

## Re: NICO Historical Review

**Source:** <http://sci.tech-archive.net/Archive/sci.med.dentistry/2005-03/3071.html>

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**From:** LadyLollipop ([LadyLollipop\\_at\\_insightbb.com](mailto:LadyLollipop_at_insightbb.com))

**Date:** 03/18/05

Date: Fri, 18 Mar 2005 05:33:45 GMT

"John Chewter" <[john@LESS\\_SPAMchewter.f9.co.uk](mailto:john@LESS_SPAMchewter.f9.co.uk)> wrote in message news:d1cnqs\$cj6\$1@hercules.btinternet.com...

> *Jan – do tell us that you understood all these papers? Some of the words  
> are longer than 'Marmalade, Can you understand trans-marmaladic words?*

John, do back up you claims and you lies, rather than stalk me, then do post something besides criticisms of everything I post.

You have number of of questions you have never answered, is that your problem?

Shall I ask them again, and post you insults, rather than answers.

Do grow up, John.

As a claimed amalgamist, I asked you why you didn't post any articles showing us why you believe amalgams are toxic, here is your reply:

> *LL Have you ever posted any studies of this toxicity????*

JC Certainly not. I am an imaging specialist.

So I kindly suggest, you shut up.

LL

> *John Chewter*

> <http://www.keyneimage.co.uk>

> *"LadyLollipop" <LadyLollipop@insightbb.com> wrote in message*

> *news:TW8\_d.76748\$Ze3.41700@attbi\_s51...*

>> <http://maxillofacialcenter.com/NICOhistory.html>

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>> *The History of Maxillofacial Osteonecrosis (NICO)*

>>

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>> *Other Links*

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>> *References*  
>> *Tables*  
>> *Painful osteonecrosis/osteomyelitis, or "phossy jaw," of upper and*  
>> *lower jaws sloughed out when dentist tried to*  
>> *extract several teeth because of "toothache." Source: American*  
>> *Journal of Dental Science, 1859.*  
>>  
>>  
>> *The Maxillofacial Center, 165 Scott Avenue, Suite 100, Morgantown, WV*  
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>> *History of Maxillofacial Osteonecrosis (NICO)*  
>>  
>> *First described in 1794 in a case of septic necrosis of the femoral head,*  
>> *this enigmatic disease is as old as the dinosaurs but has been poorly*  
>> *understood and has such subtle radiographic changes that until recently*  
>> *it was seldom diagnosed prior to end–stage damage.[11–13] Contemporary*  
>> *research has so enhanced our understanding of its basic pathophysiology*  
>> *that it now bears little resemblance to the entity once known as "aseptic*  
>> *osteomyelitis."*  
>>  
>> *Heightened awareness and improved imaging techniques have confirmed this*  
>> *once rare disorder to be one of the most common of bone disorders. In*  
>> *certain diseases, such as lupus erythematosus, almost a third of patients*  
>> *may be affected.[9] IO is able to affect any bone of the human skeleton*  
>> *and is represented by a large number of orthopedic diseases now seen as*  
>> *simple anatomic– and age–related variations of intramedullary ischemia*  
>> *and infarction.[1–5,9,14,15]*  
>>  
>> *The old, overly–simplified histopathologic definition of IO as massive*  
>> *loss of osteocytes without pus is now substantially expanded to include*  
>> *specific and often subtle signs of ischemic marrow damage which may not*

>> even include obviously dead tissues.[2–9,14–16] Histopathologically less  
>> severe or nascent involvement has begun to be consolidated under a common  
>> diagnostic term, bone marrow edema (Table 1), and the disease is now  
>> known primarily as a vascular disorder readily influenced by a variety of  
>> risk factors or trigger events ("hits") which promote  
>> thrombosis.[7,9,17–21] Persons with multifocal IO are more likely to  
>> suffer from systemic risk factors than those with single site involvement  
>> and the great majority of patients have inherited or acquired a systemic  
>> tendency toward fibrin generation (Table 2) which predisposes them to  
>> microinfarction and ischemic marrow damage.[8,9,15–22]

>>  
>> Usually associated with pain, IO can nevertheless show a surprising  
>> capacity to remain painless until great destruction has occurred, even to  
>> the point of joint collapse for hip lesions -- there is little  
>> correlation between the degree of bone involvement and the intensity of  
>> associated pain.[5,9] The pain can take on a neuralgic character but its  
>> etiology is primarily a function of intraosseous fluid dynamics and  
>> inflammatory mediators rather than damaged nerves, as discussed  
>> later.[4,5,9,11,14–16]

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>>  
>> The Pre–Antibiotic Era: 1850–1930.

