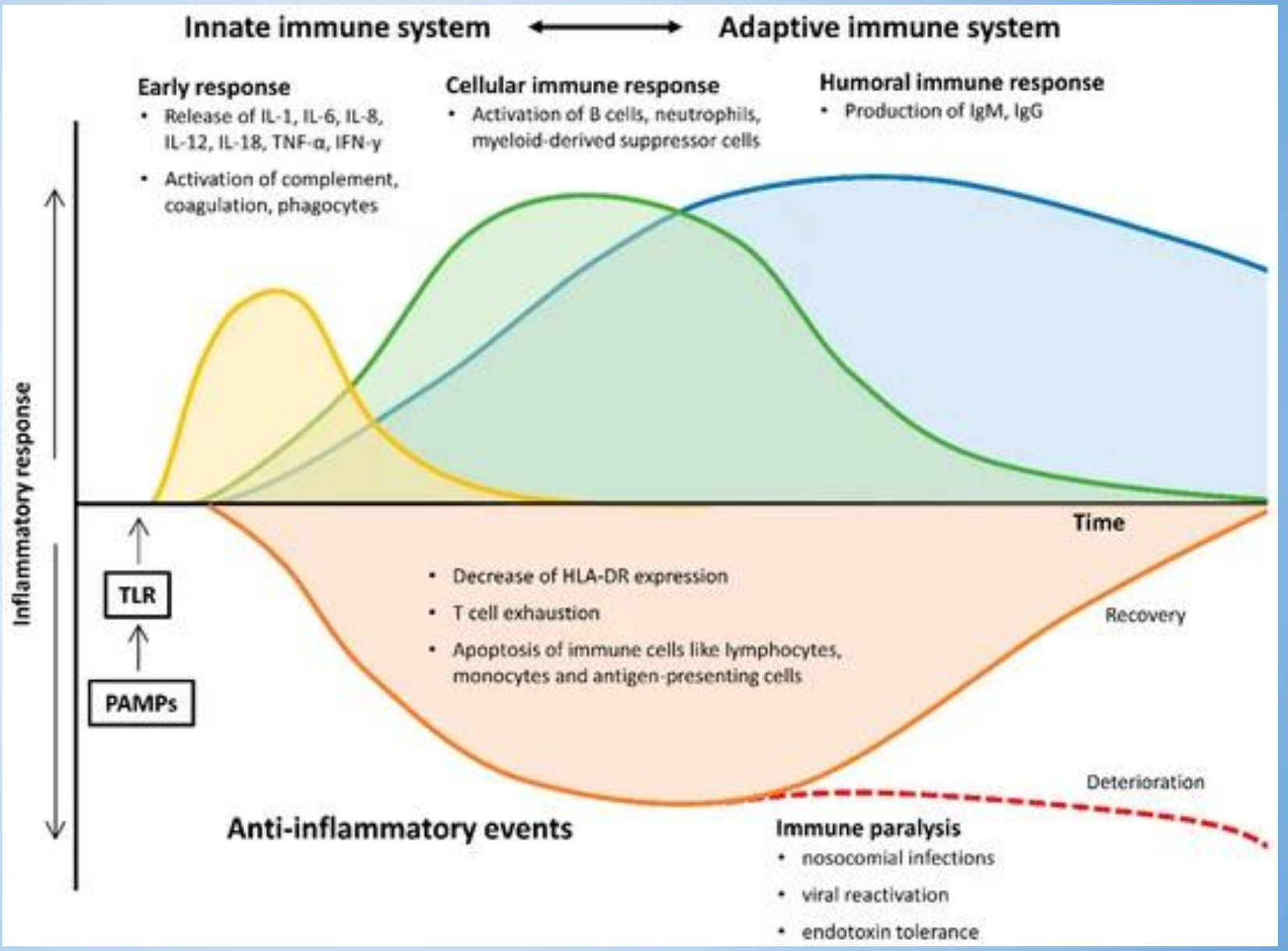
Diabetes
Cancer
Immunocompromised
Bleeding Disorders

Thomas Rowlandson (1757-1827). 1811 Print Wellcome Collection, London

Risk Factor: Immunocompromised

- Many diseases or medications cause patients to be functionally immunocompromised.
- This includes conditions like acute leukemias, HIV infection and therapeutic interventions such as bone marrow transplants
- Immune status has not been shown to have any significant impact on interventions such as implant survival these
- patients may be at significant risk of infection.
- Consideration should be given to consulting the patient’s physician to establish a safe treatment protocol for these individuals.

Degree of immunosuppression influences inflammatory response and recruitment of immune cells and antibody production



Jarczak, D.; Kluge, S.; Nierhaus, A. Use of Intravenous Immunoglobulins in Sepsis Therapy—A Clinical View. Int. J. Mol. Sci. 2020, 21, 5543. https://doi.org/10.3390/ijms21155543

Risk Factors in Oral Surgical Procedures

Disease States:

Diabetes
Cancer
Immunocompromised
Bleeding Disorders

Thomas Rowlandson (1757-1827). 1811 Print Wellcome Collection, London

Risk Factor: Bleeding disorders

- Uncontrolled bleeding conditions which can include Hemophilia A, B and C,

(also known as Factor VIII, IX and XI deficiency) or thrombocytopenia

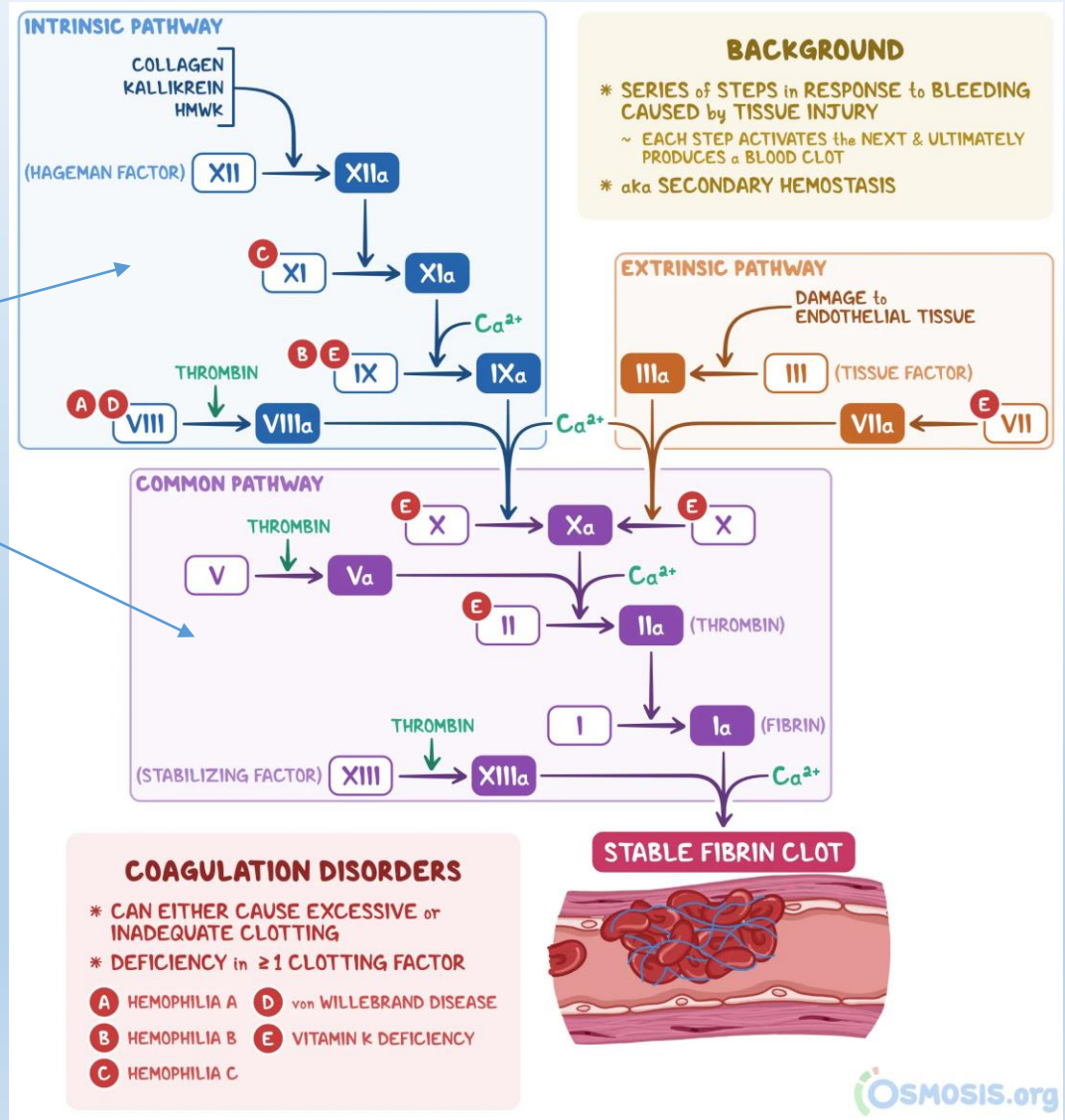
- will not affect healing, implant or graft survival but can complicate surgical procedures.
- Consideration should be given to consulting with the patient's hematologist.
- In some cases an infusion of coagulation factors is indicated prior to surgery as well as

initiation of antifibrinolytics such as tranexamic acid should be considered

Haemophilia and the Clotting Cascade

Most haemophilias affect the intrinsic pathway

Warfarin (Vit K antagonist) primarily effects the Common pathway



Risk Factors in Oral Surgical Procedures

Habits:

Smoking
Alcohol
Recreational Drugs

Thomas Rowlandson (1757-1827). 1811 Print Wellcome Collection, London

Risk Factors: Smoking

Nicotine

- vasoconstrictor - reduces oxygen delivery to healing tissues
- increases platelet adhesiveness
- raising the risk of thrombotic microvascular occlusion and tissue ischemia.
- reduces proliferation of red blood cells, fibroblasts, and macrophages

Carbon monoxide

- diminishes oxygen transport and metabolism

Hydrogen cyanide

- inhibits the enzyme systems necessary for oxidative metabolism and oxygen transport at the cellular level.

Silverstein P., Smoking and wound healing, The American Journal of Medicine Volume 93, Issue 1, Supplement 1, 15 July 1992, Pages S22-S24

Risk Factors: Smoking

- Smoking cigarettes is considered a relative contraindication to tissue regerative procedures and implant treatment.
- A recent meta-analysis demonstrated that smokers run a 140% higher risk of implant failure than non-smokers. This appears to be due to the adverse effect of cigarette smoke on bone matrix and mineralization. The bone in the anterior maxilla may be the most sensitive to the effects of cigarette smoke.
- Shorter implants also appear to fail more frequently.
- The data also demonstrates that the negative effect on implant survival is not linear.
- Smoking fewer than 10 cigarettes per day only marginally increase failure risk whereas smoking 30 or more cigarettes per day significantly increases failure. There is also a positive correlation with pack years smoked. Interestingly, exposure to second hand smoke is also a significant risk.

Wallace RH, The relationship between cigarette smoking and dental implant failure. The European Journal of Prosthodontics and Restorative Dentistry, 01 Sep 2000, 8(3):103-106
Twito and Sade (2014), The effect of cigarette smoking habits on the outcome of dental implant treatment. PeerJ 2:e546; DOI 10.7717/peerj.546
Abir Dunia Smoking and Dental Implants: A Systematic Review and Meta-Analysis Mustapha1Medicina 2022, 58, 39. https://doi.org/10.3390/medicina58010039

Risk Factors in Oral Surgical Procedures

Habits:

Smoking
Alcohol
Recreational Drugs

Thomas Rowlandson (1757-1827). 1811 Print Wellcome Collection, London

Risk Factors: Alcohol

Alcoholism is considered a relative contra-indication to regenerative procedures and implant treatment. The consumption of alcohol does not appear to interfere with soft tissue healing, bone healing or osseointegration.
May be associated with an increase in peri-implantitis causing reduced implant survival. However, a recent 5 – year retrospective study by Carr and colleagues demonstrated that the relationship of implant failure to alcohol consumption is not linear. Mild to moderate alcohol consumption significantly reduced the incidence of late implant failure while heavy consumption significantly increased implant failure when compared with non-consumption.

Carr B., Does alcohol consumption protect against late dental implant failures? Oral Surg Oral Med Oral Pathol Oral Radiol. 2021 Jun;131(6):631-637.

Risk Factors in Oral Surgical Procedures

Habits:

Smoking
Alcohol
Recreational Drugs

Thomas Rowlandson (1757-1827). 1811 Print Wellcome Collection, London

Risk Factors: Recreational Drugs

Drug addiction is a term commonly used to describe sustained abuse of mood altering substances. The FDA lists more than 170 drugs capable of being abused. This abuse occurs in all socioeconomic strata and demographics and can have a serious impact on oral health and dental treatment. Individuals who abuse drugs may or may not be addicted or dependant. Some of the more commonly abused substances include Methamphetamines, Cocaine, Heroin and Cannabis.

- Methamphetamines go by a series of names; meth, speed, ice, fire, glass and crystal. It is relatively inexpensive and gives a prolonged 'high'. Methamphetamine use is associated with 'methmouth' characterized by extensive caries, xerostomia and a tendency for significant bruxism. The concomitant use of local anesthetics with vasoconstrictor has led to heart attacks, hypertension, dysrhythmia and strokes.
- Heroin is an opiate which can be injected, snorted or smoked. Although there are no specific oral manifestations, concomitant use of sedation can cause profound respiratory suppression. Abusers who share needles are also at risk for diseases such as hepatitis and HIV.
- Cocaine also referred to as nose candy, coke and blow has no unique oral manifestations but chronic snorting can cause oral-nasal fistulas through soft and hard tissue necrosis. Concomitant use of local anesthetics with vasoconstrictors has been associated with hypertensive crisis as well as seizures.

