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GLANDELE ENDOCRINE & DINTII
Love & Hate

Doctor ALINA-ANTONELA ONICIUC-BURLACU
Medic Primar Endocrinolog

Împărtășim aceleași valori și aceeași pasiune

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AGENDA

1. Boli endocrine ce afecteaza dentitia
    A. Copii
    B. Adulti

2. Afectiuni dentare ce influenteaza sistemul endocrin

3. GOOD FOR BONES/ BAD FOR JAWS ?!?

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1. Boli endocrine ce afecteaza dentitia

A. COPII

- Multiple asocieri in sindroame genetice

- Afectari ale dentitiei provizorii si definitive

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ANOMALII DE ERUPTIE

- Dinti natali/neonatali
  - Sdr SOTO: gigantism cerebral, trasaturi dismorfice, crestere excesiva intrauterine si in prima parte a copilariei – NSD1, 5q35
  - Sdr HALLERMAN – STREIFF – nanism armonic, facies bird like, microcefalie, afectare dentara, tulburari de intellect
  - Displazie condroectodermala – displazie ectodermala [dinti, unghii], polidactilie, DSA
- Absenta eruptiei
  - Primar failure – mutatie PTHR1 – M1M2
  - Complete failure:
    - OHA: pseudohipoPTH tip1A – obezitate, talie mica, MC scurte, retard mental, TAD, loss function GNAS1
    - Sdr Williams – IUGR, facies characteristic, stenoza valvulara supraaortica, hipercalcemie, hipotiroidie
    - Displazii ectodermale
- Agenezii
  - Sdr Down – mechanism immunologic si afectari periodontale
  - Displazii ectodermale – hipo-anodontia
  - Cel mai frecvent in dentitia primara lipseste incisivul central mandibular si in cea permanenta incisivul lateral si PM2 maxilar

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ANOMALII DE ERUPTIE

- Exfoliere prematura – caderea dintilor inainte de 6 ani

  – **HIPOFOSFATAZIA**:
    - absenta FAL
    - 5 forme clinice
    - cea mai severa TAR
    - manifestari clinice sistemice: tulburari de crestere, hipotonie, bowing legs
    - manifestari dentare: pierderi dentare premature, minima inflamatie
    - a 6 a forma odontohipofosfatazia – dental loss only
    - sunt afectati primii dinti aparuti
    - Hipercalcemie, hiperfosfatemie, vitamina B6 scazuta

  - **HISTIOCITOZA LANGERHANS**
    - Manifestari sistemice: diabet insipid, intarzieri in crestere, etc
    - Manifestari dentare: gingivite, modificari de radacini, pierderi dentare

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ANOMALII DE ERUPTIE

- **Eruptie intarziata**
  - Definitie: intarzieri in aparitie a dentitiei primare/definitive cu mai mult de 6 luni sau asimetrie in eruptie
  - Hipopituitarism
    - Congenital – Sdr ce asociaza anomalii dentare sau per se
    - Dobandit
  - Hipotiroidism
    - Congenital – frecvent, asociat cu macroglosie si modificari faciale
    - Dobandit – anomalii in eruptia dintilor definitivi, carii frecvente, intarzierea vindecarii leziunilor bucale
  - Acondroplazia
  - Osteopetroza
  - Sdr Down
  - RAHITISM
    - Calcipenic
    - Deficit de vitamina D: nutritional; deficit de sinteza; catabolism crescut
    - Deficit in actiunea vitaminei D
    - Hipofosfatemic X linkat

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ANOMALII DE ERUPTIE

- **Eruptie accelerata**
  - Definitie: accelerarea aparitiei dentitiei primare si secundare
  - Apare in diabet zaharat, obezitate
  - Sdr TURNER
  - Fast maturer
  - Pubertate precoce vera si pseudopubertate precoce

ANOMALII DE NUMAR

- **Dintii supranumerari**
  - mai frecvent la baieti si la dentitia definitiva
  - 3 sindroame:
    - Sdr Rubinstein-Taybi: IUGR plus deficit de crestere postnatala, microcefalie dismorfica, anomalii oculare, retard mental, 16p133
    - Sdr OPITZ GBBB: anomalii de linie mediana, cardiace, hipospatiaz, X linkat
    - Sdr ROBINOW: nanism, fatal face, modificari acrale, WNT5A