>>  
>> IO of the maxillofacial region is not new to dentistry. During the  
>> pre–antibiotic era "phossy jaw" and other forms of "chemical  
>> osteomyelitis" resulted from environmental pollutants, such as lead and  
>> the phosphorus used in safety matches, as well as from popular  
>> medications containing mercury, arsenic or bismuth.[23–29] This disease  
>> was well established by 1867, did not often occur in individuals with  
>> good gingival health, and appeared to "attack" the mandible first.[25]  
>> It was associated with localized or generalized deep ache or pain, often  
>> of multiple jawbone sites. The teeth often appeared sound and  
>> suppuration was not present. Even so, the dentist often began extracting  
>> one tooth after another in the region of pain, often with temporary  
>> relief but usually to no real effect.[24] Occasionally, large fragments  
>> of necrotic bone would come out with the tooth, sometimes involving much  
>> of an entire quadrant, as depicted in the figure at the top of this page.  
>> Apparently, Lorinser of Vienna in 1845 was the first to call attention to  
>> the problem.[25]

>>  
>> Less severe cases of maxillofacial osteonecrosis were discussed in the  
>> classic 1898 oral pathology text by Barrett,[28] wherein he described  
>> "caries" and "necrosis" of bone with cellular "devitalization" and  
>> "inhibition of nutrient currents," characterized by a slowly progressive  
>> "breaking down" of the "territory" of marrow tissues receiving those  
>> nutrients and resulting in little or no production of granulation tissue.

>> *He had no suggested etiology for his cases. Thirty years earlier and more than a century ahead of his time, Noel[27] separated bone caries into two distinct categories: "bone death" and the less intense "reduced vitality." Even earlier, the 1848 text by Thomas Bond[23], which appears to be the first true oral pathology text, was the first book to discuss bone necrosis as such, emphasizing that this disease did not require abscessed teeth or gums, could result in the complete death of bone. Bond mentioned that "necrosis may be caused by any means which destroys the nutrition of the bone or any part of it"— usually from "constitutional vitiations, or defects of nutrition consequent upon general pravity." His recommended treatment: "when necrosis has taken place, the bone must be removed."*

>>  
>> *G. V. Black,[29] the father of modern dentistry, described in 1915 an osteomyelitis look-alike disease which he called "chronic osteitis." He described slow bone death "cell by cell" with the creation of alveolar intramedullary "cavities" up to 5 cm. in size and wondered about its unique ability to produce extensive bone destruction without pus, without redness and swelling of the overlying tissues, without an increase in the patient's body temperature, and often without pain. His suggestion to curette diseased bone reiterated the treatment proposed by Ferguson[24] in 1868 and by Bond[23] in 1848. Around the same time period osteonecrosis of the hip in children was being recognized by the author's whose names would eventually be affixed to that disease, i.e. the Legg–Calvé–Perthes disease.[31–33]*

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>> *The Forgotten Decades: 1930–1970.*

>>  
>> *For most of the twentieth century this disease was largely forgotten by the dental profession, although a few investigators made significant contributions to the advancement of our understanding. Wilensky[24] and Hankey[25] suggested that persistent regional necrosis in osteomyelitis of the jaws was secondary to vascular insufficiency, while Brosch[26] described the potential for hollow medullary spaces to enlarge and coalesce one with another. Thoma[37,38] was likely the first to specifically correlate this "residual infection" or "osteitis" with old extraction sites, many of which demonstrated focal "necrotic exudates," fibrosis and "osteoclastic resorption" of surrounding bone. His observations were affirmed in 1955 by Box,[34] who reported a very large series of limited intraosseous cavitations or "vacuolations" in old extraction sites with no production of pus or bony sequestra. Box was especially intrigued by the radiographic subtlety of the disease, by its multifocal nature, its localized tenderness without inflammatory signs, and the neuralgia-like nature of accompanying pain.*

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>> *The Over-Emphasis of Pain: 1970-1990.*