Maloney W . The Significance Of Illicit Drug Use To Dental Practice .DENTISTRY, DRUG ABUSE 2010;1(7)
Terry D. ReesOral Effects of Drug Abuse Critical Reviews in Oral Biology and Medicine, 3(3):163-184 (1992)

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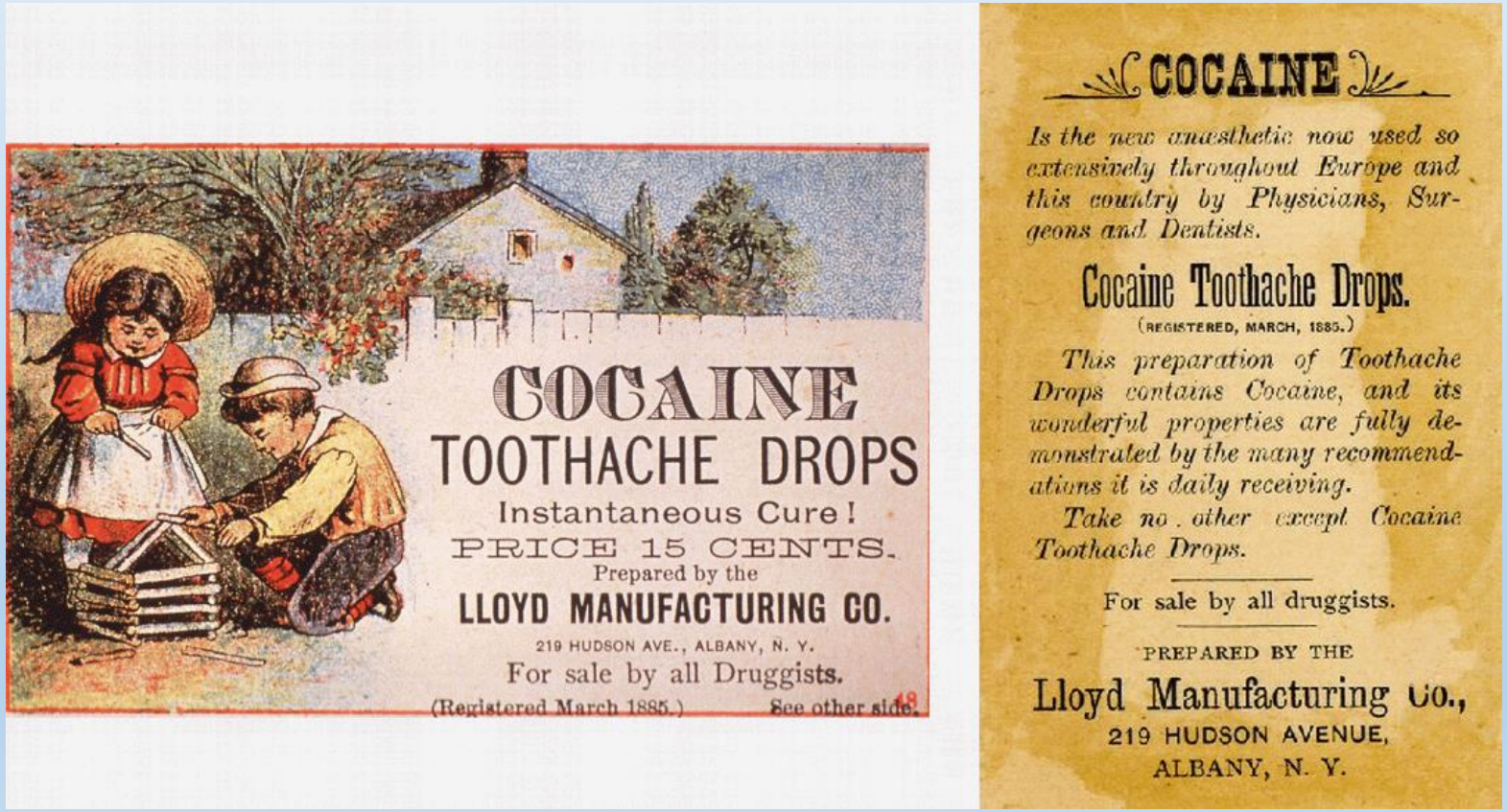
Risk Factors in Oral Surgical Procedures

Medications:

NSAIDs
PPIs
SSRIs
Clindamycin
CCBs
Bisphosphonates



Risk Factors: NSAIDs

It has been suggested that nonsteroidal anti-inflammatory medications should not be used as a post-operative analgesic in bone grafting or implant surgery.

This is mechanistically based on COX2 inhibitors ability to reduce prostaglandin levels which are necessary for bone formation.

Therefore reducing PG levels at the time bone grafts or implants are placed should inhibit osseointegration.

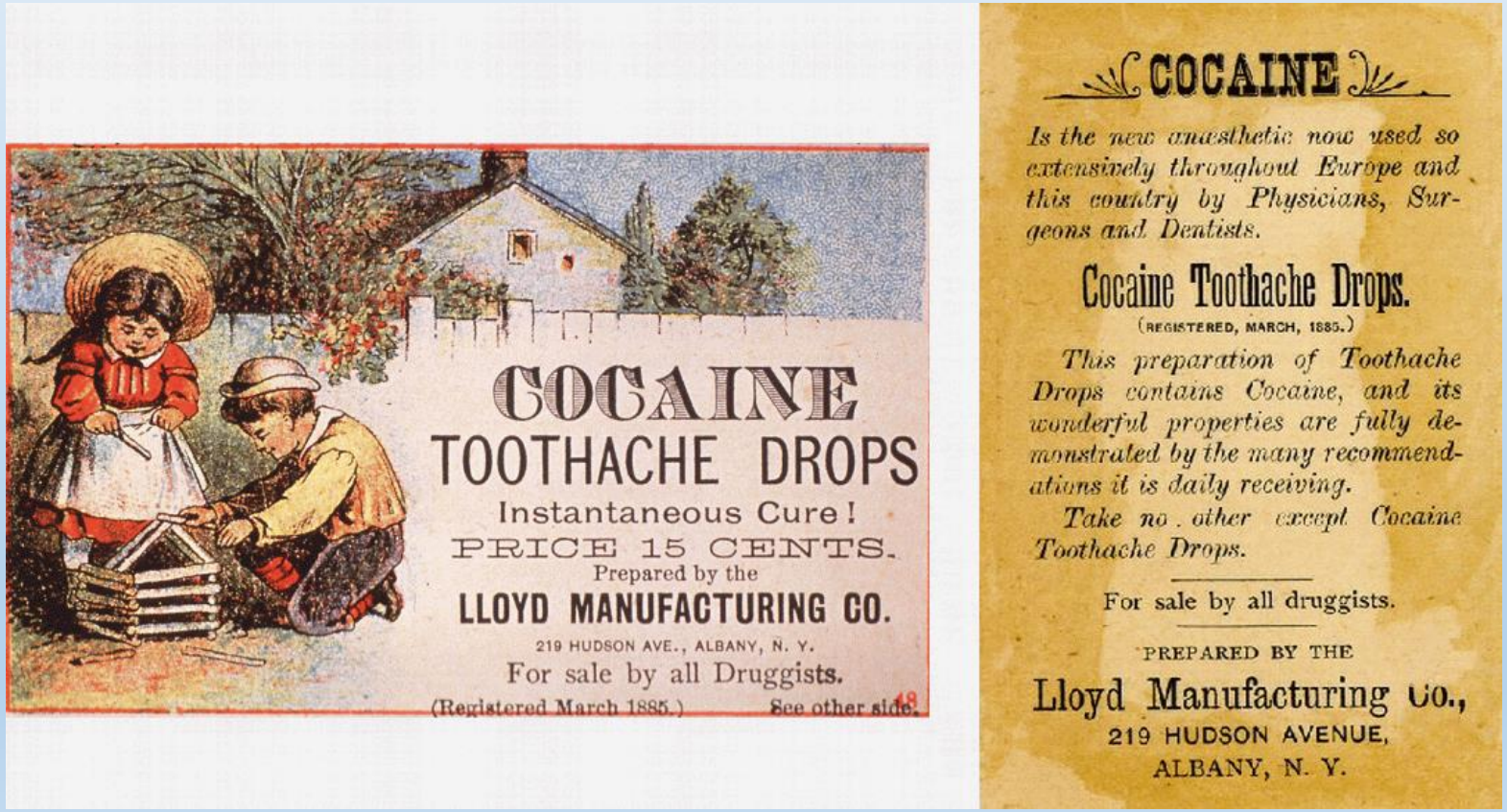
Lab and animal models however, do not bear this out. There are a number of uncontrolled clinical studies that suggest there is an early reduction in ISQ measurements which are not significant at 16 wks, increased peri-implant bone loss and increased implant integration failure rates when NSAIS are used post-operatively. Other studies could not duplicate these results. Current evidence is not convincing either way.

Perioperative use of non-steroidal anti-inflammatory drugs might impair dental implant osseointegration. Clin Oral Implants Res. 2016 Feb;27(2).
The Effect of non-steroidal anti-inflammatory drugs on the osteogenic activity in osseointegration: a systematic review. Int J Implant Dent. 2018 Dec; 4: 30.

Risk Factors in Oral Surgical Procedures

Medications:

NSAIDs
PPIs
SSRIs
Clindamycin
CCBs
Bisphosphonates



Risk Factors: PPIs

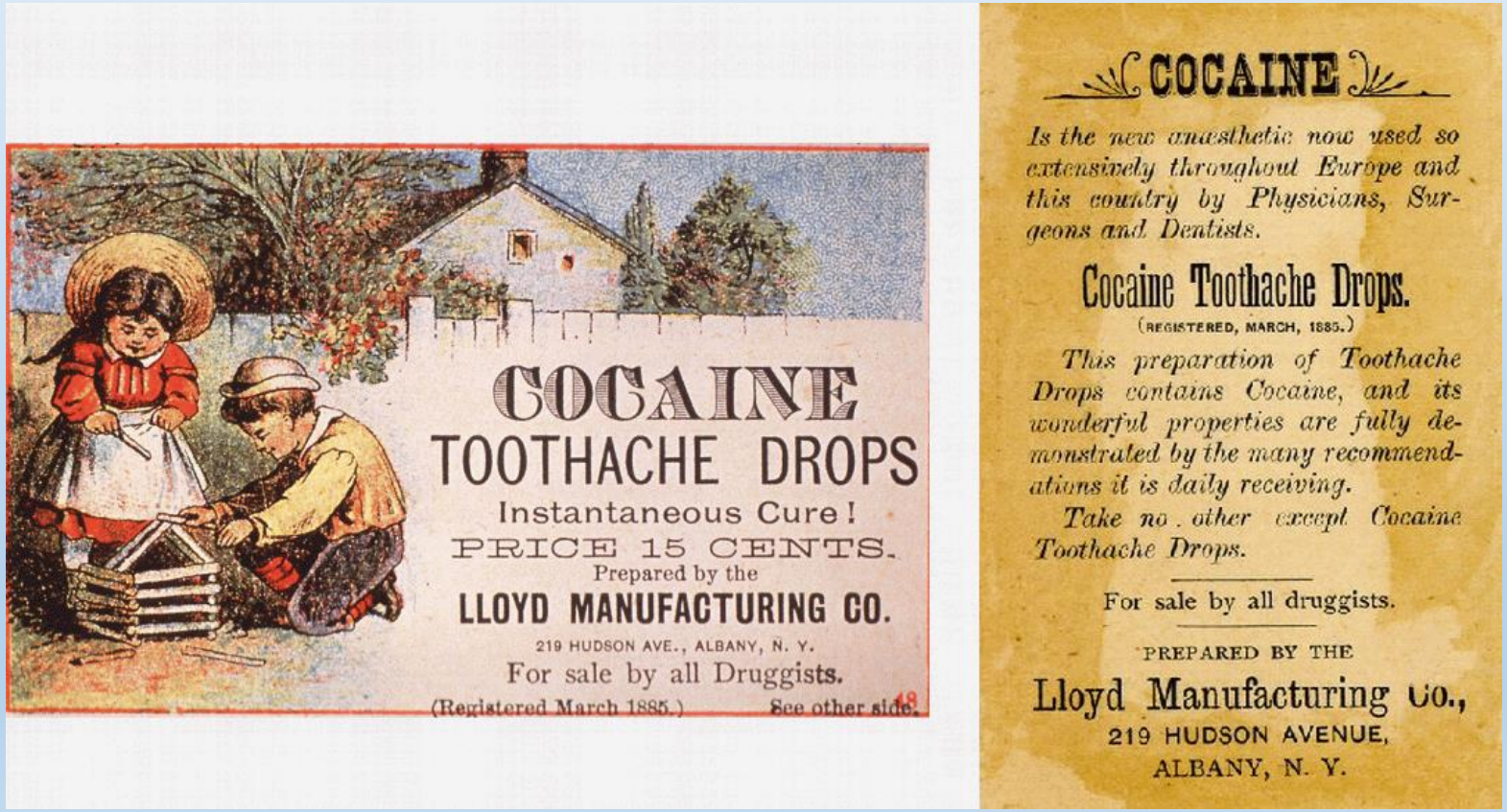
Proton pump inhibitors such as Prevacid and Nexium are typically used to treat conditions such as gastroesophageal reflux and ulcers. Mechanistically, PPIs may adversely affect osteoclast differentiation and calcium absorption leading to a reduction on bone mineralization and density. Many clinical studies and meta analysis did show significant failure rates in patients taking PPIs. These conclusions have been challenged on the basis that the studies did not adequately control for confounding factors. Current data (2022) suggests that PPIs do not contribute to graft or implant failure in any significant way once those factors are taken into account. Without randomized controlled trial it is difficult to truly evaluate any risk posed by PPIs to implant treatment.

Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology Volume 133, Issue 1, January 2022, Pages 15-20 Are proton pump inhibitors associated with implant failure and peri-implantitis?
Altay M, Proton pump inhibitor intake negatively affects the osseointegration of dental implants: a retrospective study jkaoms.2019.45.3.135

Risk Factors in Oral Surgical Procedures

Medications:

NSAIDs
PPIs
SSRIs
Clindamycin
CCBs
Bisphosphonates



Risk Factors: SSRIs

Selective serotonin reuptake inhibitors have been implicated in bone remodeling poor quality bone grafts and the failure of implants. This class of medications are typically prescribed for major depressive disorders and anxiety is used by 10% of North Americans. They include drugs like citalopram (Celexa) and fluoxetine (Prozac).

Mechanistically it has been proposed that the serotonin receptors in bone are negatively modulated by SSRIs depressing bone metabolism. Most of the studies are small and retrospective without control for confounding factors. They suggest that patients who have been on SSRIs have a higher rate of implant failure but it does not appear to matter whether patients were on SSRIs at the time of implant placement or began afterwards. Critics suggest that many studies do not adequately control for confounding factors to give clear guidance.