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ANOMALII DE SMALT

- **Deficit de 1α-hidroxilaza – TAR 27 B1**
- **Mutatia receptorului de vitamina D – TAR – alopecie + def.ectoderm dupa varsta de 2 ani**
- **Sdr PGA1: APECED – cr21 - AIRE**

Types of endocrine and nonendocrine autoimmune syndromes associated with adrenal insufficiency

Disorder	Prevalence (%)
Polyglandular autoimmune syndrome type 1	
Endocrine	
Hypoparathyroidism	89
Chronic mucocutaneous candidiasis	75
Adrenal insufficiency	60
Primary hypogonadism	45
Hypothyroidism	12
Type 1 diabetes mellitus	1
Hypopituitarism	<1
Diabetes insipidus	<1
Nonendocrine	
Malabsorption syndromes	25
Alopecia totalis or areata	20
Pernicious anemia	16
Chronic active hepatitis	9
Vitiligo	4
Polyglandular autoimmune syndrome type 2	
Endocrine	
Adrenal insufficiency	100
Autoimmune thyroid disease	70
Type 1 diabetes mellitus	50
Primary hypogonadism	5 to 50
Diabetes insipidus	<1
Nonendocrine	
Vitiligo	4
Alopecia, pernicious anemia, myasthenia gravis, immune thrombocytopenia purpura, Sjögren syndrome, rheumatoid arthritis	≤1

Data from:

1. *Leshin M. Polyglandular autoimmune syndromes. Am J Med Sci 1985; 290:77.*
2. *Neufeld M, Maclaren NK, Blizzard RM. Two types of autoimmune Addison's disease associated with different polyglandular autoimmune (PGA) syndromes. Medicine (Baltimore) 1981; 60:355.*

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ANOMALII DE DENTINA

- **Cauze congenitale – DENTINOGENEZA IMPERFECTA – 3 tipuri:**
  - **Tip 1: se asociaza cu osteogeneza imperfecta tip 1**
  - **Mutatia COL1A1, COL1A2**
  - **Talie mica, deficit de mineralizare, fracturi recurente, blue sclera**
- **Cauze sistemice**
  - **MPZoze**
  - **Sdr EHLERS DANLOS:**
    - **Multiple forme**
    - **classic TAD**
    - **mutatii COL5A1, 5A2**
    - **forma periodontala asociaza pierderi dentare, anevrisme, fenotip Marfan like**
  - **Tulburari de mineralizare:**
    - **Hipofosfatazia**
    - **Rahitismul hipofosfatemic X linkat – abcese, dentina hipoplazica, pierderi dentare**
    - **Mutatia receptorului vitaminei D**

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CORELATII PRACTICE varia

- **Afectari buco-dentare secundare: modificarilor hormonale si stilului de viata al copiilor si adolescentilor**
  - **Modificari hormonale pubertare: estradiol, progesterone, testosterone**
  - **Fluctuatii cortisol si GH**
  - **Lipsa de igiena bucala**
  - **Bad habits: fumat, dulciuri in exces, mestecat de guma, bauturi carbogazoase**
  - **BRGE netratate/ignorate**

Afectiunile cavitatii bucale determina modificari, in special la nivelul axului HT-HP-CSR si posibil functiei tiroidiene prin 3 mecanisme:

- **Modificari microbiom buccal**
- **Abcese apicale, periodontale**
- **Afectiuni periodontale**

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1. Boli endocrine ce afecteaza dentitia

B. ADULTI

- **Acromegalia** [hipersecretie de GH] cel mai frecvent adenoame hipofizare
  - Mecanism:
    - Mecanic – treme/diasteme, macroglosie, modificari de mandibula
    - Metabolic – OP, DZ, HTA, modificari microvasculare
- **Afectiuni tiroidiene**:
    - Hipertiroidism – sangerari facile, interactii cu anestezia, instabilitate CV, agitatie
    - Hipotiroidism – vindecare dificila, interactie medicatie anestezie, macroglosie
    - Tiroidita autoimuna – modificari microbiom buccal, hiposalivatie

