

Znanost
na cesti



19. oktober 2016 ob 19h, Kavarna
Union

Parodontalna bolezen: od mikrobnega neravnovesja do sistemskega vnetja

doc. dr. Rok Gašperšič, Medicinska fakulteta
Maja Ratej, Val 202



DISCOVERY!

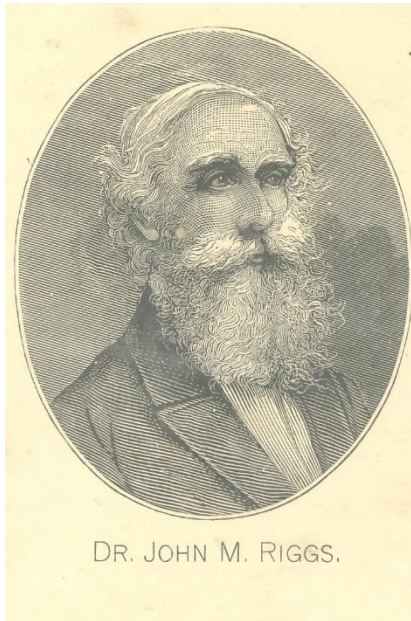
Martin Taubman, Editor

W.J. Maloney

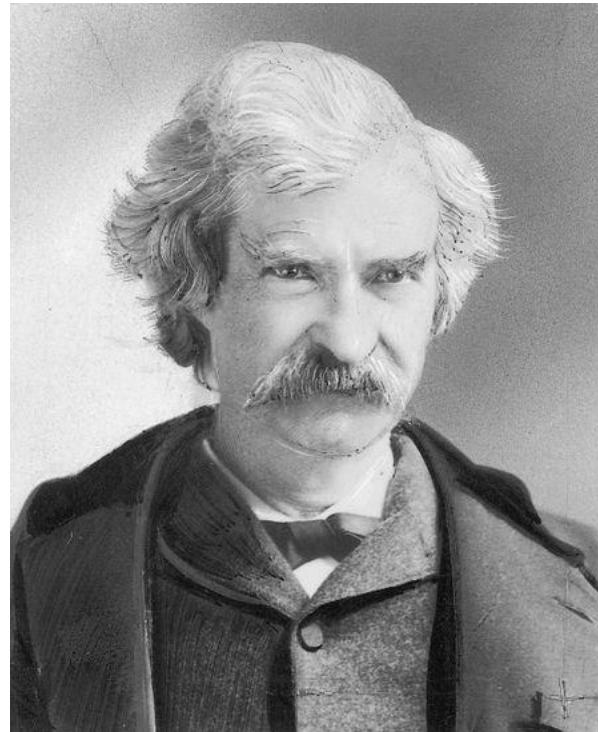
Cariology and Comprehensive Care, NYU College of Dentistry, 345 E. 24th Street, New York, NY 10010, USA; wjm10@nyu.edu

J Dent Res 89(7):676-678, 2010

A Periodontal Case Report by Dr. S.L. Clemens



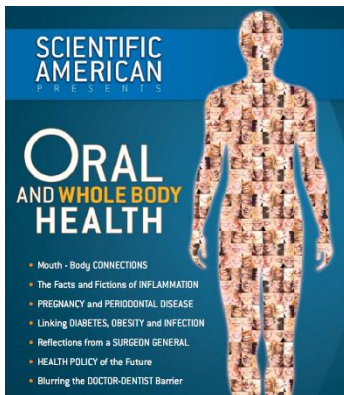
DR. JOHN M. RIGGS.



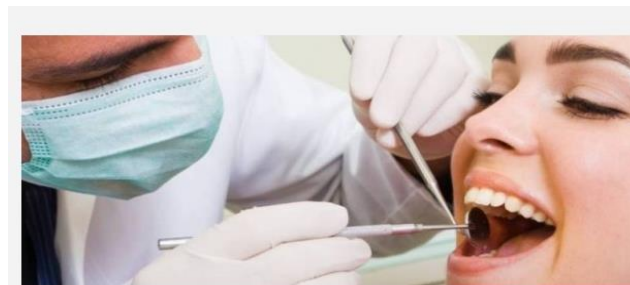
Mark Twain 1835 -1910

- Gingivitis, parodontitis
- Bakterije in vnetje
- Obzobni žepi, propad čeljustne kosti
- Večja možnost srčnega infarkta, možganske kapi, diabetesa, zapletov nosečnosti,...