Howie, R.N., Herberg, S., Durham, E. et al. Selective serotonin re-uptake inhibitor sertraline inhibits bone healing in a calvarial defect model. Int J Oral Sci 10, 25 (2018).
Carr AB, Relationship between Selective Serotonin Reuptake Inhibitors and Risk of Dental Implant FailureJ Prosthodont. 2019 Mar;28(3):252-257

Risk Factors in Oral Surgical Procedures

Medications:

NSAIDs
PPIs
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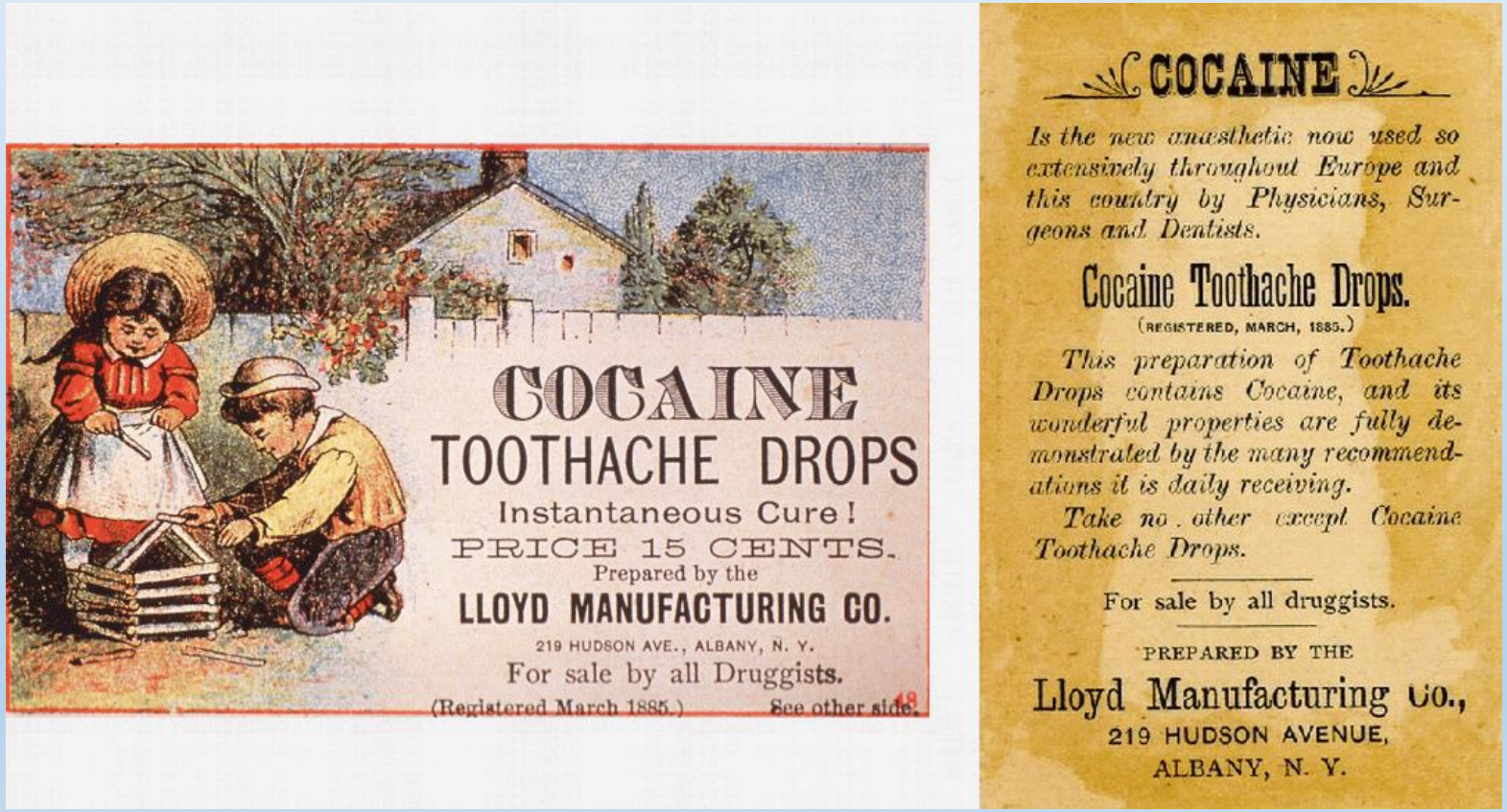
Clindamycin
CCBs
Bisphosphonates



Risk Factors: Clindamycin

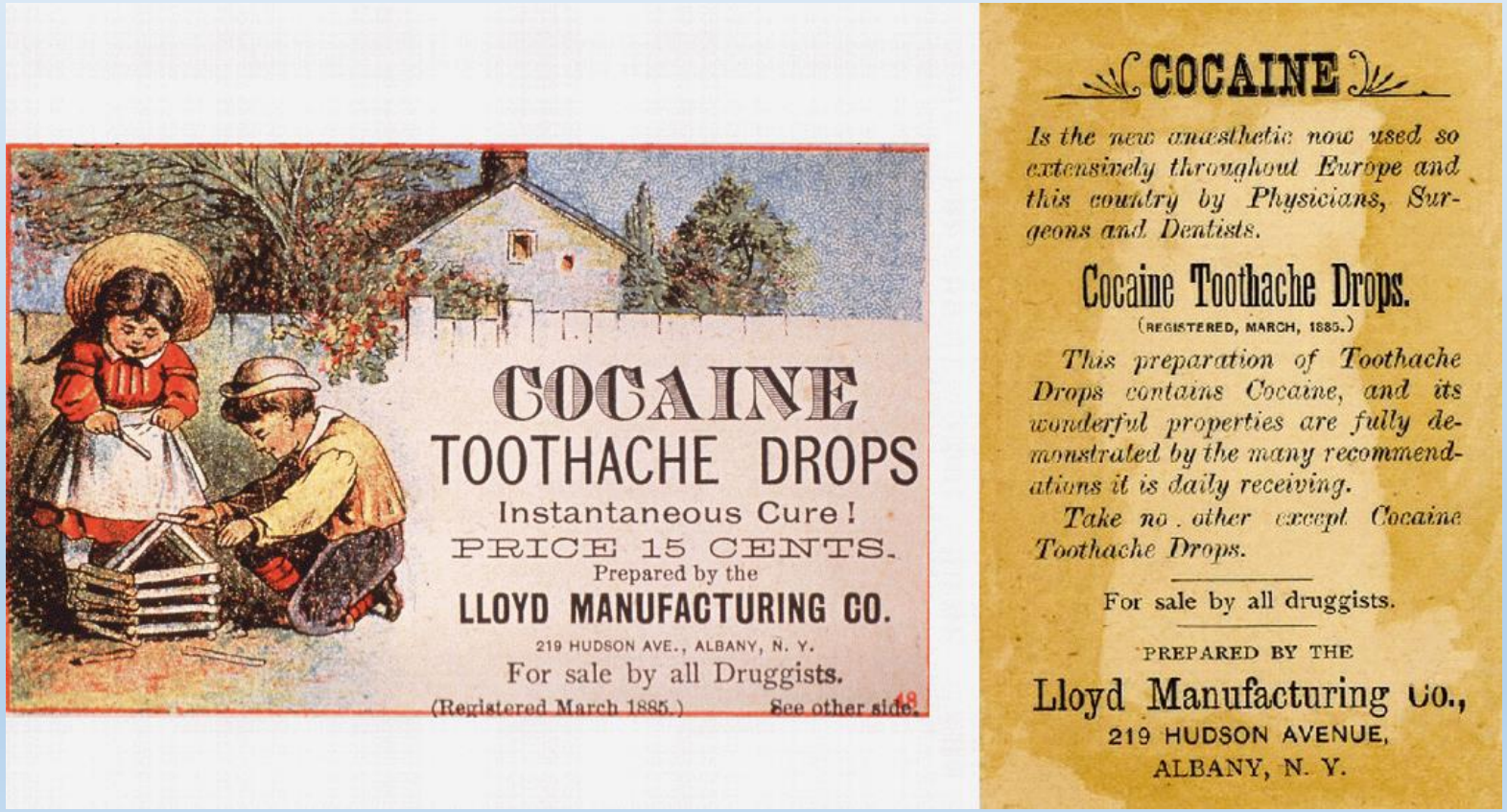
Clindamycin is typically used as an alternate antibiotic in Penicillin allergic patients. Numerous studies have been published that show a positive correlation between patients taking Clindamycin ridge augmentation failure and implant failure rates, other studies show no increase in failure rate and still other studies show an advantage to any kind of antibiotic. Some authors have suggest that the failures attributed to Clindamycin usage issue may in fact be an immunological phenomenon based on HLA differences in patient that are penicillin allergic. At this time there is no convincing evidence with respect to the risk of graft failure or implant failure posed by clindamycin or any other antibiotic.

Basma, Hussein S.; Misch, Craig M., Extraction Socket Grafting and Ridge Augmentation Failures Associated with Clindamycin Antibiotic Therapy: A Retrospective Study.Source: International Journal of Oral & Maxillofacial Implants . Jan/Feb2021, Vol. 36 Issue 1, p122-125
Salomo-Coll, Int J Oral Maxillofac Implants. Nov/Dec 2018;33(6):1390-1395.. Do Penicillin-Allergic Patients Present a Higher Rate of Implant Failure?
Binahmed A, Stoykewych A, Peterson L. Single Preoperative Dose Versus Long-term Prophylactic Antibiotic Regimens in Dental Implant Surgery. Int J Oral Maxillofac Implants 2005; 20: 115–117

Risk Factors in Oral Surgical Procedures

Medications:

NSAIDs
PPIs
SSRIs
Clindamycin
CCBs
Bisphosphonates



Risk Factors: CCBs

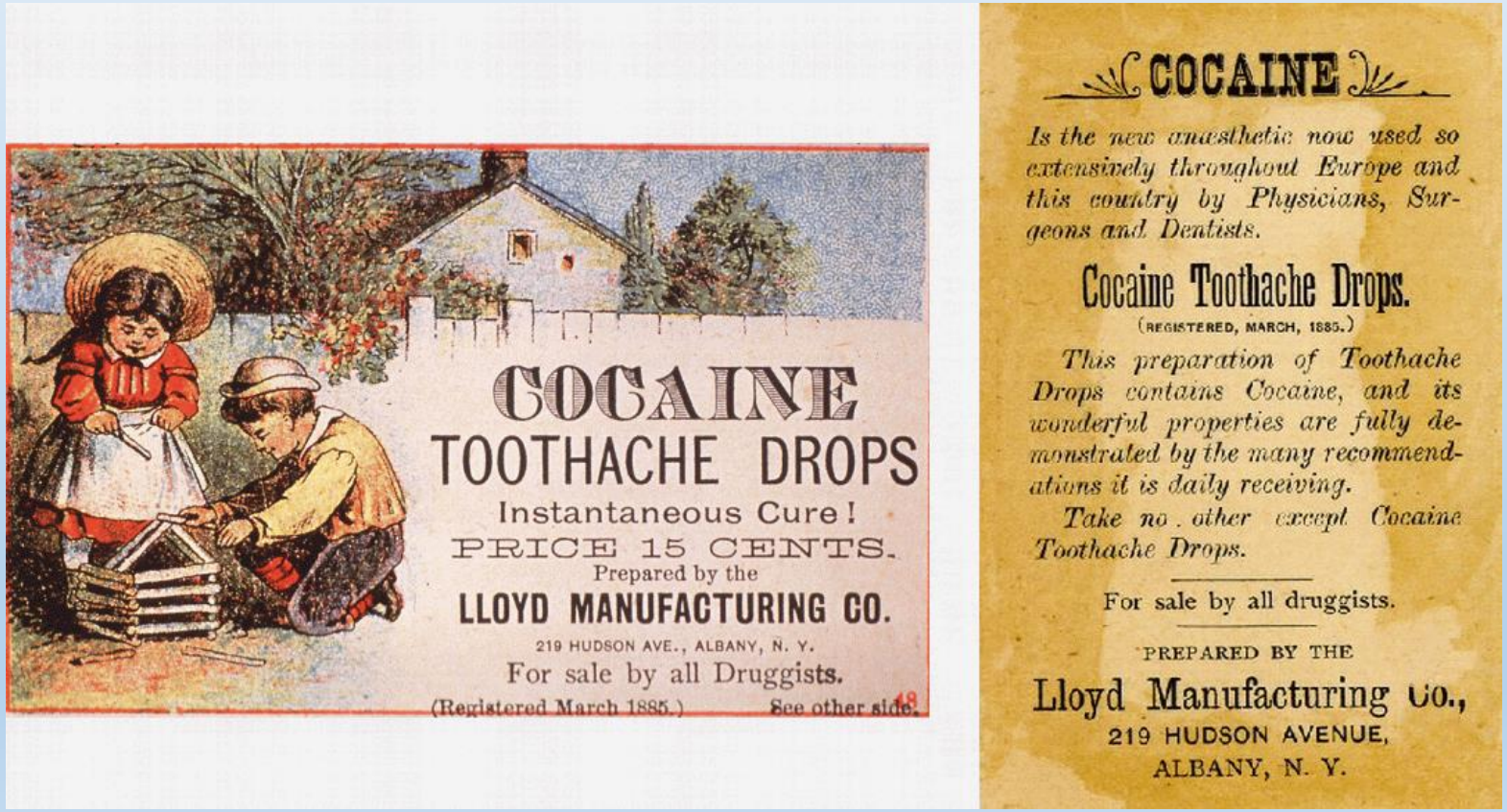
Calcium Channel Blockers typically used to control blood pressure include drugs such as Nifedipine (Procardia, Adalat) and Diltiazem (Cardizem). Older literature specifically indicated current use of CCBs as a contraindication to ridge augmentation procedures or implant treatment. Newer literature clearly shows that there is no increased risk associated with these drugs in terms of bone healing or osseointegration. They are however, strongly associated with gingival hyperplasia. Nifedipine appears to cause the greatest gingival response. The mechanism appears to be complex. These drugs cause a reduction in Ca+ through cellular channels which limits the uptake of folic acid which is necessary in the production of collagenase. Without collagenase, collagen turnover slows and connective tissue hyperplasia begins. This leads to secondary metalloproteinase over-abundance which further upregulates collagen production. It is likely although unproven in the literature that the hyperplastic gingiva makes oral hygiene difficult and could lead to a secondary peri-implantitis.

Livada, R., Shiloah, J. Calcium channel blocker-induced gingival enlargement. J Hum Hypertens 28, 10–14
Ibraheem, A., Batra, C., John, V., & Shin, D. (2019). Role of Medication in Osseointegration of Dental, Implants. Decisions in Dentistry, 5(5).

Risk Factors in Oral Surgical Procedures

Medications:

NSAIDs
PPIs
SSRIs
Clindamycin
CCBs
Bisphosphonates



Risk Factors: Bone Anti-resorptive Medications

Bone anti-resorptive therapies may in some cases be significant contra-indications to bonegraftind or implant surgery. These medications commonly include bisphosphonates which can be administered as an IV infusion such as zolendronate (Reclast) or orally such as alendronate (Fosamax), RANK Ligand inhibitors such as denosumab (Prolia) or anti-angiogenic medications. These medications have a range of indications from the control of hypercalcemia due to malignancy to the treatment of osteoporosis through modulation of bone metabolism. Although some studies have shown that low dose short term use of these drugs do not have a significant impact on grafts or implant failure, evidence is lacking for higher doses and longer duration which are associated with medication related osteonecrosis of the jaws. Both the American Association of Oral and Maxillofacial Surgeons and the European Task Force on medication related osteonecrosis of the jaws have published detailed guidelines to help practitioners assess potential risks to patients where procedures such as grafting or implants are being proposed.