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1. Boli endocrine ce afecteaza dentitia

B. ADULTI

- **Tulburari de metabolism fosfocalcic**
  - Hiperparatiroidism – tumori cu mieloplaxe, resorbtie periostala
  - Hipomineralizare:
    - Deficit de vitamina D – congenital/nutritional – anomalii de smalt si dentina
    - Hipofosfatazia – forma odontala – pierdere dentara prematura
    - Osteomalacia
    - Osteoporoza – per se + tratamente antiresorbtive – ONJ
    - Rahitismul fosfopenic X linkat – abcese dentare, anomalii de dentina, osteomelita periodontala
    - Osteomalacia tumor indusa
- **Afectiuni ale glandelor suprarenale**
  - Insuficienta CSR – lizereu Burton, vindecare dificila, necessitate dublare doza tratament de substitutie
  - Feocromocitom - !!! Atentie la anestezie, risc de declansare criza hipertensiva
  - Sdr Cushing – prin multiple mecanisme determina vindecare dificila, sangerari postinterventii, modificari microbiome buccal, agravare boli periodontale

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1. Boli endocrine ce afecteaza dentitia

B. ADULTI

- **Diabetul zaharat**
  - Relatie bidirectionala
  - Mecanism: modificari glicemie, modificari microvasculare, inflamatie cronica
  - Risc crescut de parodontopatii, abcese apicale, avulsii, etc
- **Afectiuni ale gonadelor**
  - Hiperestrogenismul de varii cause – sangerari facile, sensibilitate crescuta, risc de infectii
  - SOPC – mecanism: RI, inflamatie cronica, modificari microbiom, determina gingivite, boli parodontale
  - Sarcina fiziologica – pregnancy gingivitis
  - Menopauza – multiple mecanisme: inflamatie cronica, BMS, osteoporoza

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2. Afectiuni dentare ce influenteaza sistemul endocrin

Sunt mai putine studii si evidente clinice ce demonstreaza o influenta clara a patologiei dentare asupra sistemului endocrine.

Sunt incriminate cel putin 3 mecanisme:

1. Modificari microbiom buccal
2. Parodontopatii – boala parodontala
3. Abcese apicale periodontale, etc

Cele mai evidente asocieri sunt:

- **Diabetul zaharat –** poate fi decompensat, agravat, relevat
- **Axul HT – HP – CSR –** stresul infectios decompenseaza o patologie deja existenta sau o releva
- **Posibila afectare a glandei tiroide –** sunt necesare inca studii

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3. GOOD FOR BONES/ BAD FOR JAWS ?!?

1. **ONJ – Adevar sau Provocare ?**

- **Frecventa**:
  - 0,001–0,005 – in OP tratata cu BP si DSM
  - 1-15% - in cancere cu anumite tratamente – CTIBL, metastaze osoase
- **Definitie**: expunere tesut necrotic in mediul oral mai mult de 8 saptamani
- MR – ONJ: BP, DSM, RZM, med antiangiogenetic, inh TNF
- **Cei mai incriminati**:
  - BP orali – ALN
  - BP iv – ZOL
  - DSM
  - Medicatia IBL

- **Mecanisme fiziopatologice**
  - Inhibitia osteoclastica
  - Infectie si Inflamatie
  - Inhibitia angiogenezei
  - Disfunctie imuna
  - Factori genetici
  - Distrugerea barierei orale
  - **TRIGGERI: extractii dentare, implanturi, malpozitii proteze**

