DOI: 10.21276/sjds

Scholars Journal of Dental Sciences (SJDS) **ISSN 2394-496X (Online)**
Sch. J. Dent. Sci., 2017; 4(5):233-238 **ISSN 2394-4951 (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjds.2017.v04i05.005

Case Report

Osteoradionecrosis of the Jaws –A New Cause and a New Cure - A Case Report and Review Article

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Abstract: Osteoradionecrosis is a radiation induced disease of the jaw bones. During the past 80 years, a number of theories for the pathogenesis of ORN have been proposed, with consequent implications for its treatment. Until recently, the triad of hypoxia, hypocellularity, and hypo vascularity proposed by Robert Marx was accepted as the primary cause, leading to the use of hyberbaric oxygen therapy for both treatment and prevention of the disease. This article deals with a new theory of pathogenesis of ORN, which proposes that damage to bone is caused by "radiation induced fibrosis". New treatments have therefore been devised, which include the use of pentoxyphylline and tocopherol for future treatment and prevention of ORN.
Keywords: Osteo radionecros, Robert Marx, hypo vascularity

INTRODUCTION-

Definition **-** Osteoradionecrosis of the jaws is a disease characterized by chronic non-healing wound secondary to irradiation and superimposed infection.

Synonyms

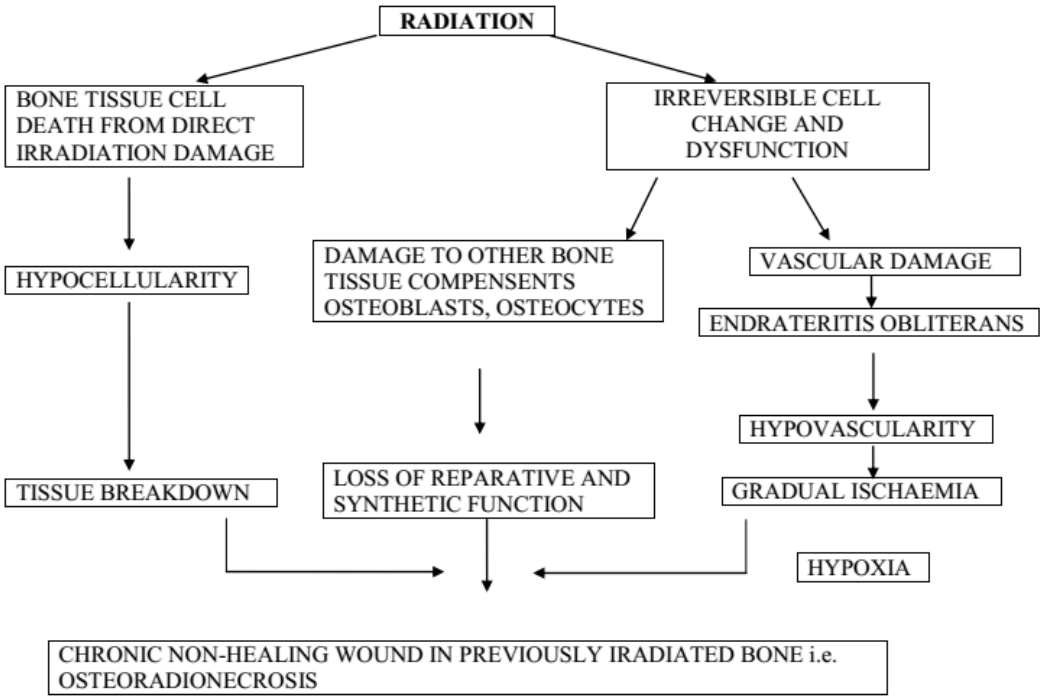
Radiation osteitis,
Radio-osteonecrosis,
Radio-osteitis,
Septic osteoradionecrosis