Morten Schiodt, Workshop of European task force on medication-related osteonecrosis of the jaw—Current challenges Oral Diseases. 2019;25:1815–1821.
Salvatore L.Ruggiero, American Association of Oral and Maxillofacial Surgeons' Position Paper on Medication-Related Osteonecrosis of the Jaws—2022 Update, Journal of Oral and Maxillofacial Surgery Volume 80, Issue 5, May 2022, Pages 920-943

Medications Associated with MRONJ

Table 1. Pharmaceutical agents associated with MRONJ

Pharmaceutical agents associated with MRONJ	Mode of action
For osteoporosis/bone conditions (trade name)	
Alendronate (Fosamax)	Nitrogen containing BP inhibits mevalonate pathway
Ibandronate (Boniva)	Nitrogen containing BP inhibits mevalonate pathway
Pamidronate (Aredia)	Nitrogen containing BP inhibits mevalonate pathway
Risedronate (Actonel)	Nitrogen containing BP inhibits mevalonate pathway
Zoledronate (Zometa)	Nitrogen containing BP inhibits mevalonate pathway
Denosumab (Xgeva)	Antibody binds to RANK ligand
Clodronate (Bonefos, Loron)	Nonnitrogen containing BP competes with ATP as metabolite
Etidronate (Didronel)	Nonnitrogen containing BP competes with ATP as metabolite
Tiludronate (Skelid)	Nonnitrogen containing BP competes with ATP as metabolite
For Oncologic use	(all these compounds affect angiogenesis)
Imatinib, Sunitinib (Sutent)	Tyrosine kinase inhibitors
Sorafenib (Nexavar)	VEGF inhibitor
Bevacizumab (Avastin)	Angiogenic inhibitor

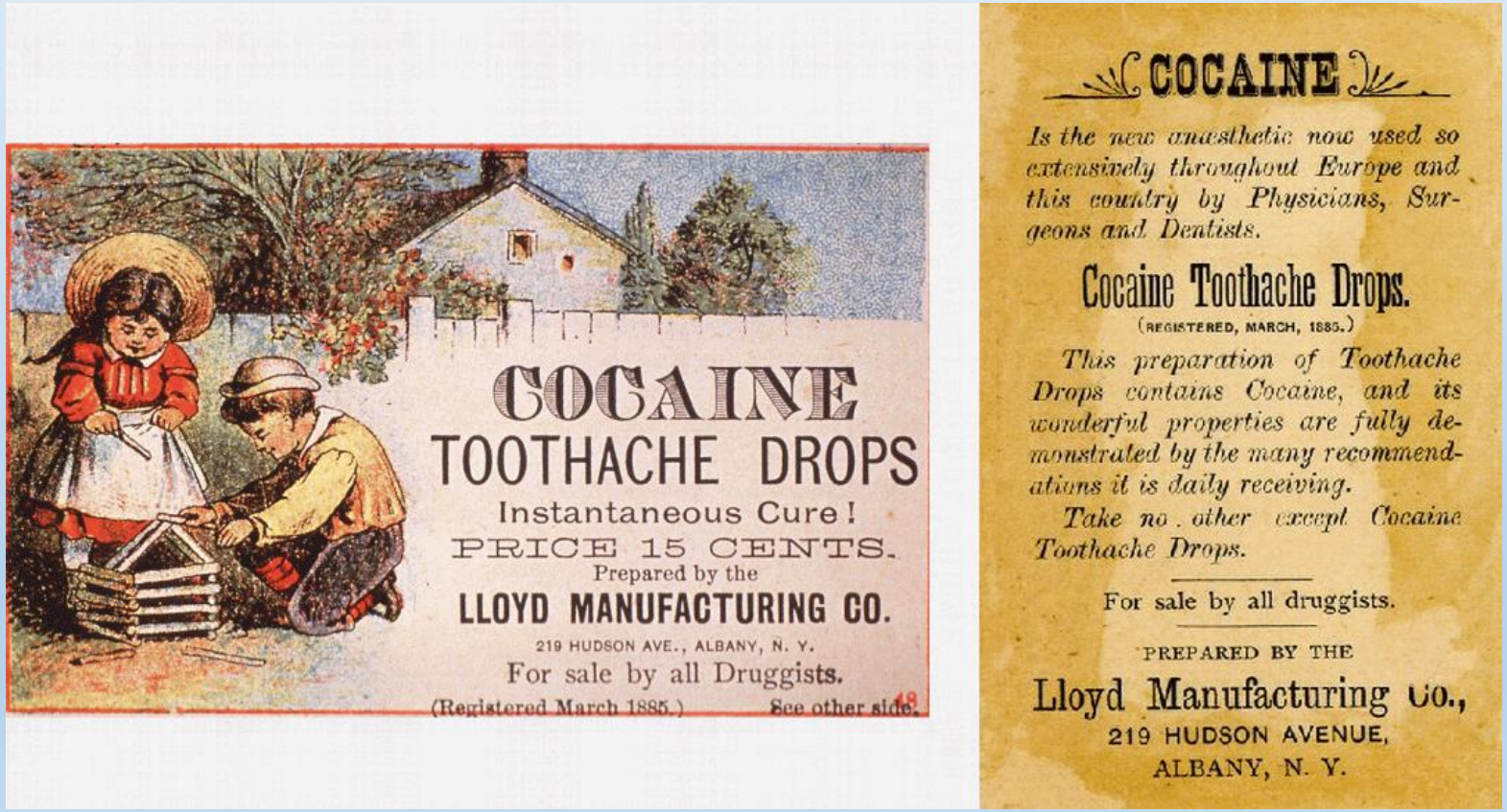
BP Bisphosphonate, *RANK* receptor activator of nuclear factor kappa-B, *ATP* adenosine triphosphate, *VEGF* vascular endothelial growth factor

Wan, J.T., Sheeley, D.M., Somerman, M.J. et al. Mitigating osteonecrosis of the jaw (ONJ) through preventive dental care and understanding of risk factors. Bone Res 8, 14 (2020).

Risk Factors in Oral Surgical Procedures

Medications:

NSAIDs
PPIs
SSRIs
Clindamycin
CCBs
Bisphosphonates



Critical Review of Therapies:

Soft Tissue Grafting

Hard Tissue Grafting

Platelet Rich Fibrin

Thomas Rowlandson (1756-1827). 1787. Engraving.

Bone Grafting

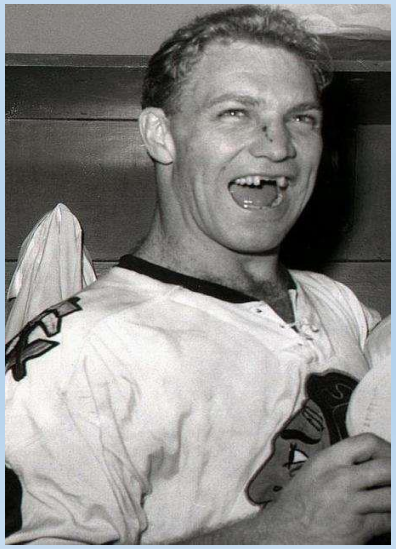
The biologic mechanisms that provide a rationale for bone grafting are:

- Osteoconduction – scaffold for native bone to grow into
- Osteoinduction – cause osteoprogenitor cells to differentiate
- Osteogenesis – graft osteocytes as well as peripheral osteocytes continue to produce new bone

Grafting Materials

Bone Materials:

- Autografts – harvested from patient
- Allografts – harvested from someone else (bone banks)
- Xenografts – harvested from something else



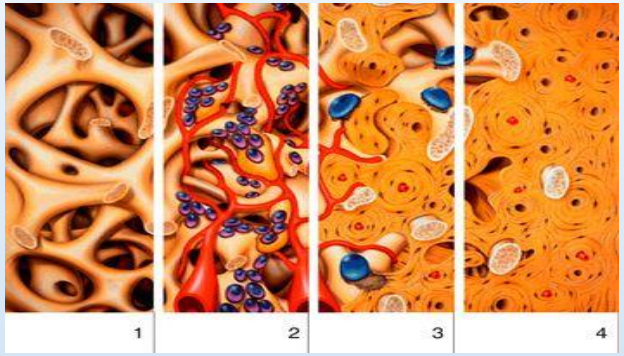
Grafting Materials

- Fresh Bone
- Fresh Frozen Bone
- Demineralized Bone Matrix (DBM)
- Demineralized Freeze Dried Bone (DFDBA)
- Composites/Synthetics - HA, Ceramics (Ca based), Calcium triphosphate, Bioglass (Silica based), polymers (MMA)
- Bone Morphogenic Proteins (BMP)

(A) Figures showing bone substitutes in various physical forms – particulate form of mineralized and (B) demineralized bone allograft. (C) Particulated xenograft, (D) particulated form of HA + β-Tcp mixture, (E) demineralized allograft in putty form, (F) allograft in the form of corticocancellous chips, (G) cortical block allograft, (H) cancellous block allograft, (I) corticocancellous block allograft *(Courtesy: Zimmer Dental)*, (J) cancellous strip allograft, (K) cortical strip allograft.

Courtesy of: https://pocketdentistry.com/basics-of-bone-grafting-and-graft-materials

What Makes Grafting Products Different

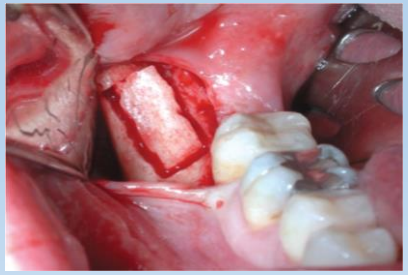


Osteoconduction – bone grows into graft (one way)

Courtesy of: https://pocketdentistry.com/basics-of-bone-grafting-and-graft-materials

Osteoinduction – recruitment of undifferentiated cells by growth factors (BMP)

http://web.orthofix.com/Products/Products/Trinity%20ELITE/Trinity-ELITE-Brochure.pdf



Osteogenesis – osteoblasts grow from the periphery as well as within the graft (bidirectional)

https://www.oralhealthgroup.com/features/botox-reduction-post-bone-graft-resorption-anterior-mandibular-dental-implant-reconstruction-preliminary-study

Why So Many Products?

Bacterial (clostridia + gm-ve)
Viral (Hep C + HIV)
Prion (BSE)

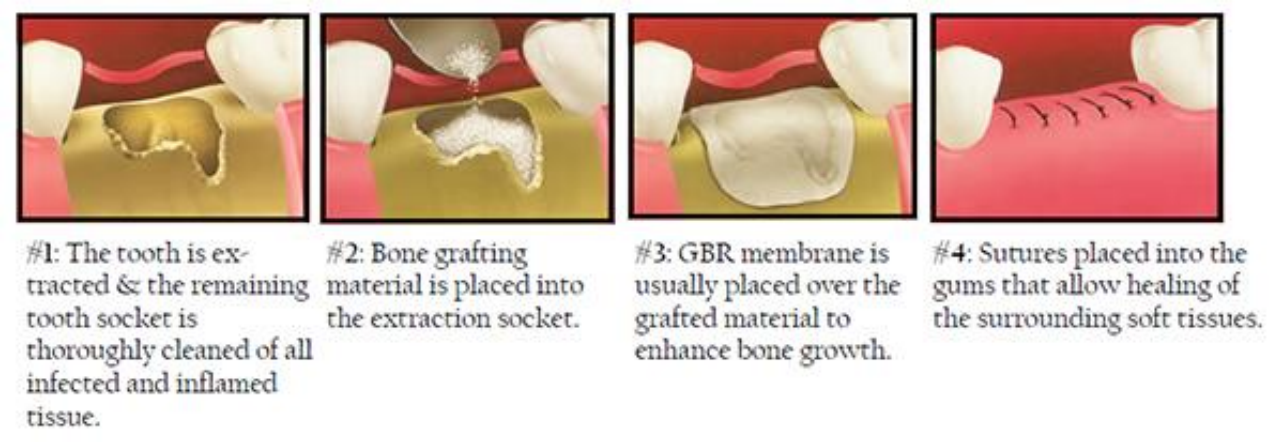
Bone Morphogenic Protein (BMP)
Endothelial Derived Growth Factor (EGF)
Fibroblast Growth Factor (FGF)
Insulin Like Growth Factor (IGF)
Platelet Derived Growth Factor (PDGF)
Transforming Growth Factor (TGF)
LIM-Mineralizing Protein (LMP)

More processing = safer graft material but fewer active ingredients

Options?

- Use a scaffolding product at minimal cost (osteoconduction only) and rely on normal healing
- Use expensive products that contains some of the factors (osteocnduction/induction)
- Do an autograft – second surgical site (osteoconduction/induction/genesis)
- Add factors yourself to an inexpensive product (osteoconduction/induction)

Traditional Guided Bone Regeneration (GBR)



#1: The tooth is extracted & the remaining tooth socket is thoroughly cleaned of all infected and inflamed tissue.

#2: Bone grafting material is placed into the extraction socket.

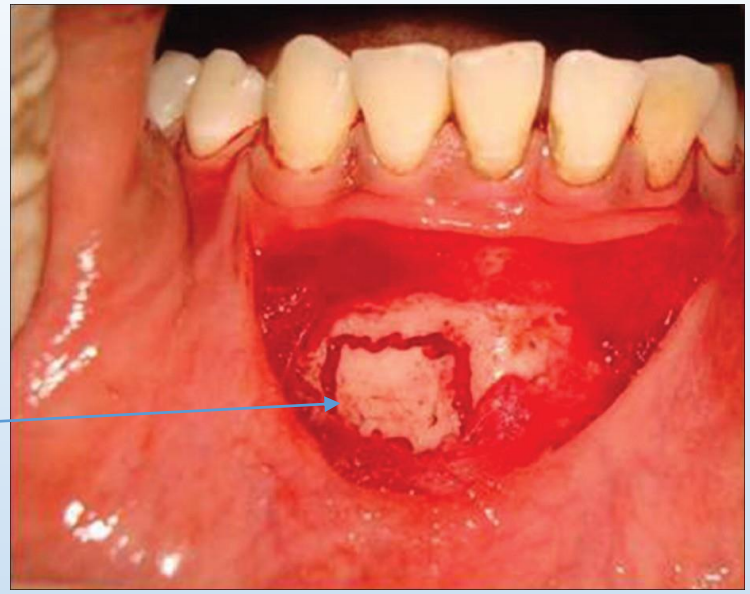
#3: GBR membrane is usually placed over the grafted material to enhance bone growth.

#4: Sutures placed into the gums that allow healing of the surrounding soft tissues.