- Gingivitis, parodontitis
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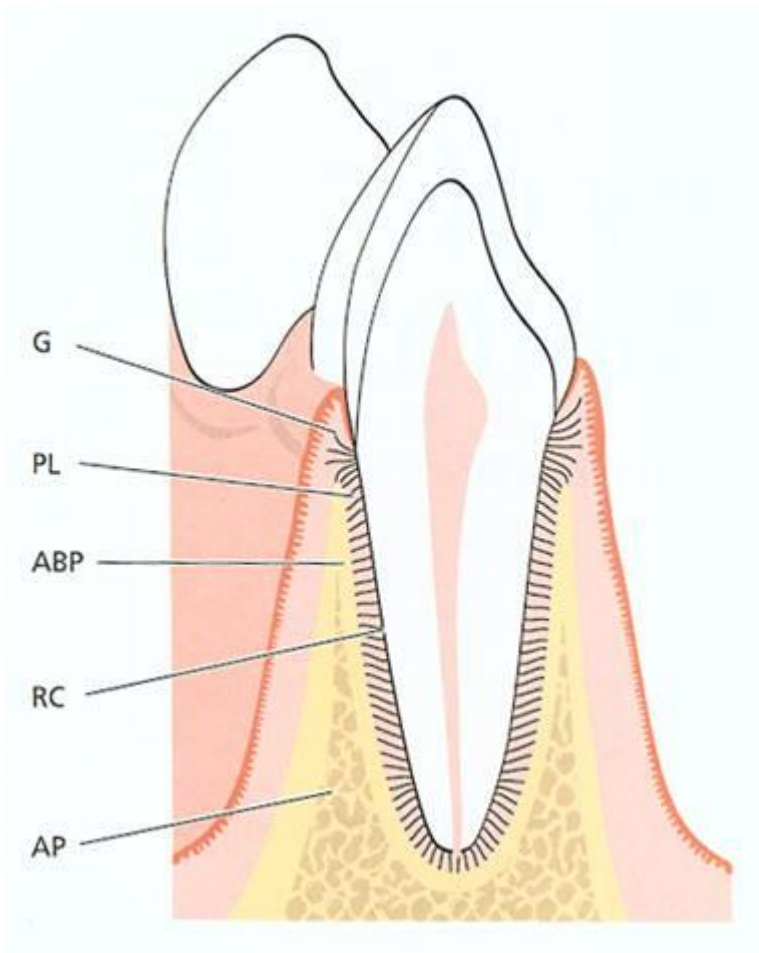
2006



Parodontalna bolezen – tihi ubijalec

2016

Obzobna tkiva



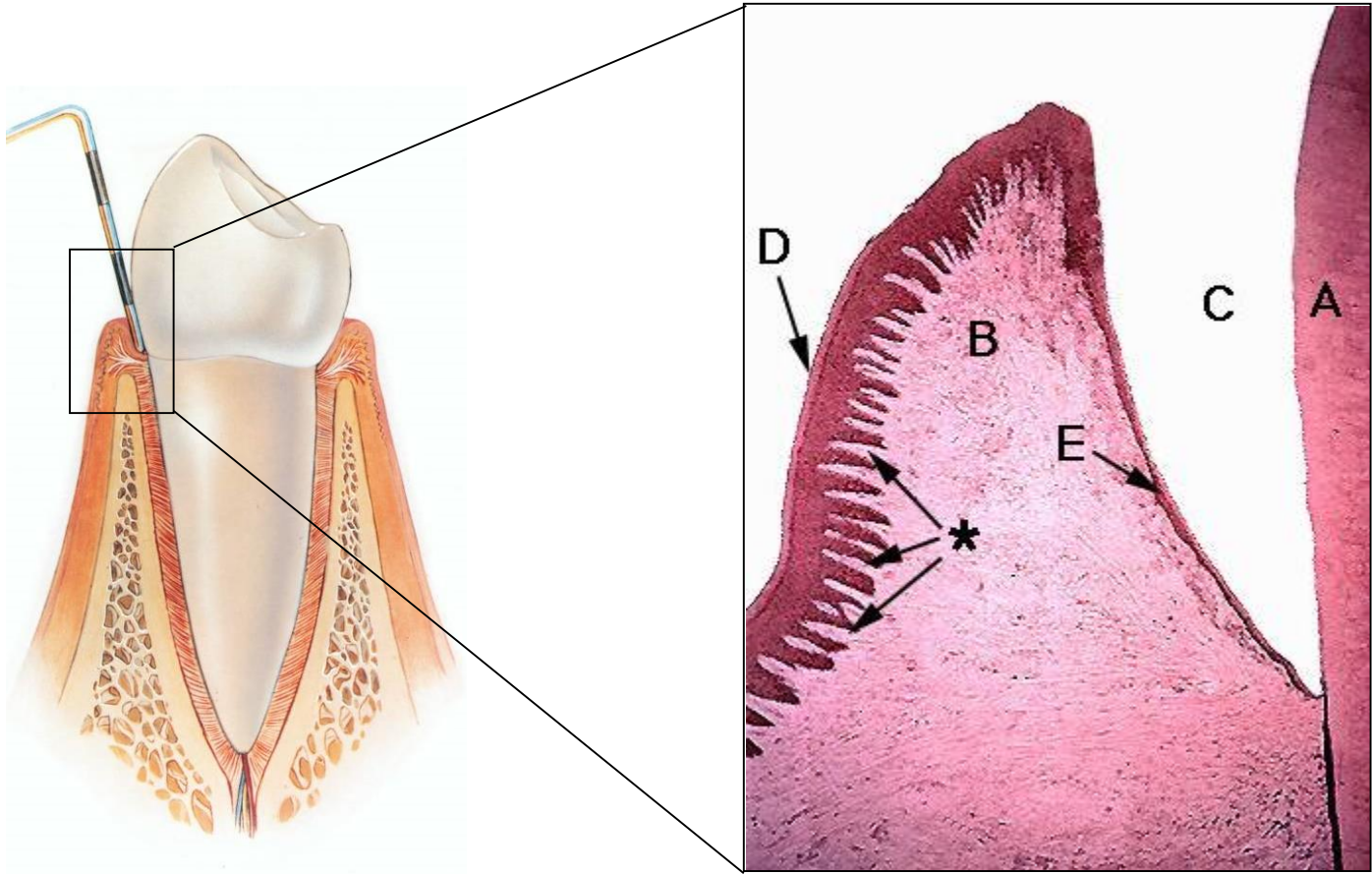
- ❑ Dlesen (G)
- ❑ Pozobnica (PL)
- ❑ Koreninski cement (RC)
- ❑ Alveolarna kost (ABP)