Clinical presentation –

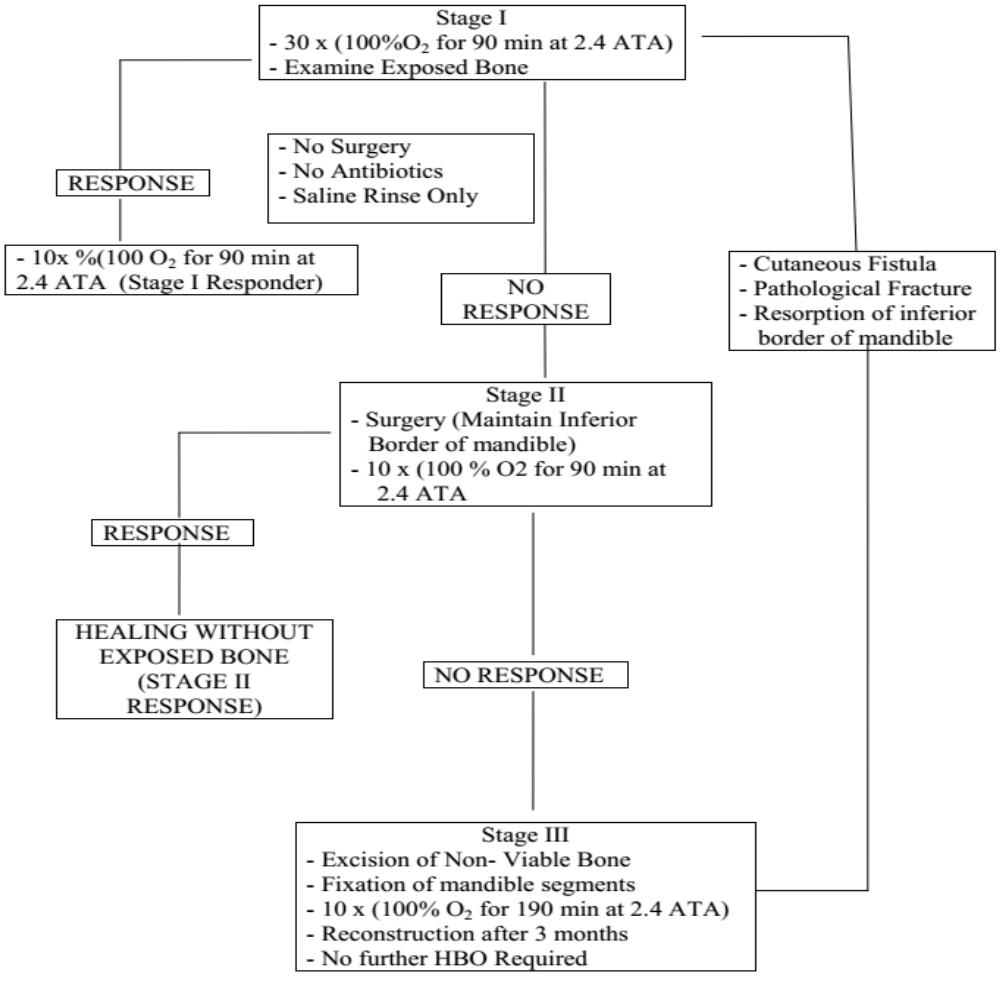
- Affects the mandible more often than the maxilla [1]
- Seen after radiation of more than 60Gy and more commonly when *brachytherapy* is used
- Interval between radiotherapy & onset of ORN is usually 6-12 months [2]
- Exposed devitalized bone through ulcerated mucosa or skin
- Pain is a common symptom
- Dysaesthesia [3]
- Food impaction in area of exposed sequestra [4]
- Fistulation from the oral mucosa or skin
- Pathological fractures
- Predisposing factors include – dental extractions [5, 6], injuries, infections, immune deficiencies malnutrition, etc