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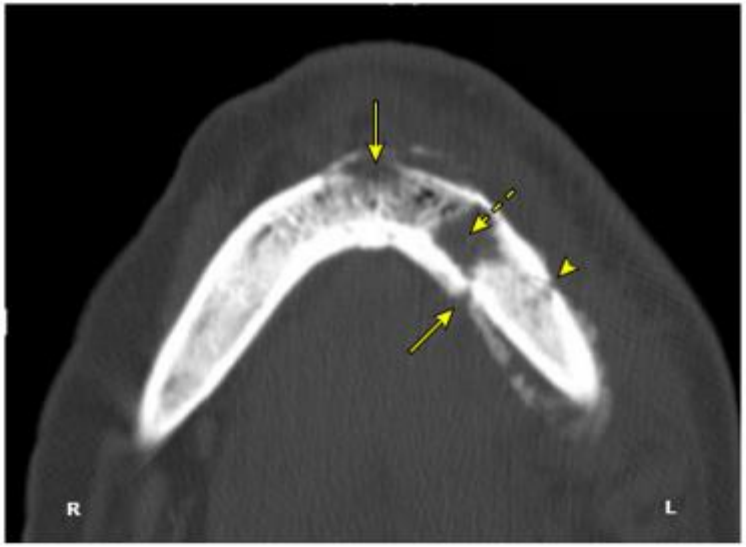
Punctul de Vedere al Endocrinologului

1. **ONJ – Adevar sau Provocare ?**

- NU EXISTA MARKERI UTILI IN DETECTAREA PRECOCE !
- Imagistica utila ?: rgr panoramica; cone beam CT
- Clinica variabila si progresiva; 4 stadii de evolutie

- **GOOD FOR BONE BUT BAD FOR JAW?**
  - BP previne fractura de Coloana Vertebrala cu **41,77%** si Sold **30%-51%**
  - DSM previne fractura de Coloana Vertebrala cu **68%** si Sold **40%**

Osteonecrosis of the jaw: radiographic appearance



This is a section from a CT scan of a 72-year-old woman with multiple myeloma treated with monthly bisphosphonate injections. She complained of left-sided jaw pain and swelling following dental extraction. This coronal view of the mandible shows several areas of disruption of cortical bone (arrows), a pathologic fracture line (arrowhead), and a large area of central bone loss (dashed arrow) suggestive of tumor and/or abscess formation.

CT: computed tomography.

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Bisphosphonates for the treatment of osteoporosis

Bisphosphonate	Formulations	Dosing	Vertebral fracture reduction	Hip fracture reduction	Nonvertebral fracture reduction	Discontinuation of therapy (in selected patients*); after:
Alendronate	Oral¶	• 10 mg once daily, **or** • 70 mg once weekly△	Yes	Yes	Yes	5 years
Risedronate	Oral, immediate release¶	• 5 mg once daily, **or** • 35 mg once weekly, **or** • 150 mg once monthly	Yes	Yes	Yes	5 years◇
	Oral, delayed-release (enteric-coated)§	• 35 mg once weekly				5 years◇
Zoledronic acid	Intravenous	• 5 mg once every 12 months	Yes	Yes	Yes	3 years
Ibandronate	Oral¶	• 150 mg once monthly	Yes	No	+/-	Limited data
	Intravenous	• 3 mg every 3 months				Limited data

Refer to UpToDate clinical topic reviews for detail on appropriate use of these agents. Dosing in this table is for adult patients with normal kidney function.

* For patients at low risk for fracture in the near future (eg, stable bone density, no previous vertebral or hip fractures), we suggest discontinuing therapy to reduce potential risks of long-term therapy, as there appears to be residual fracture benefit post-treatment.

¶ Most oral bisphosphonates should be taken alone on an empty stomach first thing in the morning with at least 240 mL (8 oz) of water. After administration, the patient should not have food, drink, medications, or supplements and should remain upright for at least one half-hour (alendronate, risedronate) or one hour (ibandronate).

△ The 70 mg dose is also available in an effervescent formulation (dissolved over at least 5 minutes in 4 oz of tap water) and an oral solution (follow administration with at least 2 oz of water).

◇ Based on indirect evidence from the alendronate extension trial.

§ The enteric-coated, delayed-release formulation is taken immediately after breakfast with 4 oz of water.