- Parodoncij = obzobna tkiva
- Parodontalna bolezen = bolezen obzobnih tkiv

Zdrava obzobna tkiva



Prerez dlesni – shema in slika



Različne vrste in debelina epitelijev

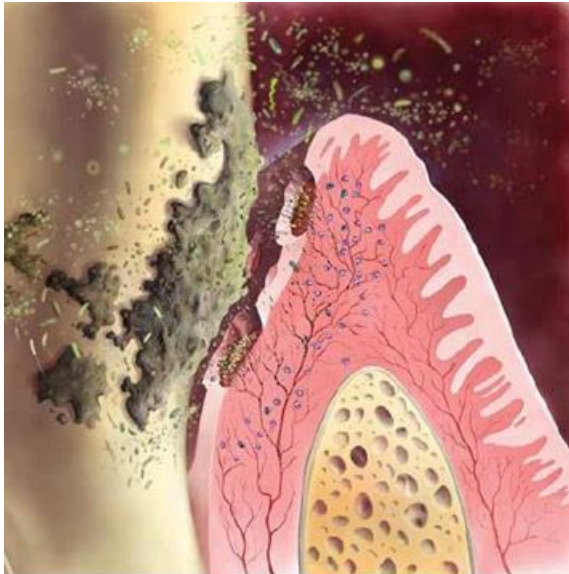