Theories of pathophysiology – A critical appraisal

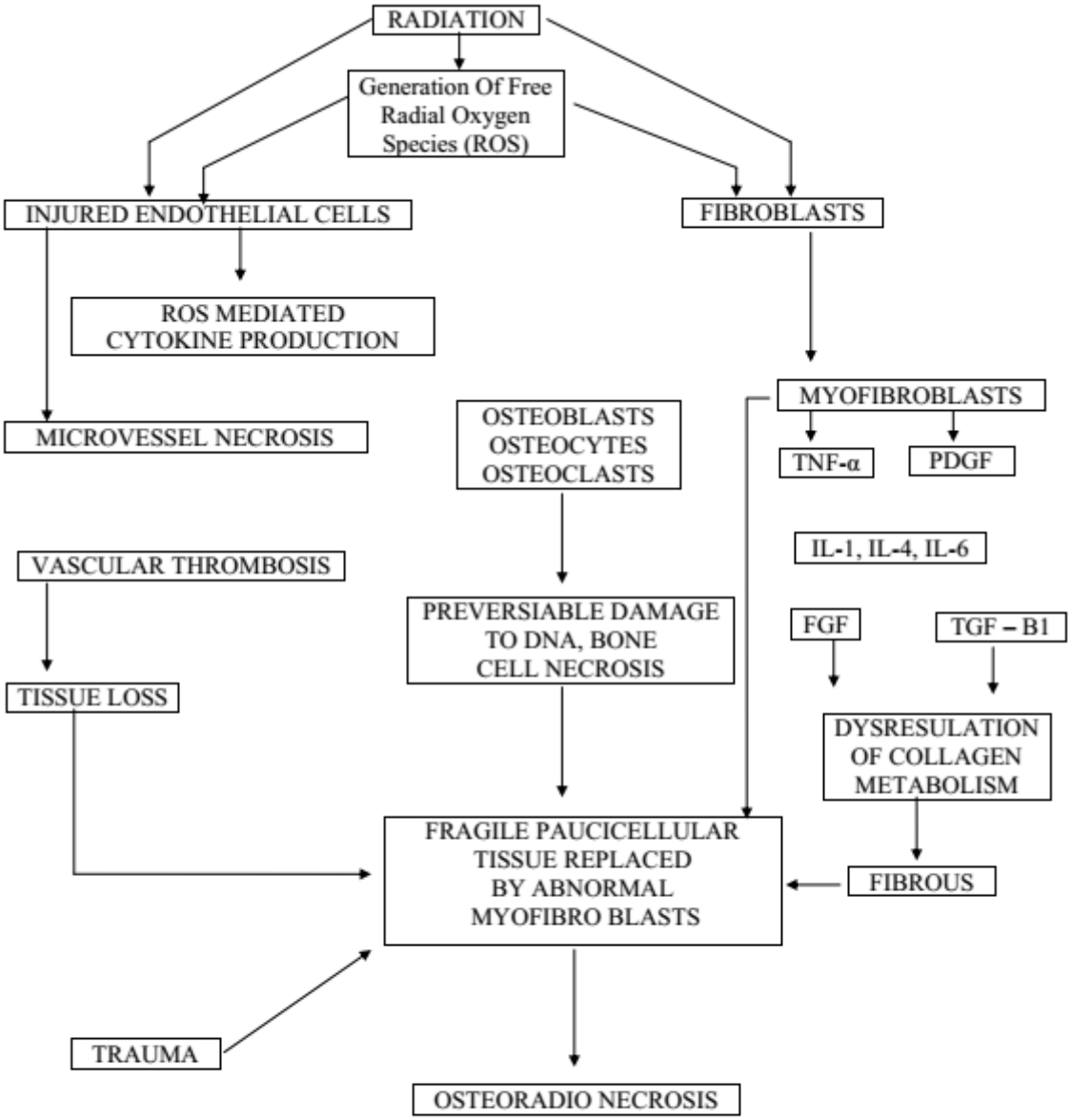
- Watson & Scarborough reported 3 crucial factors in the development of ORN-exposure to radiotherapy above a critical done local injury & infection [7].
- Meyer then proposed his radiation, trauma & infection theory [8].
- Marx's theory of hypoxia, hypocellularity & hypo vascularity was the most popular [9].