References:

1. *Black DM, Schwartz AV, Ensrud KE, et al. Effects of continuing or stopping alendronate after 5 years of treatment: the Fracture Intervention Trial Long-term Extension (FLEX): A randomized trial. JAMA 2006; 296:2927.*
2. *Black DM, Reid IR, Boonen S, et al. The effect of 3 versus 6 years of zoledronic acid treatment of osteoporosis: A randomized extension to the HORIZON-Pivotal Fracture Trial (PFT). J Bone Miner Res 2012; 27:243.*

Mecanism de actiune **BP**/ Caracteristici:

- Inhiba FPP – modifica metabolismul osteoclastelor
- In doze de 1000 de ori mai mari inhiba mineralizarea
- T1/2 = 1 h – dar raman in os forever
- Absorbtia in os este direct proportionala cu turnoverul

Mecanism de actiune **Denosumab**/ Caracteristici:

- Anticorp monoclonal – RANKL
- Inhiba formarea osteoclastelor
- Inhiba resorbtia osoasa
- Creste BMD
- Scade riscul de fractura
- Dispare din os la oprirea tratamentului
- Durata tratamentului: 10 ani

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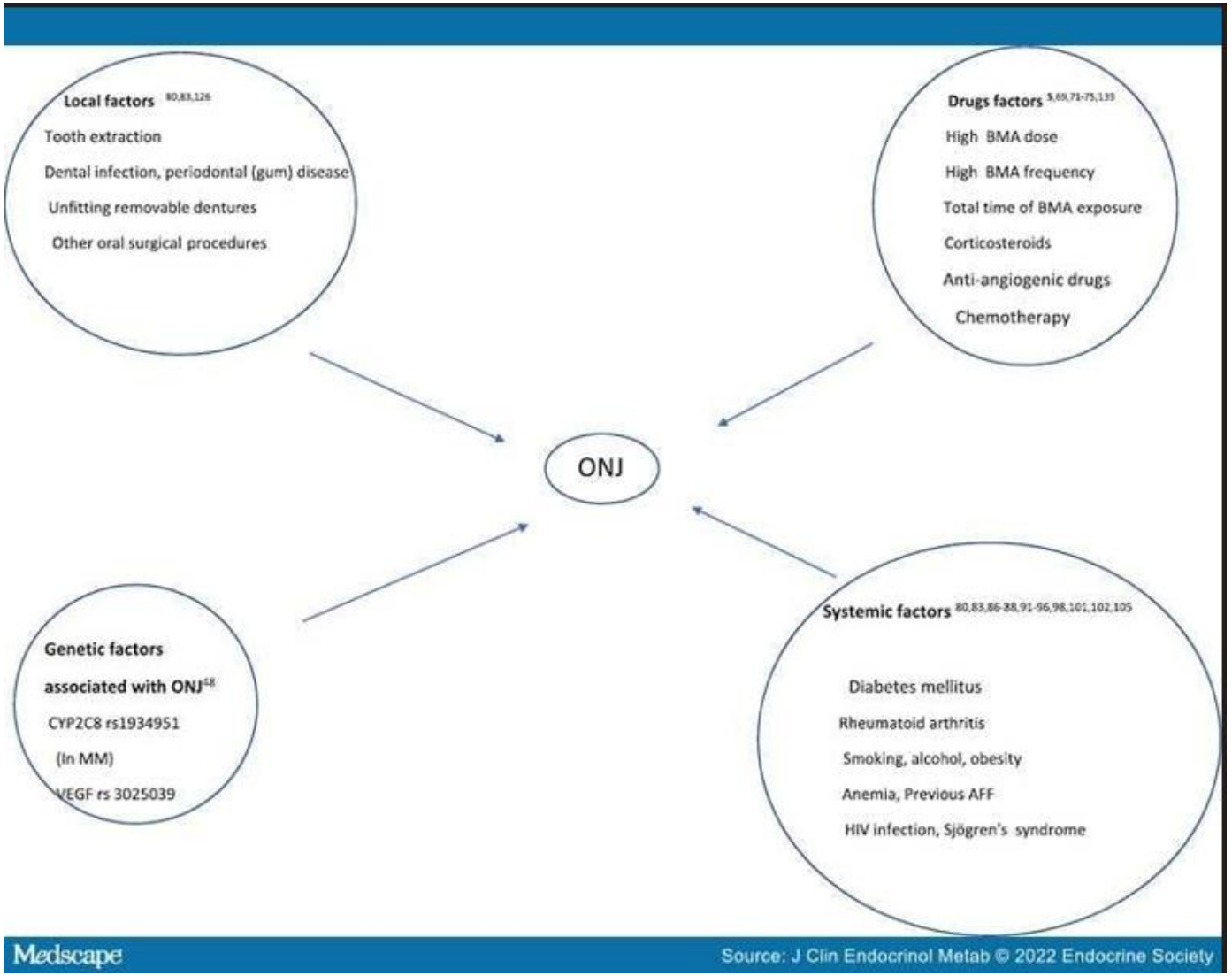