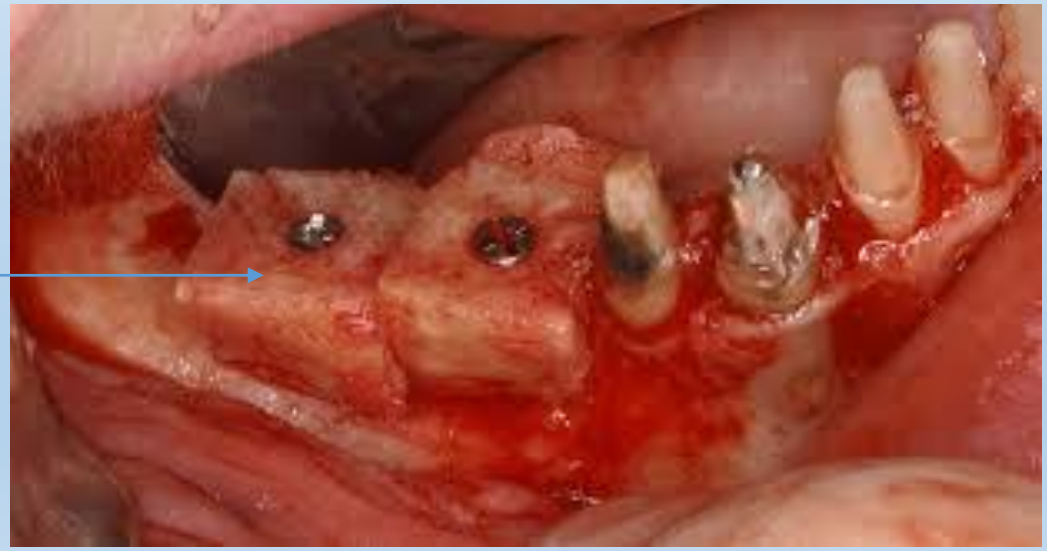
https://www.baysidedentist.com/procedures/extractions-bone-grafts-guided-bone-regeneration/

Autograft

Autogenous bone is harvested from a secondary site



Graft is then fixed into position in new site



http://www.jofs.in/article.asp?issn=0975-8844;year=2012;volume=4;issue=2;spage=148;epage=152;aulast=Prabhakara

Analysis of Outcomes

Elnayef: vertical augmentation in atrophic mandibles – 4 mm or less all techniques (block grafts, distraction, GBR) had same success rates, GBR had lower complication rate, for >4 mm distraction and blocks are better. Optimal local conditions are the key to success.

Perez-Gonzalez: vertical ridge augmentation and implant survival – equal success with allogenic and autogenous block grafting, no difference in resorption

Bassir: socket preservation – grafting at time of extraction reduces dimensional loss, damaged sockets benefit more than sound sockets, primary closure may be beneficial

Al-Nawas: autogenous vs bone substitutes – analysis revealed no differences in implant survival rates

Corbella: comparison of biomaterials for socket grafting – no superiority (new bone formation) in any biomaterial, xenografts showed lower resorption than allografts, “Allograft was not related to higher new bone volume than sites healed without any biomaterial”

Elnayef, Basel, Vertical Ridge Augmentation in the Atrophic Mandible: A Systematic Review and Meta-Analysis. International Journal of Oral & Maxillofacial Implants . 2017, Vol. 32 Issue 2, p291-312. 22p.

Pérez-González F, Molinero-Mourelle P, Sánchez-Labrador L, et al. Assessment of clinical outcomes and histomorphometric findings in alveolar ridge augmentation procedures with allogeneic bone block grafts: A systematic review and meta-analysis. Med Oral Patol Oral Cir Bucal. 2020;25(2):e291-e298. Published 2020 Mar 1. doi:10.4317/medoral.23353

Bassir, Seyed Hossein, et al. "Systematic review and meta-analysis of hard tissue outcomes of alveolar ridge preservation." Int J Oral Maxillofac Implants 33.5 (2018): 979-994.

Al-Nawas, Bilal, and Eik Schiegnitz. "Augmentation procedures using bone substitute materials or autogenous bone-a systematic review and meta-analysis." Eur J Oral Implantol 7.Suppl 2 (2014): S219-S234.

Corbella, Stefano, et al. "Histomorphometric Results After Postextraction Socket Healing with Different Biomaterials: A Systematic Review of the Literature and Meta-Analysis." International Journal of Oral & Maxillofacial Implants 32.5 (2017).

Critical Review of Therapies:

Soft Tissue Grafting

Hard tissue Grafting

Platelet Rich Fibrin

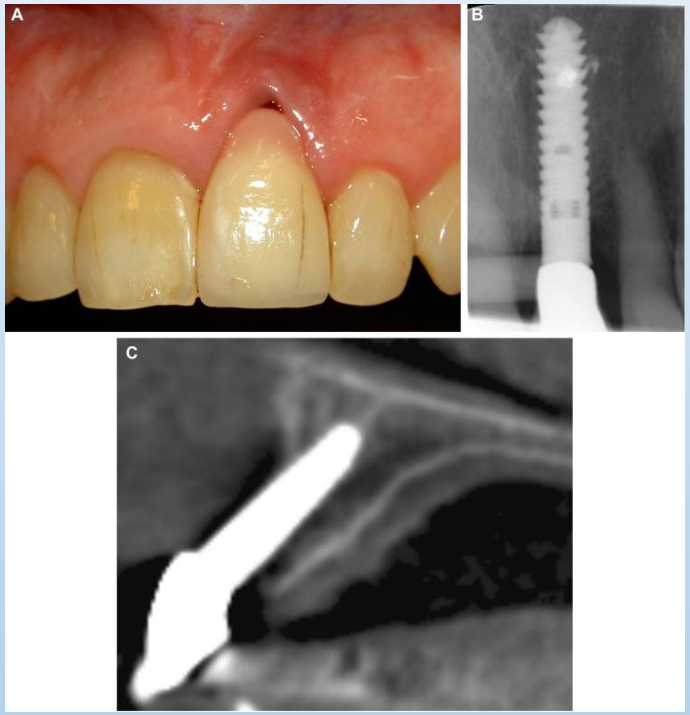
Thomas Rowlandson (1756-1827). 1787. Engraving.

Critical Review of Therapies: Soft tissue Procedures

Procedures to increase peri-implant coverage and keratinized width

long term success of any soft tissue procedure (repositioning, free gingival graft or connective tissue graft) is dependant on:

- volume and position of overlying hard and soft tissue,
- position of implant in three dimensions,
- platform and emergence profile of prosthesis
- interproximal distance
- interproximal height



Raghoebar GM, Immediate Reconstruction of Failed Implants in the Esthetic Zone Using a Flapless Technique and Autogenous Composite Tuberosity Graft. J Oral Maxillofac Surg. 2018 Mar;76(3)

Giovanni Zucchelli, Autogenous soft tissue grafting for periodontal and peri-implant plastic surgical reconstruction, J Periodontol. 2020;91:9–16
Frizzera F, Treatment of peri-implant soft tissue defects: a narrative review. Braz Oral Res. 2019 Sep 30;33(suppl 1)

Critical Review of Therapies: Soft tissue Procedures

Repositioning

- requires sufficient keratinized width
- requires sufficient vestibular depth
- process that stimulated recession (eg. thin buccal bone) may continue to effect outcome

Free Gingival Graft

- requires second surgical site
- graft shrinks by 30% during healing
- Success rates >90% 1 year, >75% 5 year

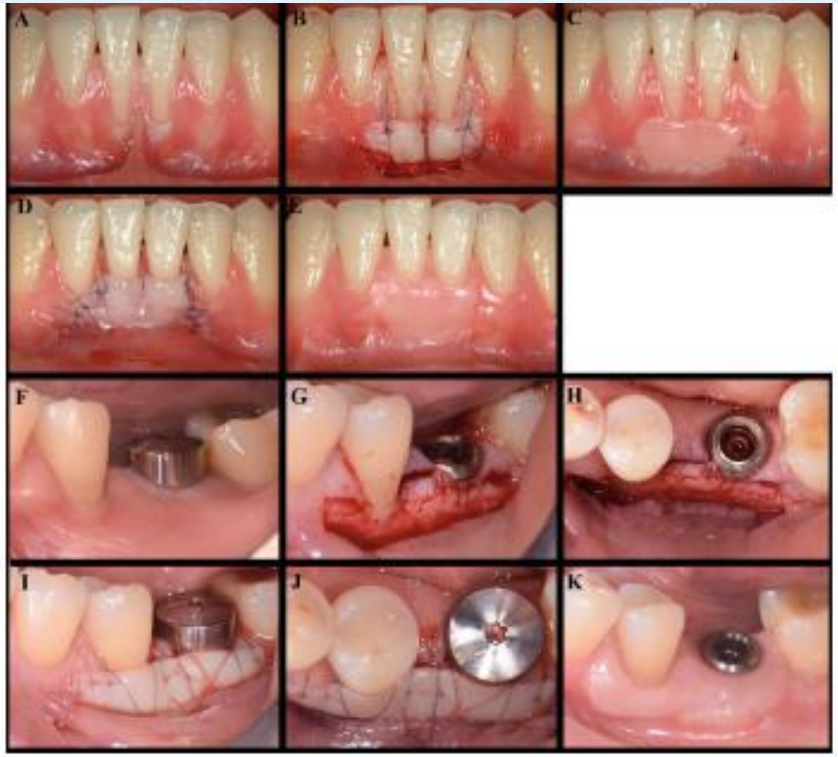


FIGURE 1 **A through E**) Free gingival graft at lower central incisors. **A**) baseline; **B**) immediately postoperative; **C**) 5-months postoperative; **D**) coronally advanced flap; **E**) 6-months postoperative showing the complete root coverage of the recession defects together with increased keratinized gingiva. **F through K**) Free gingival graft around a posterior implant with minimal keratinized mucosa on the buccal aspect. **F**) baseline; **G** and **H**) flap preparation and suturing to the periosteum; **I** and **J**) free gingival graft sutured to the periosteum and to the adjacent soft tissue; **K**) 6-month healing

Giovanni Zucchelli, Autogenous soft tissue grafting for periodontal and peri-implant plastic surgical reconstruction, J Periodontol. 2020;91:9–16

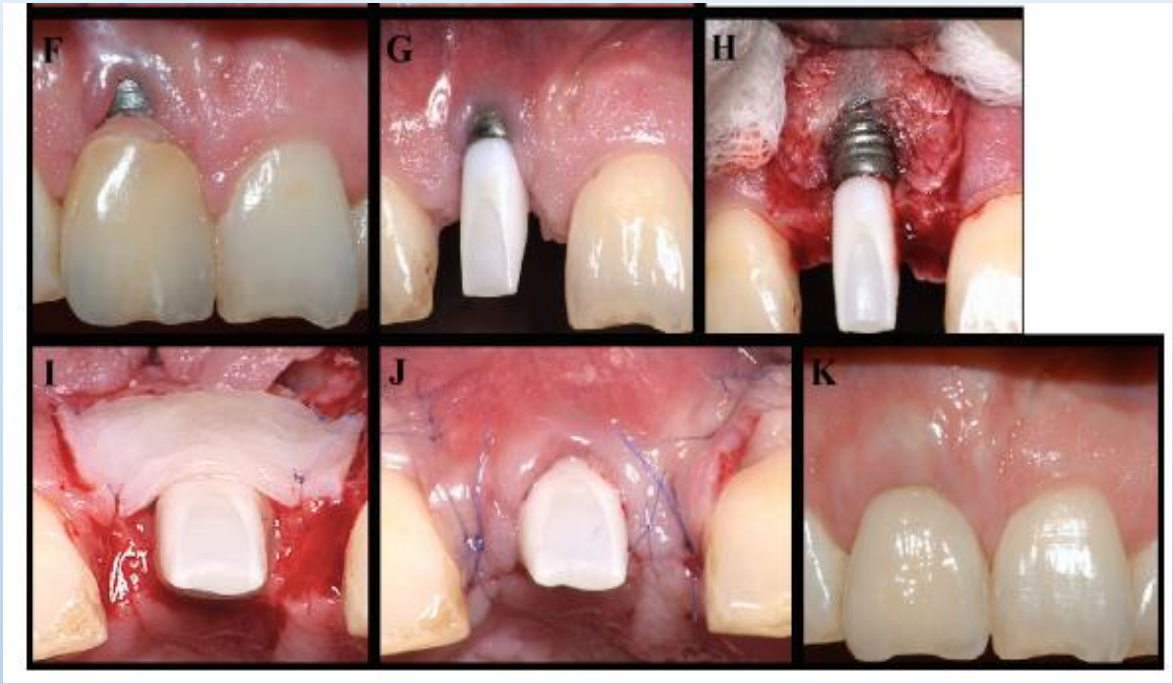
Frizzera F, Treatment of peri-implant soft tissue defects: a narrative review. Braz Oral Res. 2019 Sep 30;33(suppl 1)

Bassetti, Renzo (2016). Soft tissue augmentation procedures at second-stage surgery: a systematic review. Clinical Oral Investigations. 20. 10.1007/s00784-016-1815-2.

Critical Review of Therapies: Soft tissue Procedures

Connective tissue grafts

- tx of choice for recession
- thickening the thin biotype
- masking discolouration
- papilla reconstruction
- can be used with a variety of flaps or tunneling techniques
- requires harvest site
- Dimensions of graft influence outcome (4mm x 14 mm appears ideal)
- Success reported at 90% at 1 year and 80% at 5 years



Giovanni Zucchelli, Autogenous soft tissue grafting for periodontal and peri-implant plastic surgical reconstruction, J Periodontol. 2020;91:9–16

Frizzera F, Treatment of peri-implant soft tissue defects: a narrative review. Braz Oral Res. 2019 Sep 30;33(suppl 1)

Bassetti, Renzo (2016). Soft tissue augmentation procedures at second-stage surgery: a systematic review. Clinical Oral Investigations. 20. 10.1007/s00784-016-1815-2.