Pathophysiology of ORN according to Marx

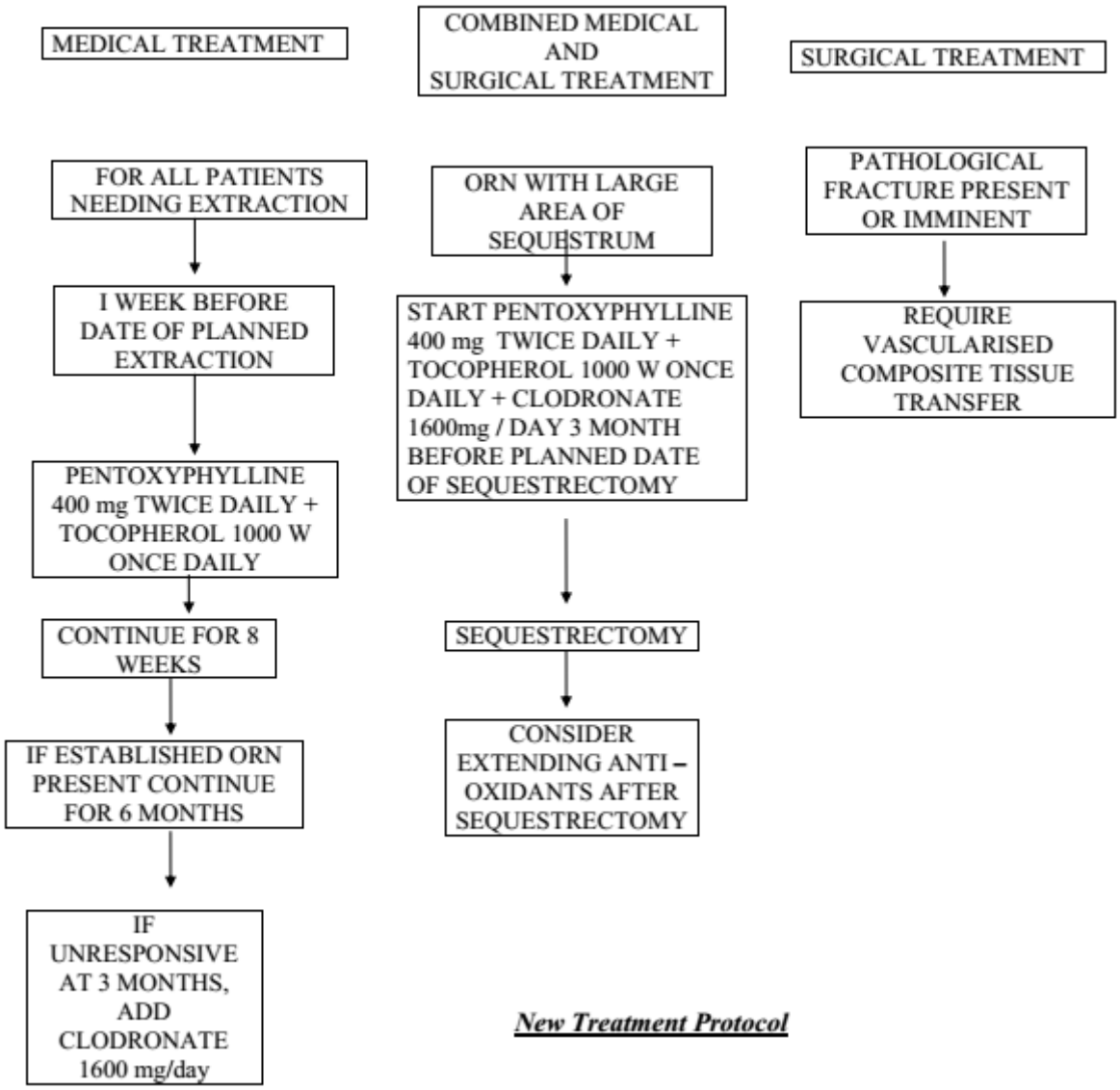


Treatment protocol for ORN according to Marx



RADIATION INDUCED FIBROATROPHIC THEORY

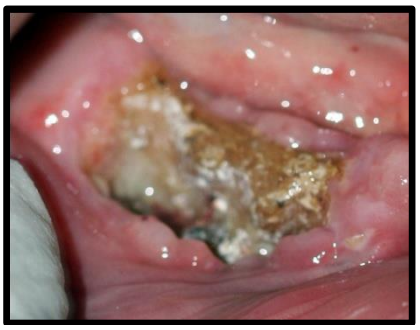
Current understanding of the pathophysiology of ORN