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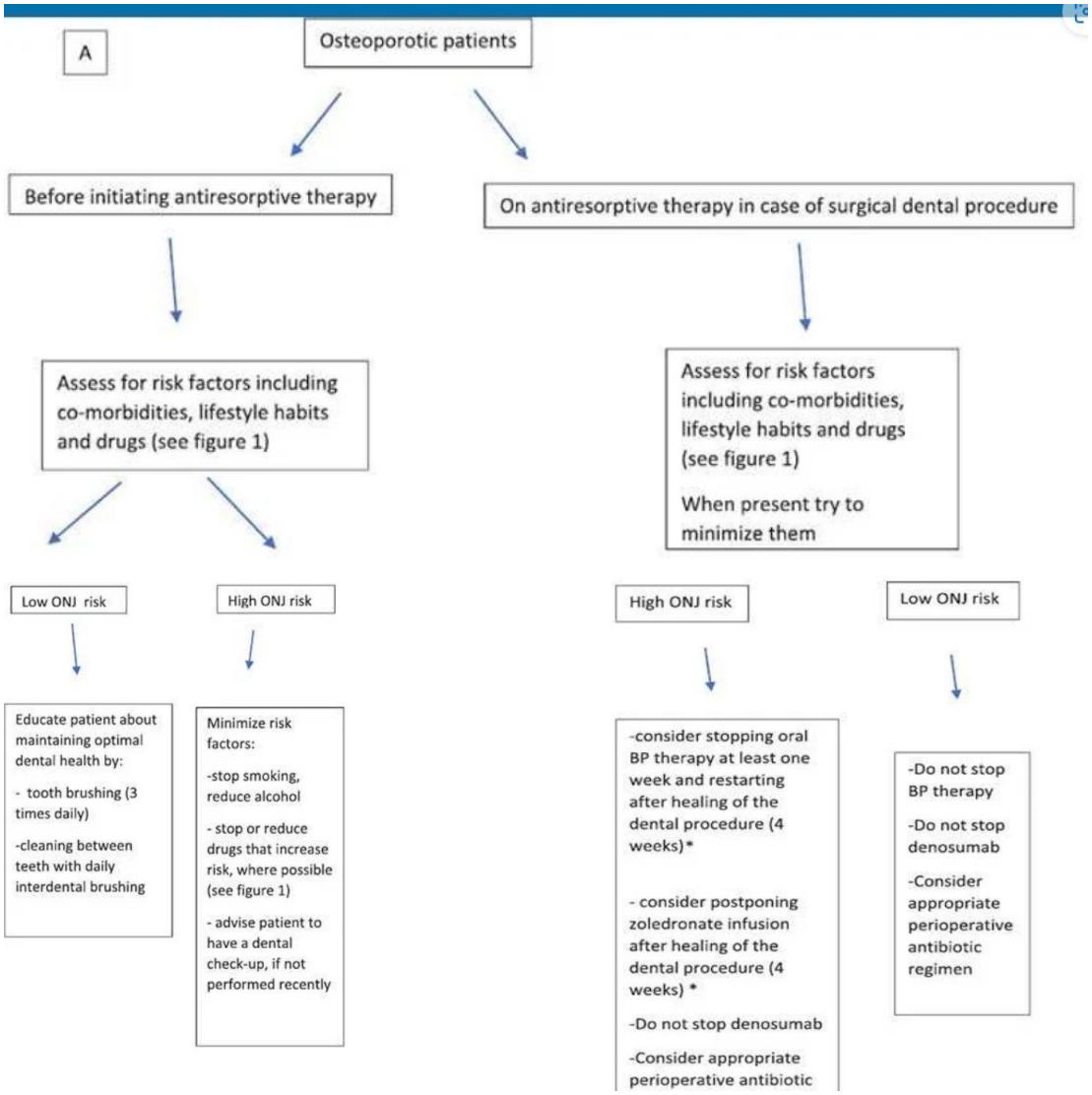