>>

>> *The 1970s and 1980s saw a strong emphasis placed on the neuralgia-like*

>> *pains often accompanying osteonecrosis of the maxillofacial region, an*

>> *influence embodied in the currently popular diagnostic name NICO*

>> *(neuralgia-inducing cavitational osteonecrosis).[40-48] Significant or*

>> *complete pain reduction was achieved in chronic "idiopathic" facial pain*

>> *by the simple expedient of decortication and curettage of damaged*

>> *alveolar bone (Table 3), supporting the contention by neural researchers*

>> *that persistent odontogenic and osseous disease can be important*

>> *contributing factors for such neuralgias.44-49 None of these*

>> *investigations included a control group, nor has any facial neuralgia*

>> *follow-up study. Ethical considerations and the ever-present potential*

>> *for silent or subclinical disease will likely prevent valid control*

>> *groups from being identified, but a 1995 NICO follow-up investigation*

>> *confirming earlier surgical successes went so far as to guarantee patient*

>> *anonymity, to use a well-established pain evaluation instrument instead*

>> *of surgeon records to determine outcomes, and to use a third party to*

>> *collect and analyze data in order to reduce potential biases.[50]*

>>

>> *Unfortunately, the major emphasis on the association with neuralgic pain*

>> *initiated significant controversy among professionals treating*

>> *"idiopathic" facial pain and kept involved researchers from focusing on*

>> *other features of the disease process, such as more appropriate diagnoses*

>> *and diagnostic techniques, and better understanding of the*

>> *pathophysiology and pathoetiology of the disease. Early lesions were*

>> *diagnosed by a number of independent pathologists as chronic*

>> *osteomyelitis, and microorganisms cultured from many NICO lesions,*

>> *combined with occasional facial pain relief with antibiotic therapy,*

>> *assured that these cases would be diagnosed and treated as chronic*

>> *osteomyelitis. And yet, a significant number of patients did not respond*

>> *in a fashion appropriate to that diagnosis. This led some investigators*

>> *to seek alternative interpretations for the biological behavior and*

>> *histopathology. A critical shift in perspective (return to the original*

>> *concepts?) occurred in 1989 when this odd alveolar disease began to be*

>> *viewed primarily as a problem of compromised medullary blood flow driven*

>> *by progressive thrombosis, rather than as a unique infection unknown to*

>> *other bones.[56,57]*

>>

>> *This new perspective as a maxillofacial manifestation of IO provided, for*

>> *the first time, a logical explanation for the curiously multifocal nature*

>> *of the disease; its frequent intermingling of ischemically damaged and*

>> *normal marrow (also influenced by the perfusion irregularities of fatty*

>> *marrow[58]), its frequent lack of inflammatory cells, its remarkably*

>> *chronic and recurring character, its deep bone pain and varied pain*

>> syndromes, its relatively high failure rate with local interventions, and  
>> its primary localization at the ends of the arterial inflow (retromolar  
>> and subcrestal alveolar regions) where weak, irregular blood flow favors  
>> the formation of intravascular thrombi.[5,7,9,14,15,59]  
>>  
>> This is not to say that intraosseous microorganisms do not represent a  
>> significant risk factor or triggering mechanism for thrombosis in these  
>> stagnant zones of cancellous bone. Affected bone is ideal fodder for  
>> periodontal and periapical bacteria chronically stimulating inflammatory  
>> and immune responses.[60–62] Impaired medullary circulation prevents  
>> proper healing in these instances and the chronic infection, in turn,  
>> enhances local and systemic clotting. This further exacerbates the  
>> medullary ischemia and initiates a slow, ever-increasing spiral of  
>> thrombosis and microinfarction with progressively elevating  
>> intramedullary pressures, additional thrombosis, and frequent propagation  
>> of spontaneous pain. Prothrombotic factors, especially fibrinogen, also  
>> allow increased adherence of bacteria to thrombin-activated endothelial  
>> cells.[63]  
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>> Decade of Major Advances: 1990–2000.  
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>> Once it became clear that this disease of the jaws resembled avascular  
>> necrosis of other bones, investigators used newly available laboratory  
>> tests, including allele-specific polymerase chain reaction, to identify  
>> in NICO patients heritable disorders predisposing to adverse thrombotic  
>> events. At least 72% proved to be afflicted with a variety of such  
>> disorders, as compared to 70–87% for patients with IO of the hip and  
>> knee.[9,19–21,64–67 This was seen as a major breakthrough, eventuating in  
>> the use of anticoagulants (without surgery or antibiotics) in persons  
>> with NICO and hip osteonecrosis.[68–71] Although not all affected  
>> individuals benefited, the significant pain relief experienced by a large  
>> proportion of treated patients confirms an association in those persons  
>> between the symptoms of IO and the hypercoagulable disorders.[69,71]  
>>  
>> Viewing NICO as the oral manifestation of a systemic disease also allowed  
>> application of the clinicopathologic qualities of long bone disease to  
>> maxillofacial cases, especially the use of diagnostic imaging techniques  
>> such as 99technetium-MDP (99mTc-MDP) scintigraphy and Single Photon  
>> Emission Computed Tomography (SPECT) scans, instead of the indium and  
>> gallium scans typically used for bone infections.[64,72–74] The small  
>> number of chronic inflammatory cells found in NICO lesions makes  
>> radioisotopes which attach to leukocytes much less useful than those  
>> which attach to new or exposed bone matrix. There is usually a small  
>> amount of ongoing healing in IO lesions and so they present as "hot  
>> spots" of increased radioisotope uptake, with "cold spots" of extremely