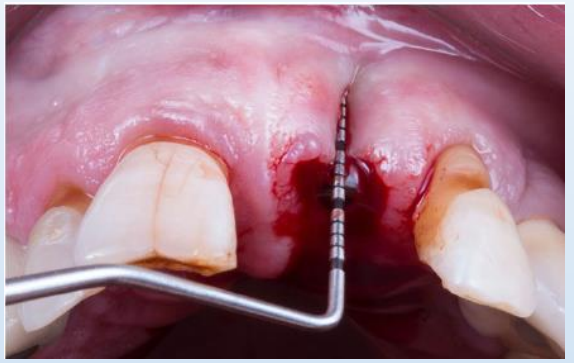
Critical Review of Therapies: Soft tissue Procedures

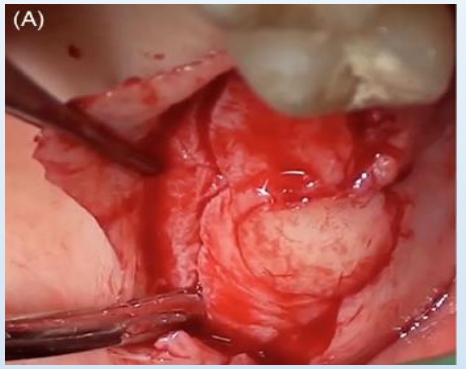
Composite Grafts

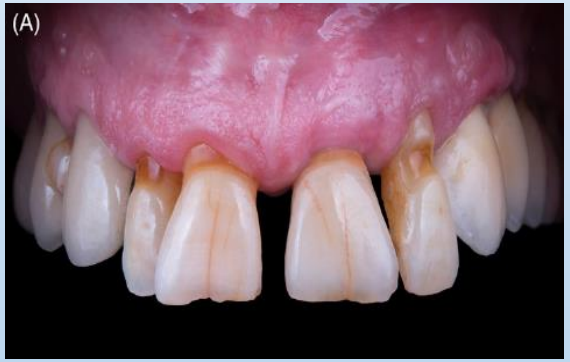
designed to address both hard tissue deficits (incomplete buccal plate) and soft tissue deficiencies (thin biotype)

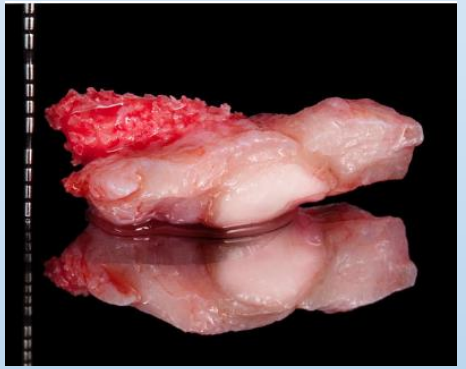
4 layers thick – extensive harvest and morbidity

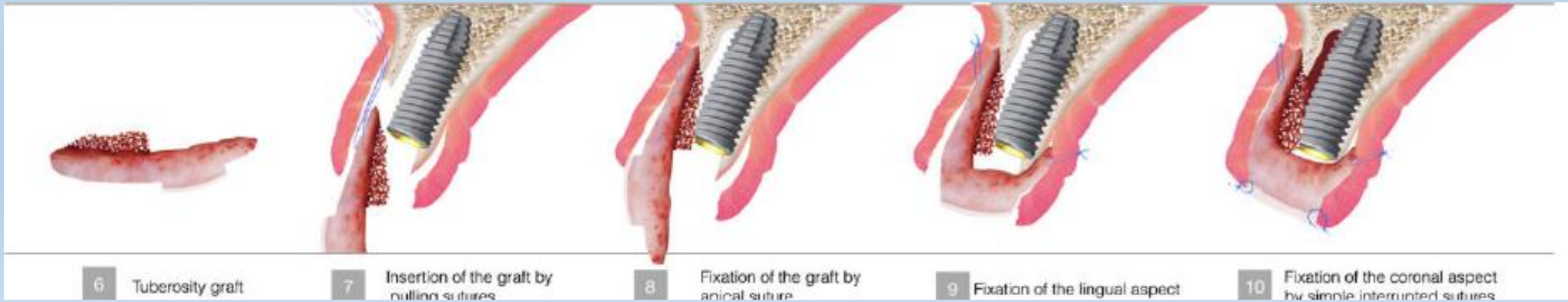
No studies on superiority over regular CTG or FGG











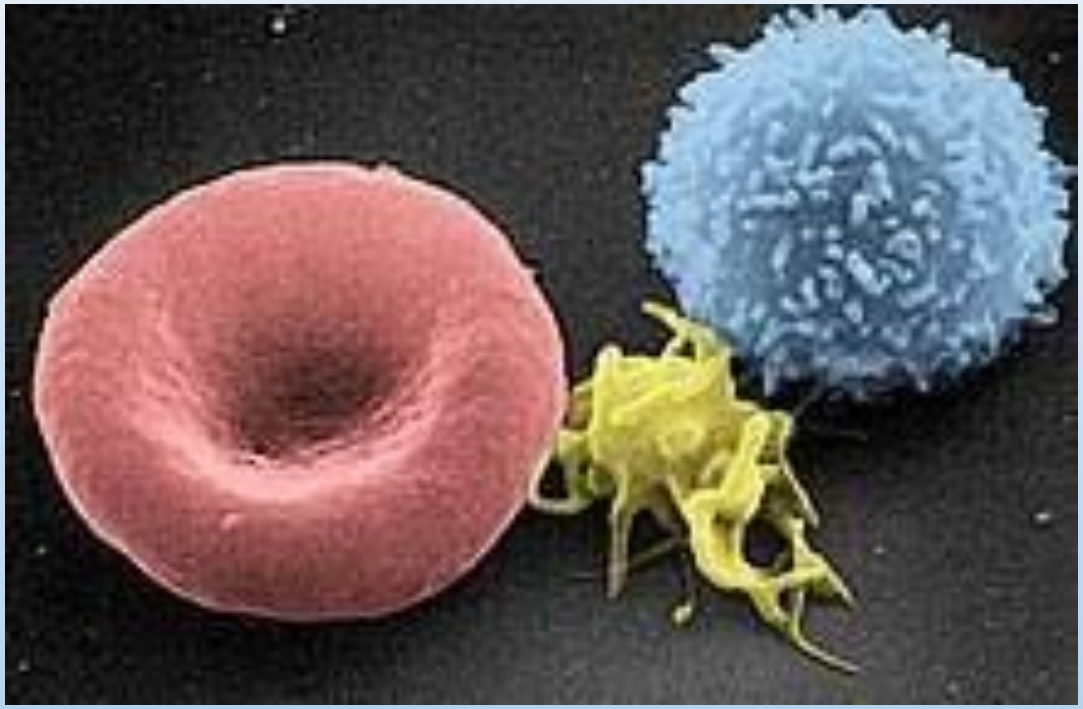
Zufia J, The four-layer graft technique, a hard and soft tissue graft from the tuberosity in one piece, J Esthet Restor Dent. 2019;1–7.

Critical Review of Therapies:

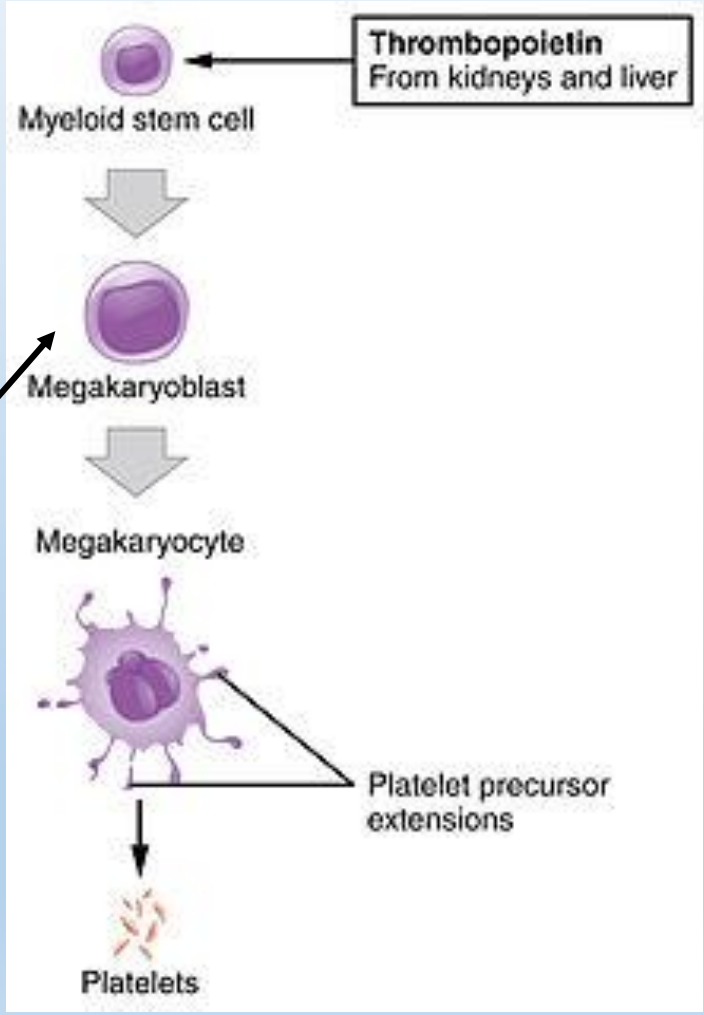
Soft Tissue Grafting
Hard tissue Grafting
Platelet Rich Fibrin

Thomas Rowlandson (1756-1827). 1787. Engraving.

Critical Review of Therapies: Platelet Rich Fibrin



https://en.wikipedia.org/wiki/Platelet



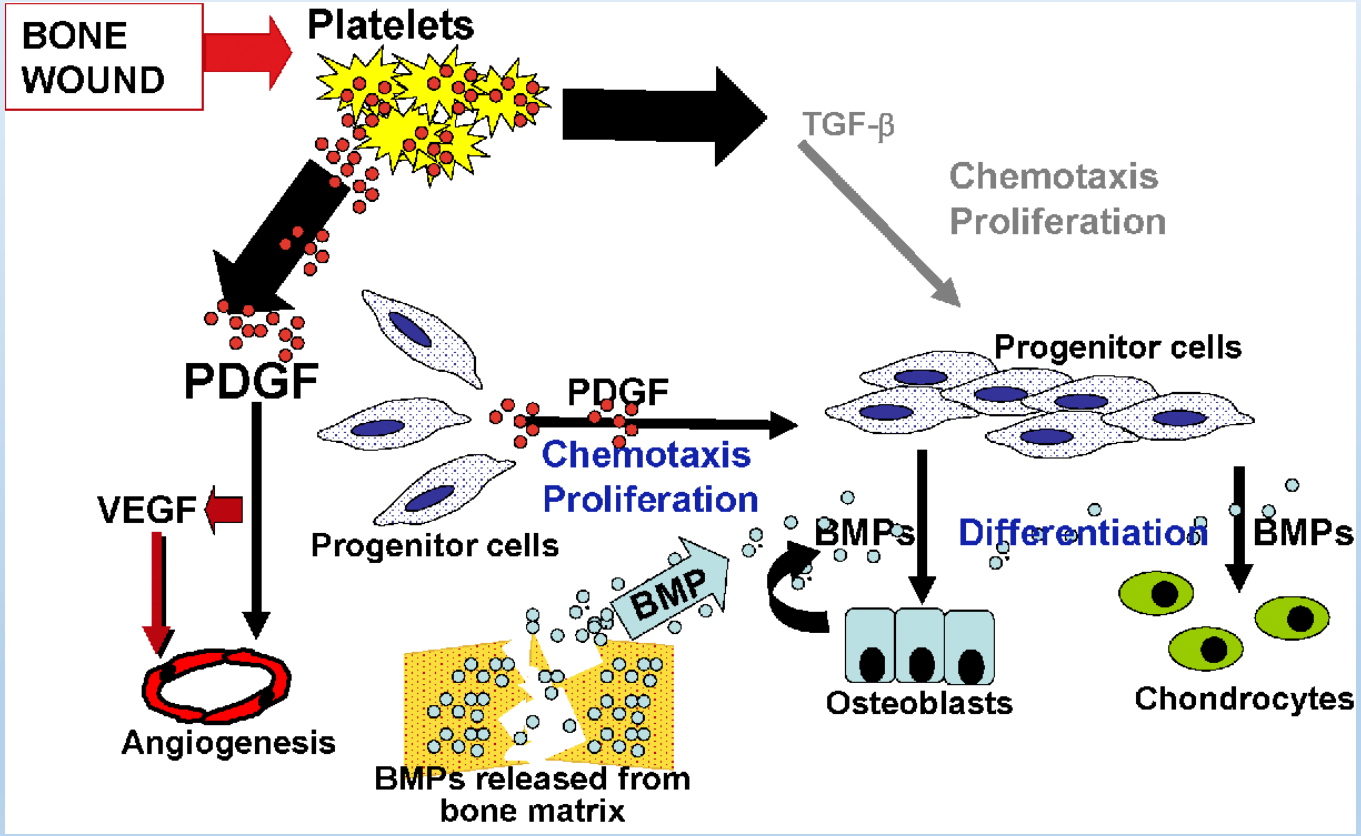
https://en.wikipedia.org/wiki/Thrombopoiesis

Platelets: Derived from megakaryoblasts/cytes in the bone marrow
150K – 350K/ul of whole blood

Platelets: Growth Factors

TGF-B (transforming growth factor)
- Stimulate bone deposition
PDGF (platelet derived growth factor
- Promotes bone healing through bone marrow stem cell upregulation
bFGF (basic fibroblast growth factor)
- Promotes osteogenesis and angiogenesis
IGF-1 (insulin like growth factor 1)
- Proliferation and migration of fibroblasts
VEGF (vascular endothelial growth factor)
- Migration of endothelial cells leading to angiogenesis and ossification in damaged bone

Yun Qian, Platelet-Rich Plasma Derived Growth Factors Contribute to Stem Cell Differentiation in Musculoskeletal Regeneration, Front. Chem., 31 October 2017



https://www.semanticscholar.org/paper/Recombinant-human-platelet-derived-growth-factor%3A-Hollinger-Hart/a9ef5008f200f23618c68dd1637b0047d3dbf50e

Platelet Rich Plasma (PRP) vs Plasma Rich Fibrin (PRF)

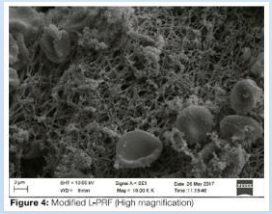
- Historically these products derive from the search for a better ‘fibrin glue’ – intended as a ‘surgical patch’
- Fibrin glues were developed as adjuncts to surgical healing particularly in populations with coagulation issues
- Limitations on the use of ‘blood products’ (risk of Hepatitis) pushed development of modified protocols
- PRP protocols use Thrombin and CaCl which makes them ‘blood products’
- Choukroun et al bypassed legal restrictions in France by introducing a protocol (PRF) which used no ‘gelling ingredients’

PRP (Platelet Rich Plasma)

First Generation
Thrombin, CaCl added
'liquid form for injection'
Leukocyte poor

PRF (no anticoagulants or activation agents)

Second Generation
'Gel form'
Natural clotting/activation

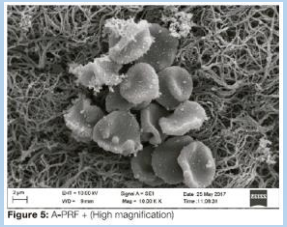


L-PRF
(Leukocyte rich PRF)

G-PRF
(Dry gauze PRF)

C-PRF
(Compression PRF)

Single spin, Only difference is how you squeeze the clot



A-PRF
(Advanced PRF)