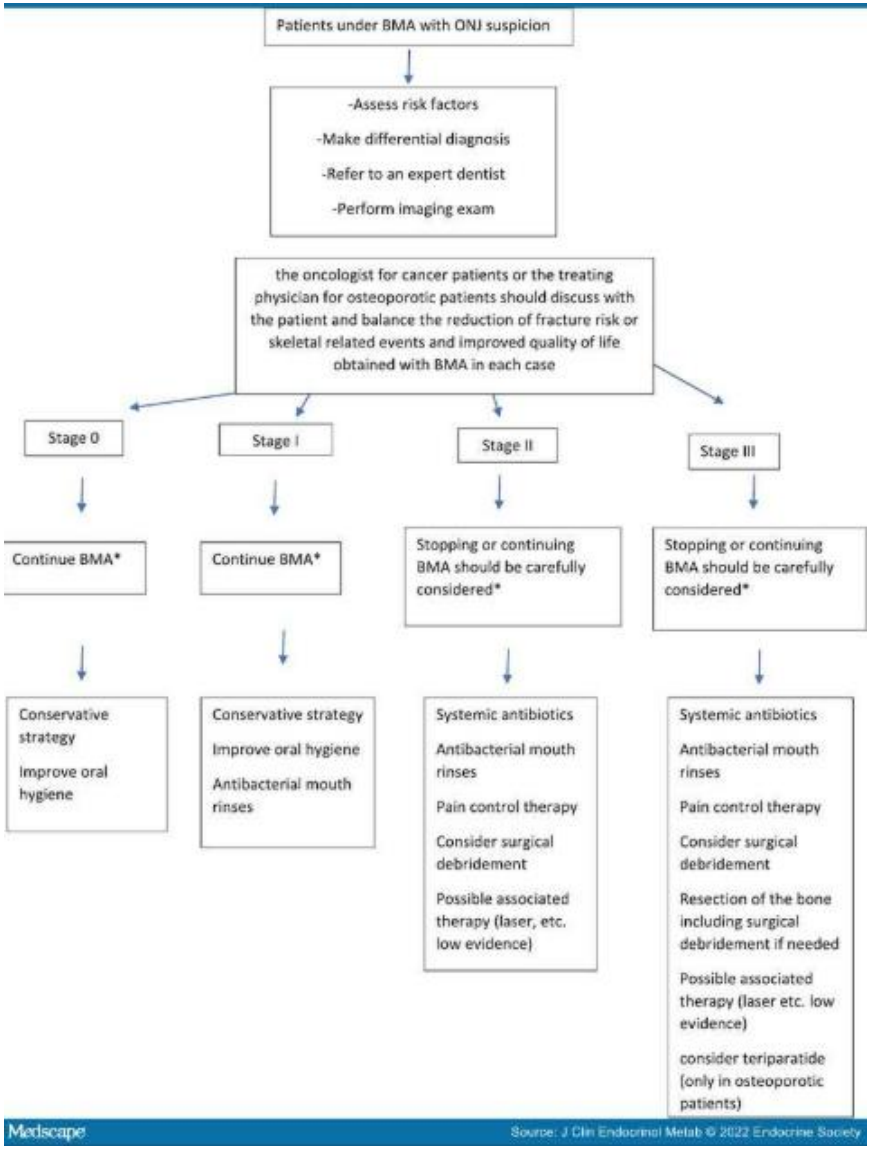
Patients under BMA with ONJ suspicion
-Assess risk factors
-Make differential diagnosis
-Refer to an expert dentist
-Perform imaging exam
the oncologist for cancer patients or the treating physician for osteoporotic patients should discuss with the patient and balance the reduction of fracture risk or skeletal related events and improved quality of life obtained with BMA in each case
Stage 0
Stage I
Stage II
Stage III
Continue BMA*
Continue BMA*
Stopping or continuing BMA should be carefully considered*
Stopping or continuing BMA should be carefully considered*
Conservative strategy
Improve oral hygiene
Conservative strategy
Improve oral hygiene
Antibacterial mouth rinses
Systemic antibiotics
Antibacterial mouth rinses
Pain control therapy
Consider surgical debridement
Possible associated therapy (laser, etc. low evidence)
Systemic antibiotics
Antibacterial mouth rinses
Pain control therapy
Consider surgical debridement
Resection of the bone including surgical debridement if needed
Possible associated therapy (laser etc. low evidence)
consider teriparatide (only in osteoporotic patients)
Medscape
Source: J Clin Endocrinol Metab © 2022 Endocrine Society