>> *reduced uptake in the occasional severely desiccated lesion. Newly developed 99mTc isotopes directed at fibrin "–chain peptide may prove useful for patients actively forming microclots.[75]*

>>

>> *A substantial proportion (25–35%) of scans will be falsely negative because the disease has long periods during which no bone is destroyed or regenerated, even as symptoms and marrow damage progress. This holds true regardless of the affected bone, but maxillofacial involvement suffers from an unexpected false–negative phenomenon: radiologists not attuned to jawbone ischemia often interpret a hot spot of alveolar bone as "normal," presuming it to relate to ubiquitous dental and periodontal disease. We recommend, therefore, that the surgeon review all films interpreted as negative. Thin–sliced spiral CT scans and ultrasonic scans have also proven effective in localizing NICO, although they require very careful evaluation.[76] MRI scans are valuable for the rounded ends of bones but in our experience are of little benefit in alveolar cases.[77,78]*

>>

>> *In a similar fashion the more contemporary histopathologic features of ischemic osteonecrosis and bone marrow edema (its less severe counterpart) often overlooked by or unfamiliar to oral pathologists, could be applied to maxillofacial examples with the notable caveat that there are no features of cortical collapse in jaw lesions and odontogenic infections are often superimposed.[1–9,57] Additionally, microscopic evaluation of maxillofacial biopsy samples is made much more difficult by the small number and size of available curettage fragments, especially when an intramedullary cavitation exists, in contradistinction to the large specimens available for study after resection and core biopsies of long bone cases. Recent analyses have, significantly, reported that almost 3/4 of jawbone biopsy samples of ischemic osteonecrosis and NICO can be classified as the histologically more subtle variants called bone marrow edema or regional ischemic osteoporosis.[81,82] This has helped to explain why some oral pathologists, certainly not the majority, have difficulty distinguishing the classic features from "normal" bone and bone marrow.*

>>

>> *The first microscopic review of a large series of biopsied cases of NICO was reported during the 1990s, as was the first necropsy example.[57,82] These papers strongly emphasized the multifocal nature of the disease, while others reinforced the strong association between chronic facial pain and inflammatory or ischemic marrow disease.[55,83] In this light, one of the most important advances was the refinement of the old anesthesia/hyperesthesia and microanesthesia diagnostic tests to more successfully localize areas of medullary disease in facial pain patients.[84–86]*

>>

>> *During the 1990s sophisticated assays were also applied, for the first time, to maxillofacial osteonecrosis. Haley and Pendergras[87] used a well–established neurotoxicity assay on a very large number of tissue samples, finding almost all to be extremely toxic –– often more toxic than hydrogen sulfide, the chemical normally used to establish maximum level of neurotoxicity. The exact nature of the toxin is not yet known,*