Slow (lower G) spin

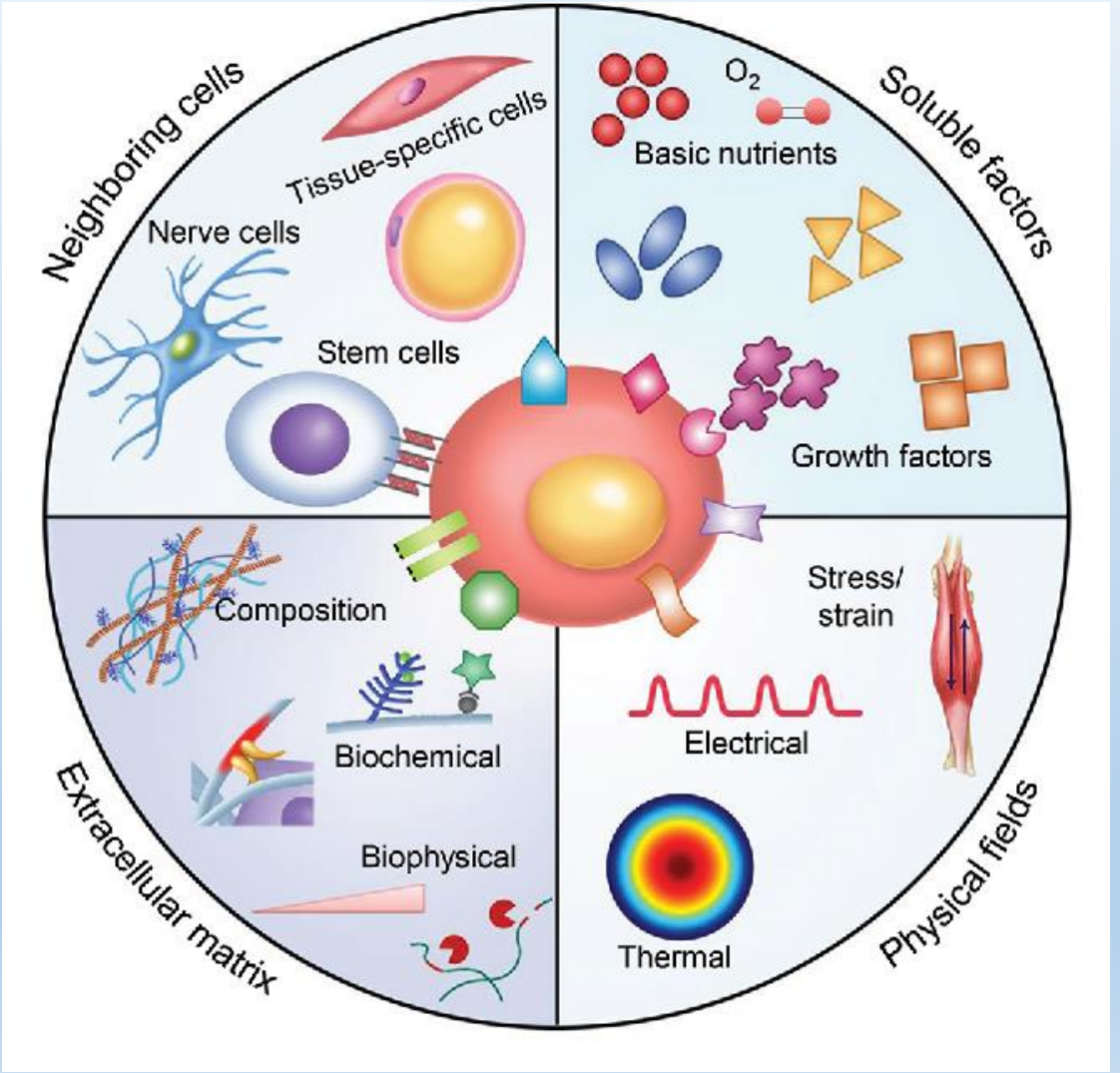
i-PRF
Injectable PRF

Short spin (more fluid – less clotting time)

Peck MT[I]; Hiss D[II]; Stephen LXG[III] The effect of preparation method on the fibrin diameter of leukocyte- and platelet-rich fibrin (L-PRF) S. Afr. dent. . vol.73 no.4

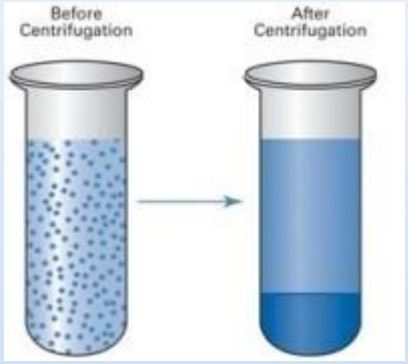
PRF in Tissue Healing/Regeneration

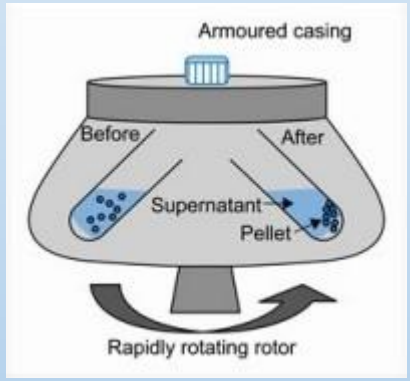
- Growth factors from platelets are present as a response to trauma and bleeding.
- PRF is a way of concentrating some of those factors
- Theoretically tissue regeneration should improve, in reality healing and selective regeneration is tightly controlled through the ECM components
- Blood supply and physical stressors, may ultimately be more important to regenerative outcome



https://www.semanticscholar.org/paper/Functional-and-Biomimetic-Materials-for-Engineering-Huang-Li/9d5fe62d1427b613d8f2a982fc619b7bee4250b2

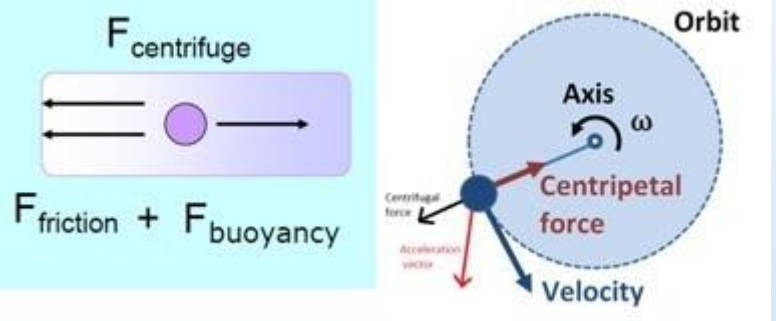
Separating Blood Components: Centrifuge Principles

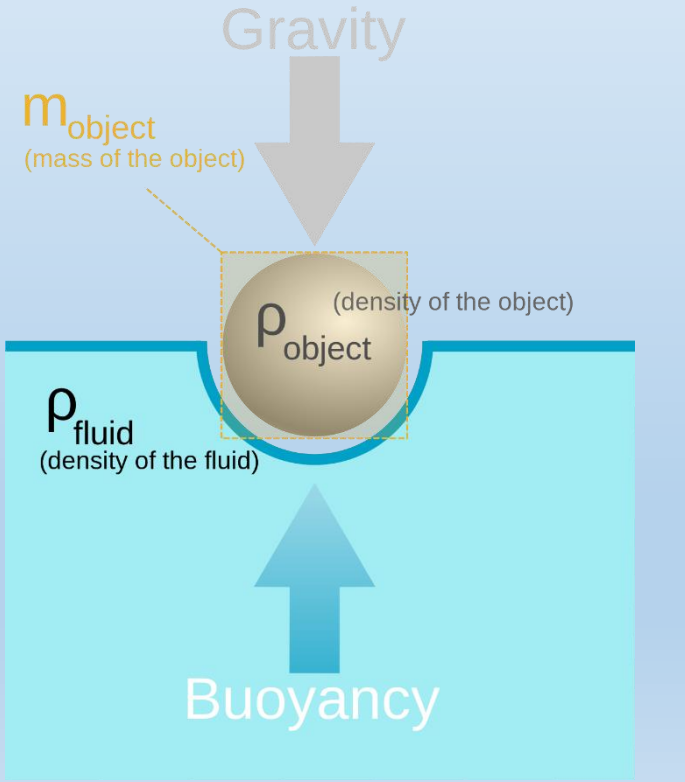




Separation of particles in a fluid can be enhanced by centripetal acceleration

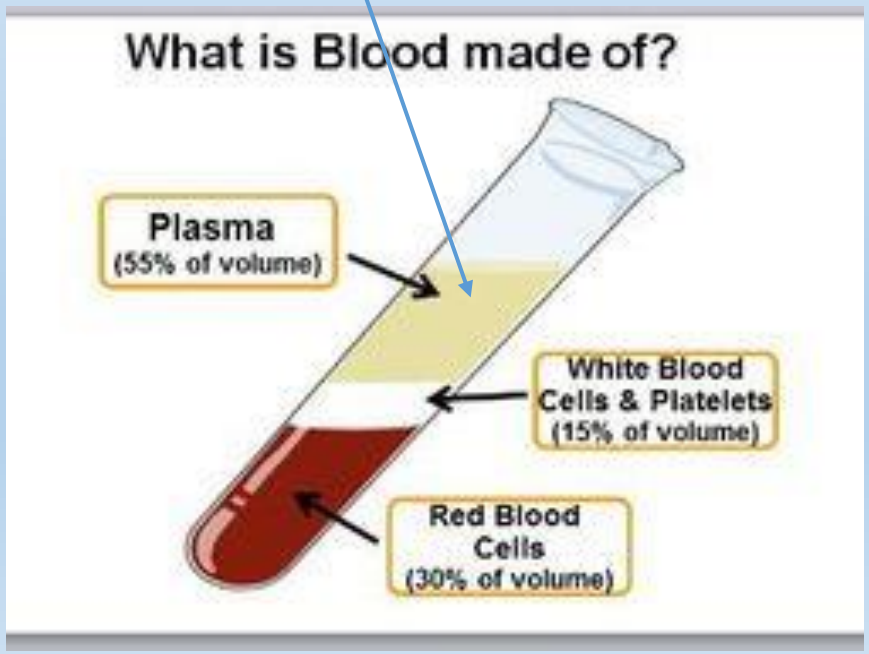
The force applied to particles in the fluid is a function of the rotational speed (rpm), the radius of the rotor and the relative mass of the particles (buoyancy)



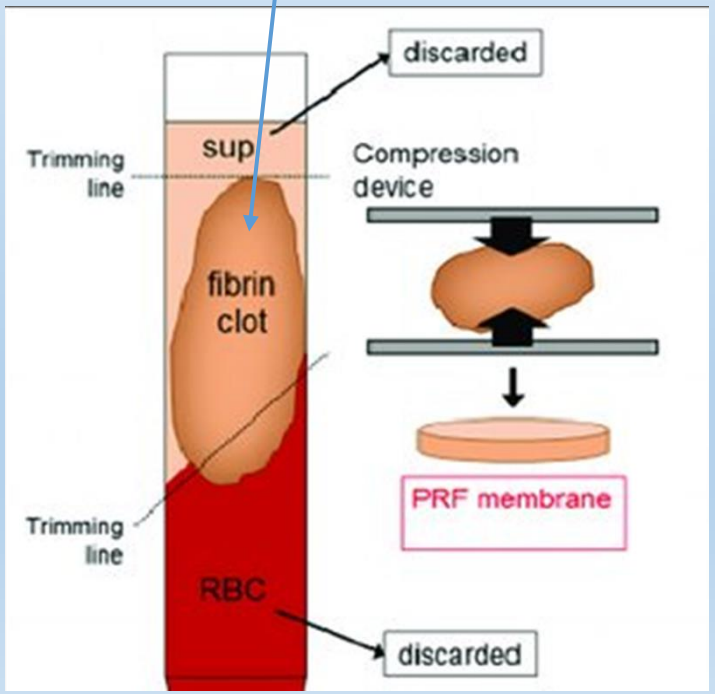


Platelet Rich Fibrin: Blood components

In a blood collection tube with anticoagulant, components remain fluid (no fibrin clot)



In tube with no anticoagulant blood components separate and platelet/fibrin clot forms



Platelet rich fibrin clot is removed and trimmed (RBSs are considered a contaminant)

Release of growth Factors PRP vs PRF

Table 1 Final growth factor released over a 10-day period from the various platelet concentrates including PRP, PRF, and A-PRF

	PRP	PRF	A-PRF
PDGF-AA	6176 (2812–9184)	9262 (2877–13839)	11048 (5036–18817)
PDGF-AB	4131 (1837–5492)	4396 (862–7563)	6007 (3455–10298)
PDGF-BB	1155 (531–1371)	680 (220–1147)	1010 (643–1803)
TGF-beta1	1105 (619–1453)	1110 (302–1714)	1589 (1052–2315)
VEGF	847 (693–1009)	732 (537–914)	847 (814–1063)
EGF	363 (210–497)	512 (146–715)	659 (447–795)
IGF	54 (44–67)	166 (55–252)	129 (81–179)

Data represents averages (pg/ml) with ranges (minimum to maximum values)

Eizaburo Kobayashi Comparative release of growth factors from PRP, PRF, and advanced-PRF, Clin Oral Invest Jan 2016

Efficacy of PRP and PRF as an augmentation product

Quantitatively unknown

-reproducible studies are few

-protocols and armamentarium differ extensively

-early influence on bone healing appears significant (1st week)

-late effects on bone final bone volume and quality equivocal

Qualitatively better than many products available for GBR based on concentration of growth factors not on clinical outcomes

Lolas et al. Res Rep Oral Maxillofac Surg 2018, 2:007

Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, et al. (1998) Platelet-rich plasma: Growth factor enhancement for bone grafts. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 85: 638-646.