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Punctul de Vedere al Endocrinologului

Staging and treatment of medication-related osteonecrosis of the jaw (MRONJ)

MRONJ* staging	Treatment strategies¶
At risk: No apparent necrotic bone in patients who have been treated with either oral or intravenous bone-modifying agents	• No treatment indicated • Patient education and reduction of modifiable risk factors
Stage 0 (Increased risk): No clinical evidence of necrotic bone, but nonspecific clinical findings, radiographic changes, and symptoms	• Systemic management, including the use of pain medication, and close scrutiny and follow-up • Refer to dental specialist and follow up every 8 weeks with communication of lesion status to the oncologist • Patient education and reduction of modifiable risk factors
Stage 1: Exposed and necrotic bone, or fistulas that probe to bone in patients who are asymptomatic and have no evidence of infection	• Antibacterial mouth rinse • Clinical follow-up on an every-8-week basis by a dental specialist with communication of lesion status to the oncologist • Patient education and reduction of modifiable risk factors
Stage 2: Exposed and necrotic bone or fistulas that probe to bone, associated with infection as evidenced by pain and erythema in the region of the exposed bone with or without purulent drainage	• Symptomatic treatment with oral antibiotics and topical antibacterial rinse • Pain control • Debridement to relieve soft tissue irritation and infection control • Clinical follow-up on an every-8-week basis by a dental specialist with communication of lesion status to the oncologist • Patient education and reduction of modifiable risk factors
Stage 3: Exposed and necrotic bone or a fistula that probes to bone in a patient with pain, infection, and one or more of the following: exposed and necrotic bone extending beyond the region of alveolar bone (ie, inferior border and ramus in mandible maxillary sinus, and zygoma in the maxilla), resulting in pathologic fracture, extraoral fistula, oral antral or oral nasal communication, or osteolysis extending to the inferior border of the mandible or sinus floor	• Symptomatic treatment with oral antibiotics and topical antibacterial rinse • Pain control • Surgical debridement or resection for long-term palliation of infection and pain • Clinical follow-up on an every-8-week basis by a dental specialist with communication of lesion status to the oncologist • Patient education and reduction of modifiable risk factors

* Exposed or probable exposed bone in the maxillofacial region without resolution for greater than 8 weeks in patients treated with an antiresorptive and/or an antiangiogenic agent who have not received radiation therapy to the jaws.

¶ Regardless of the disease stage, mobile segments of bony sequestrum should be removed without exposing uninvolved bone. The extraction of symptomatic teeth within exposed, necrotic bone should be considered since it is unlikely that the extraction will exacerbate the established necrotic process.

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Take away message

- **Multiple sindroame genetice asociaza modificari dentare si tulburari endocrine ce afecteaza cresterea si dezvoltarea normala a copiilor**
- **Desi, in diagnosticarea tulburarilor endocrine la copii examinarea dentara nu este prioritara, identificarea precoce a anomaliilor de eruptie numar si structura pot facilita algoritmul de diagnostic**

- **La randul ei, patologia dentoalveolara poate afecta sau decompensa o patologie tiroidiana, suprarenala, diabet zaharat, etc**
- **Anumite boli endocrine produc prin propriile mecanisme patogenice, prin complicatii sau orin tratament, modificari la nivelul dentitiei si cavitatii bucale**

- **Osteoporoza netratata poate ucide dar si complicatiile dentare datorate tratamentelor ei, pot avea implicatii severe**
- **Scopul nostru este sa ne tratam correct pacientii cu minim de reactii adverse**

- **Consider utila colaborarea Stomatolog – Endocrinolog in dublu sens!!!**

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