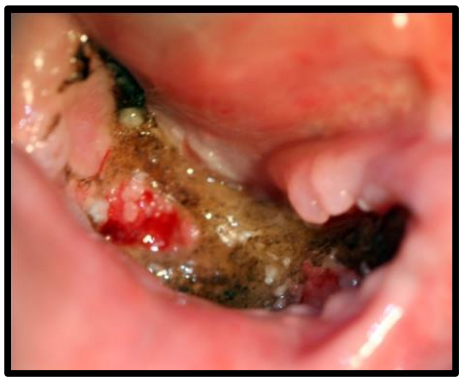
New Treatment Protocol

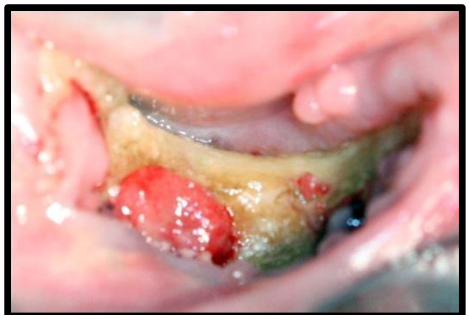
CASE REPORT

A 62 year old female patient reported to the Department of Oral and Maxillofacial Surgery with a chief complaint of a non-healing wound in the lower left side of the mouth since two weeks. History of surgery and radiation therapy for carcinoma of upper lip one year ago and extraction of 45 and 46 fifteen days ago. Extraction wounds have failed to heal indicating osteoradionecrosis of the lower right side of the mandible.

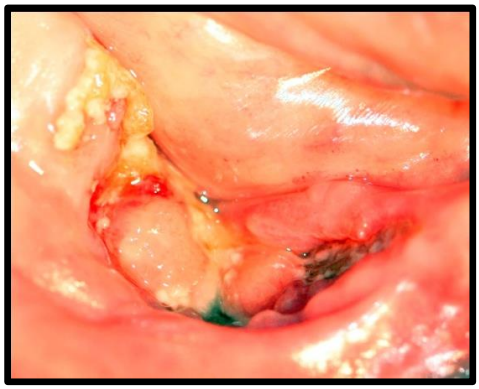


A combined approach was decided for the case. A sequestrectomy of the affected area was carried out to remove the necrotic bone and induce fresh bleeding. Simultaneously the patient was started on the above mentioned regimen.





Post-operative after 2 months



Post-operative after 4 months

Current understanding of the pathophysiology and new protocol for the prevention & treatment of ORN-

Radiation induced fibrosis is a new theory that accounts for the damage to normal tissues, including bone after radiotherapy. This theory suggests that the key event in the progression of ORN is the activation and dysregulation of fibroblastic activity that leads to atrophic tissue within a previously irradiated area.

After radiotherapy, endothelial cells are injured both directly from radiation, and indirectly from reactive oxygen species or free radicals. These reactive oxygen species then mediate the release of cytokines, which result in unregulated fibroblast activation and the myofibroblast phenotype characterized by unusually high rate of proliferation, excretion of abnormal products of the extracellular matrix, and a reduced ability to degrade such components persists. Ultimately these myofibroblasts undergo apoptosis, and even decades after radiotherapy, the bone remains pauci cellular, poorly vascularised and fibrosed, so that they have an increased tendency to develop ORN.

To reverse changes in these reactive oxygen species, new therapeutic regimens have been developed, which include the use of-

1-*Pentoxyphylline* - a methyl xanthine derivative that dilates blood vessels increases erythrocyte flexibility, inhibits inflammatory reactions in –vivo, inhibits proliferation of human deprival fibroblasts & increases collagenase activity in-vitro.

2-*Tocopherol (Vitamin E)* - Scavenges the reactive oxygen species that were generated during oxidative stress by protecting cell membranes against perioxidation of lipids, partial inhibition of TGF –β1, reduction of fibrosis.

3-Clodronate - a new generation bisphosphonate that inhibits bone resorption by reducing the numbers & activity of osteoclasts [10].

All patients having dental extractions could be given 8 weeks of pentoxyphylline 400 mg twice daily with tocopherol 1000 IU, starting a week before the procedure. If ORN develops, they could be used for a further 6 months, with clodronate prescribed after three months, if there has been no appreciable response. Patients with established ORN follow this regimen for 6 months, with clodronate added after three months if there is no appreciable response. Antibiotics should be used for established ORN, where there is clinical evidence of infection and frank pus, including draining sinuses or collections.

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