Albanese et al. Immunity & Ageing 2013, 10:23

Critical Review: Conclusions

- All bone and soft tissue remodels secondary to functional and anatomical parameters
- Tissue preservation is more successful than reconstruction
- Surgical techniques should aim for minimal necessary trauma
- No material or technique is clearly or consistently superior to another
- Blood supply is paramount to effective healing
- Understanding and preserving the vascular supply is the key to improved surgical outcomes

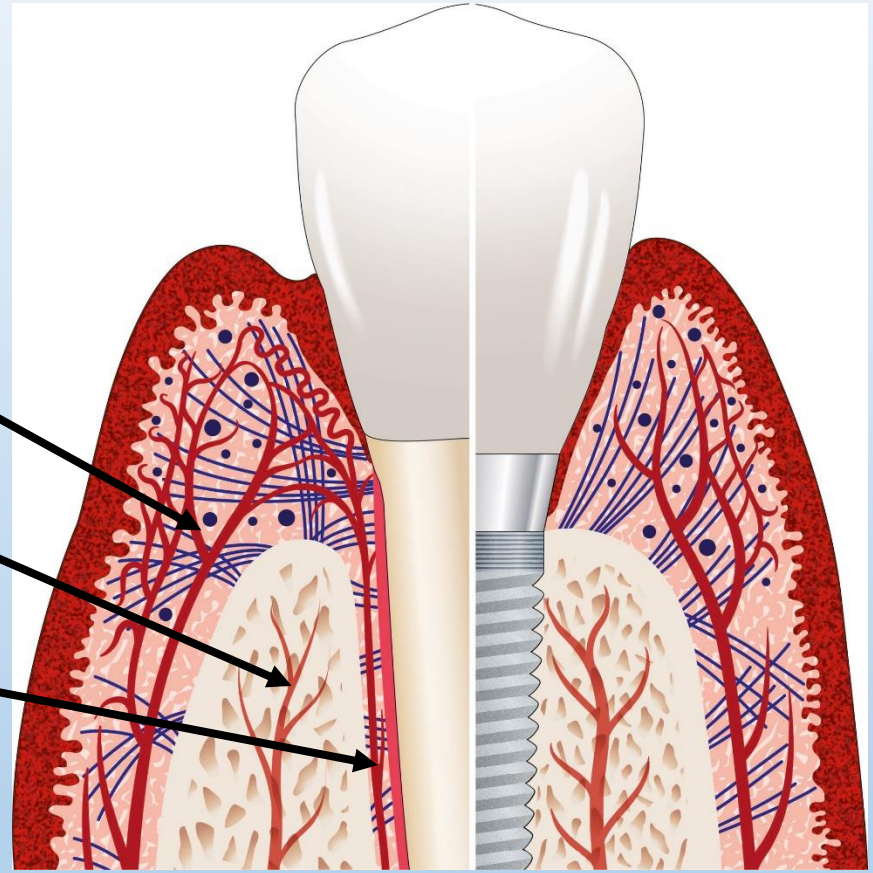
Vascular Supply to the Alveolar Complex

Only 3 vascular sources

1. Soft tissue Arteries (mucosa and periosteal)

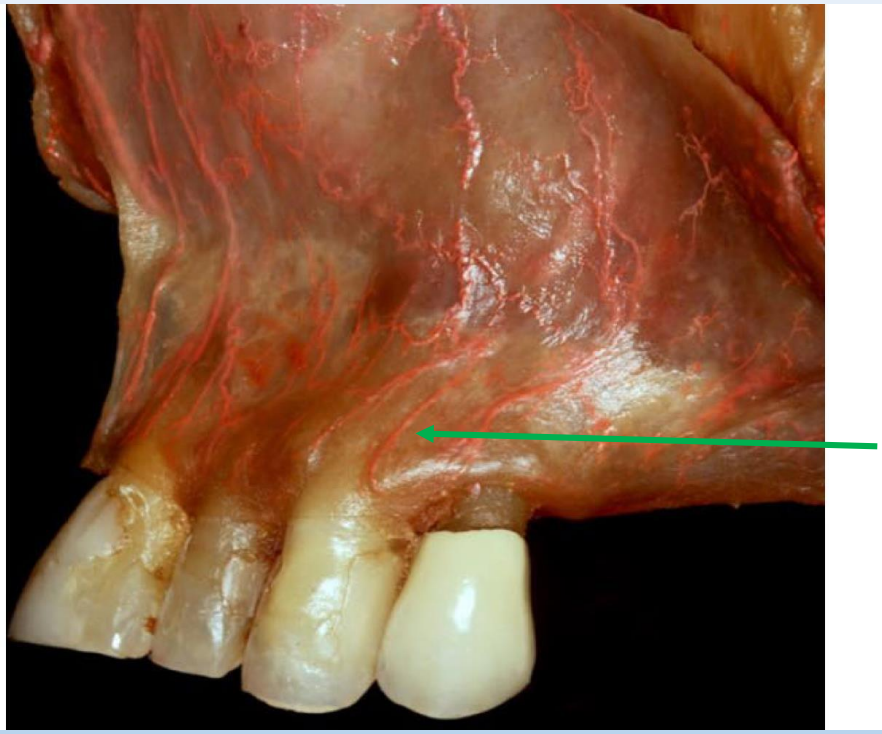
2. Interproximal Arteries

3. PDL Arteries (arise from Dental Artery which penetrates root apex to supply pulp)

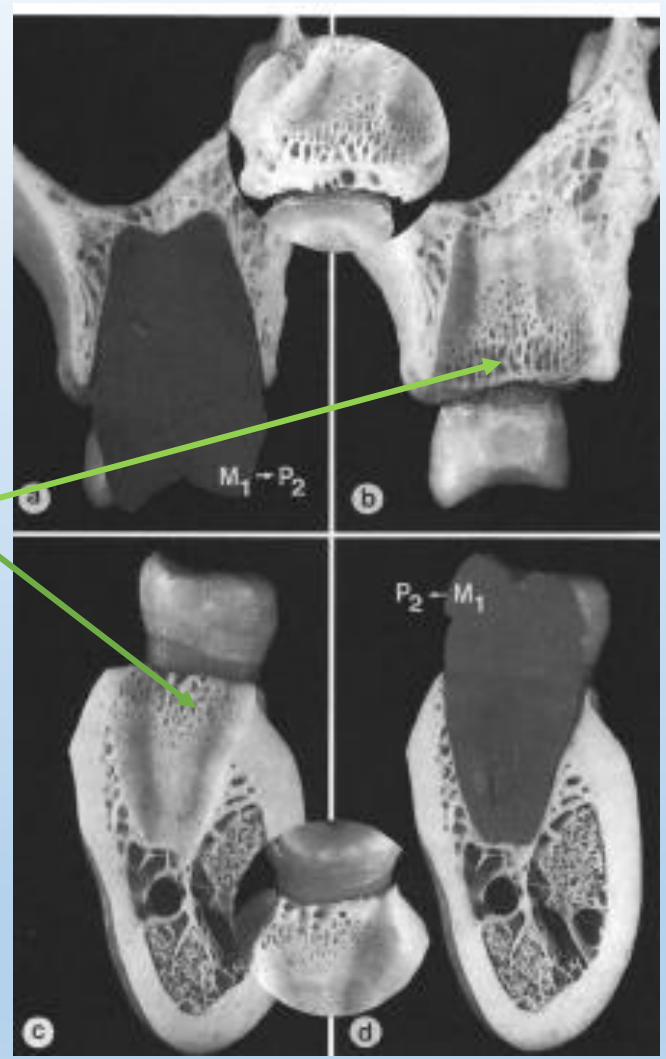


Handbook of Microscopic Anatomy, Volume V/5: The Periodontium, Professor Dr. H.E. Schroeder, Zahniirtliches Institut der Universitiit, Abteilung fiir Orale Strukturbiologie, PlattenstraBe 11, CH-8028 Ziirich

Vascular Supply Is Not Evenly Distributed



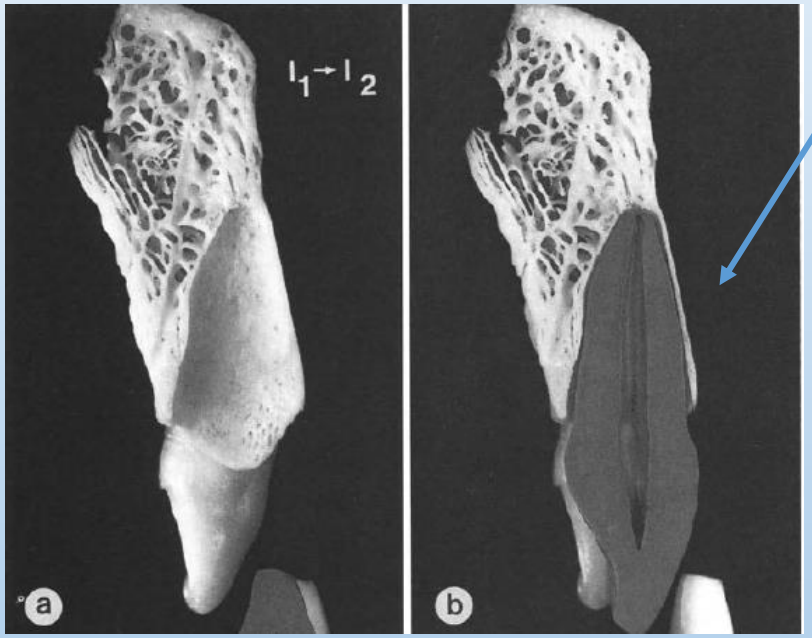
Periosteal and mucosal vessels selectively anastomose with the interproximal vessels in the crestal 1/3 of socket.

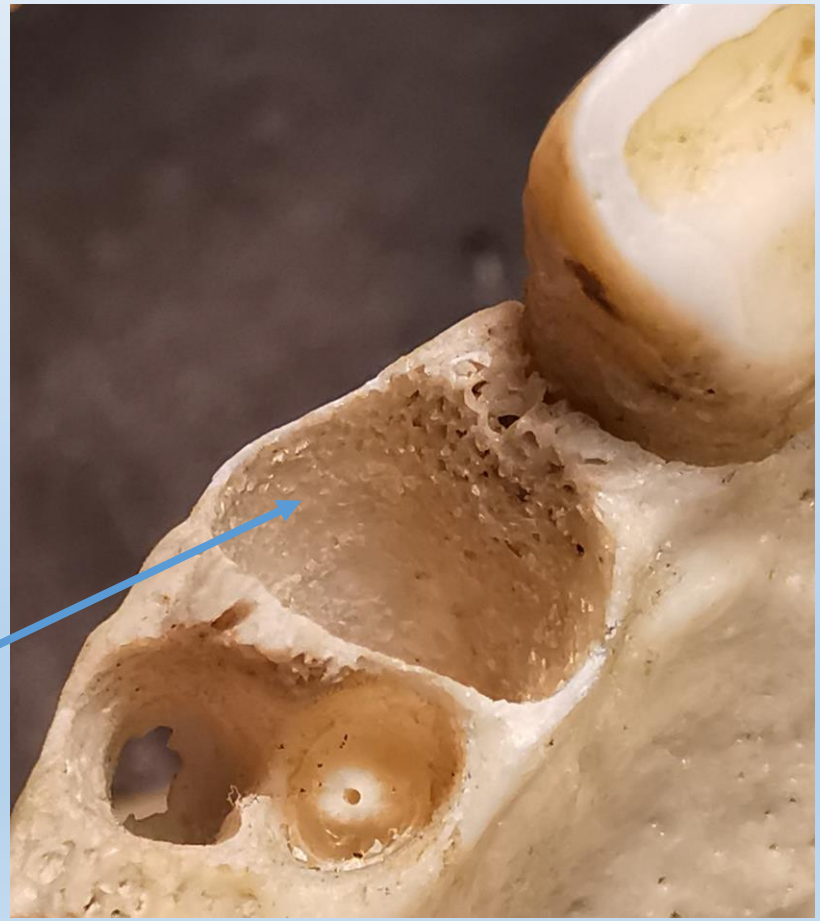


Vascular survey of the maxillary vestibule and gingiva—clinical, impact on incision and flap design in periodontal and implant surgeries, Arvin Shahbazi, Clinical Oral Invest 2021

The Buccal Plate

In the anterior the buccal bone and the alveolar socket often fuse, therefore no internal vascular supply



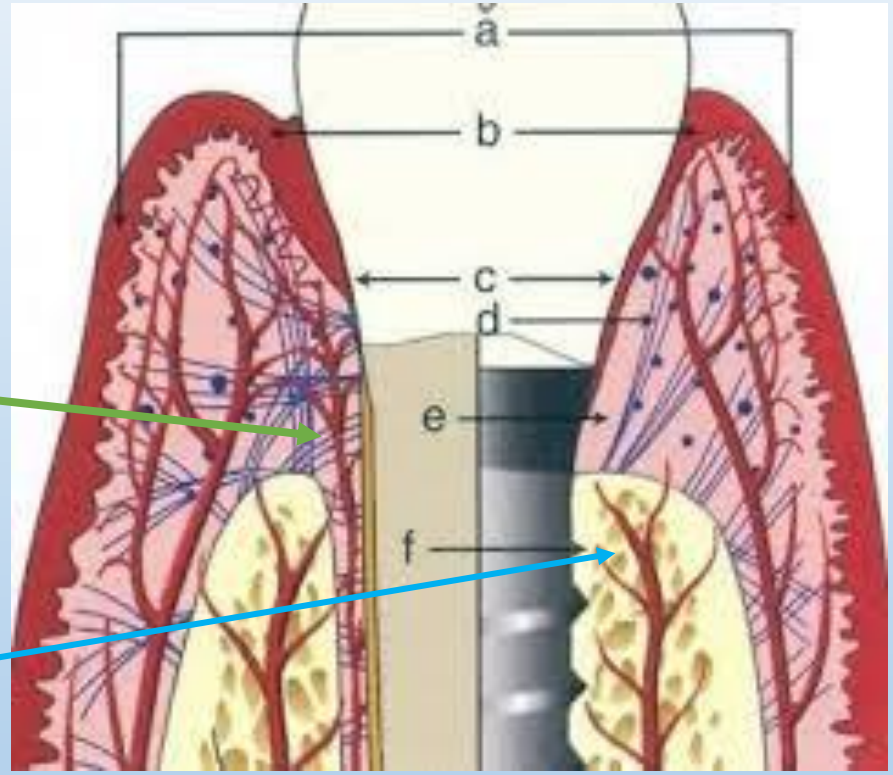


When the gingival tissue and buccal bone are thin, very few vessels perforate from the facial surface

Consequences of Immediacy on Blood Supply

After flapless tooth removal the PDL vessels are lost, leaving only the periosteal and interproximal vessels.

If a flap is raised only the interproximal vessels are left and they are predominantly in the coronal third



Clinical Relevance

- Proximal crestal bone must be protected during surgical procedures
  - during extraction sacrifice relatively avascular buccal bone if necessary
  - Choose implant diameter to preserve width of interproximal bone
- Buccal blood supply must be preserved if possible
  - Do not raise flap if possible
  - Do not incise papillae if possible
- Allow blood vessels to anastomose
  - If grafting of defects necessary avoid impenetrable membranes between vascular supply and graft

Saghiri, M-A et al. “The role of angiogenesis in implant dentistry part II: The effect of bone-grafting and barrier membrane materials on angiogenesis.” Medicina oral, patologia oral y cirugia bucal vol. 21,4 e526-37. 1 Jul. 2016, doi:10.4317/medoral.21200

Key Points

- Plan ahead – surgery is only the first step in rehabilitation
- Consider risk factors which may compromise desired outcomes
- Reconstructive techniques may be no better than natural healing
- Effective healing is always contingent on adequate blood supply
- Preservation of tissue is always more desirable than reconstruction