>> *but the discovery of the neurotoxicity led some to question whether or*  
>> *not this process damaged the peripheral nerve myelin of the alveolar*  
>> *nerves. This idea was further stimulated by the finding in a small*  
>> *number of NICO biopsy samples of an unusual form of nonwallerian*  
>> *degeneration in the majority of visible nerves.[55] To this end the*  
>> *blood of another small sample of NICO patients was evaluated by a*  
>> *newly-established assay which, for the first time, allowed the*  
>> *determination of circulating antibodies against peripheral nerve*  
>> *myelin.[88] The sera of healthy humans normally show none of these*  
>> *antibodies, as was true for a few of the NICO patients, but other NICO*  
>> *patients had antibody levels as high as or higher than those found in the*  
>> *classic demyelination disease, the Guillain-Barré syndrome.[89,90] This*  
>> *suggests chronic exposure of the peripheral myelin to the immune system,*  
>> *either as a primary attack (autoimmune) or secondary to myelin exposed or*  
>> *partially destroyed by a local inflammatory/ischemic phenomenon.*  
>>  
>> *While some patients had no such antibodies, others demonstrated Elevated*  
>> *levels of circulating anti-peripheral nerve myelin (anti-PNM) antibodies*  
>> *have been found in NICO patients, suggesting .120-122 Chronic nerve*  
>> *damage is likely enhanced by the very high levels of neurotoxicity found*  
>> *by bioassay in virtually all tissue samples of maxillofacial*  
>> *osteonecrosis, although the responsible neurotoxins have not yet been*  
>> *identified.123*

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>> *Table 1: Alternative diagnostic names used for bone marrow  
>> edema and ischemic osteonecrosis.1–9,14–16*

>>  
>> *Bone Marrow Edema*  
>> *Ischemic Osteonecrosis*  
>>  
>> *Arlet Type I osteonecrosis*  
>> *Bone compartment disease*  
>> *Bone marrow edema syndrome*  
>> *Chronic traumatic edema*  
>> *Medullary engorgement–pain syndrome*  
>> *Migratory osteolysis*  
>> *Migratory osteoporosis*  
>> *NICO \**  
>> *Post–traumatic painful osteoporosis*  
>> *Post–traumatic reflex dystrophy*  
>> *Primary algodystrophy*  
>> *Regional ischemic osteoporosis*  
>> *Regional osteoporosis*  
>> *Roentgenologic transient osteoporosis*  
>> *Sudeck's disease (RSD) \*\**  
>> *Transient bone marrow edema syndrome*  
>> *Transient demineralization*  
>> *Transient ischemic osteoporosis*  
>> *Transient marrow edema*  
>> *Transient osteoporosis*  
>> *Transitory demineralization in pregnancy*  
>> *Aseptic necrosis*  
>> *Aseptic osteomyelitis*  
>> *Aseptic osteonecrosis*  
>> *Avascular necrosis*  
>> *Bone infarction*  
>> *Coronary disease of bone*  
>> *Ischemic necrosis*  
>> *NICO \**  
>> *Osteochondrosis desiccans*  
>> *Perthe's disease*

>>  
>>  
>> *\* NICO: neuralgia–inducing cavitational osteonecrosis*  
>> *\*\* RSD: reflex sympathetic dystrophy*

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>> *Table 2: Coagulation disorders found in patients with ischemic*

>> *osteonecrosis of the hips, knees and jaws. These are compared to the*

>> *proportions found in patients with deep vein thrombosis of soft tissues*

>> *and with the normal population. Resulting proportions do not total 100%*

>> *because some patients had multiple disorders. Modified from Bouquot JE,*

>> *LaMarche MG. J Pros Dent 1999; 81:148–158.*

>>

>> *Normal Population*

>> *Deep Vein Thrombosis*

>> *Osteonecrosis*

>>

>> *Thrombophilia*

>>

>> *Hereditary types\**

>> *2–5%*

>> *5–9%*

>> *50–70%*

>>

>> *Acquired types*

>> *3–7%*

>> *20–50%*

>> *33%*

>>

>> *Hypofibrinolysis:*

>>

>> *Hereditary types \**

>> *<1%*

>> *5–15%*

>> *18–22%*

>>

>> *Acquired types*

>> *<1%*

>> *20–25%*

>> *50%*

>>

>> *Total (includes multiple coagulopathies):*

>> *5–9%*

>> *20–50%*

>> *65–87%*

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>> *\* usually autosomal dominant*

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>> *Table 2: Results of surgical curettage of jawbone NICO (Neuralgia-Induced Cavitational Osteonecrosis) lesions, an average of 4.5 years after last surgery, in 103 patients with "idiopathic" chronic facial pain for an average of 6 years (range: 2-18 years) prior to NICO surgery.*

>>

>> *Reference: Bouquot JE, Christian J. Long-term effects of jawbone curettage on the pain of facial neuralgia. J Oral Maxillofac Surg 1995;*