Vnetje dlesni - gingivitis



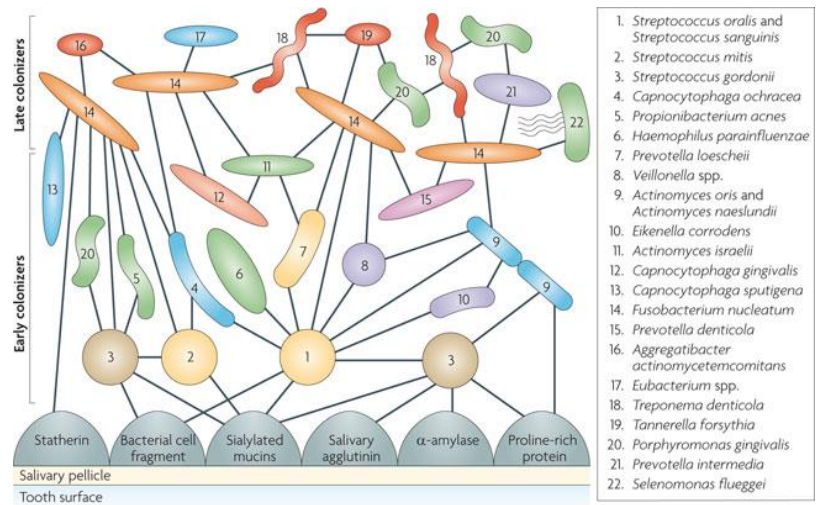
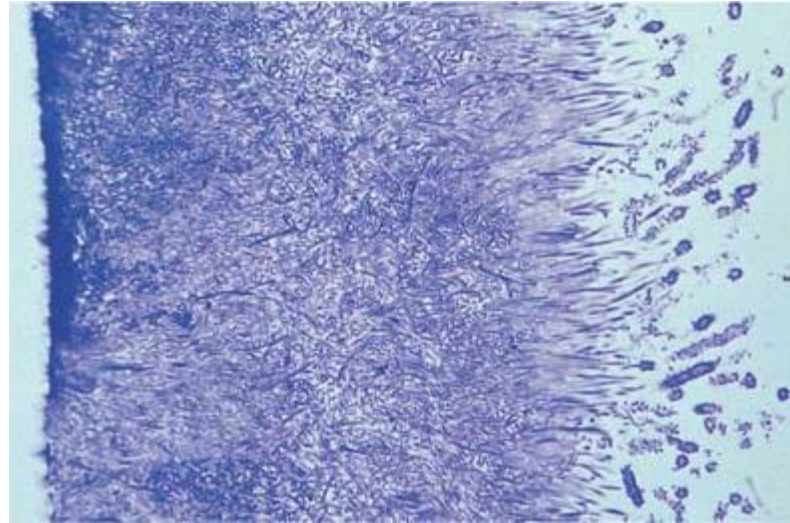
Bakterijske zobne obloge



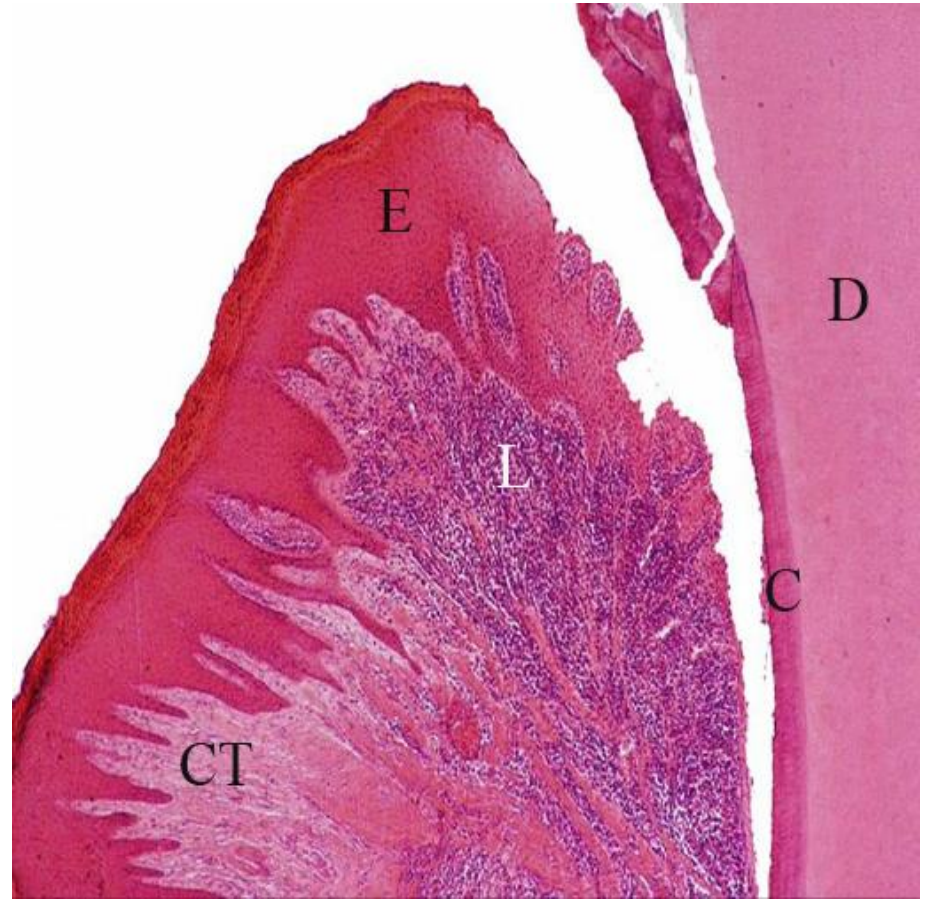
Vzrok gingivitisa



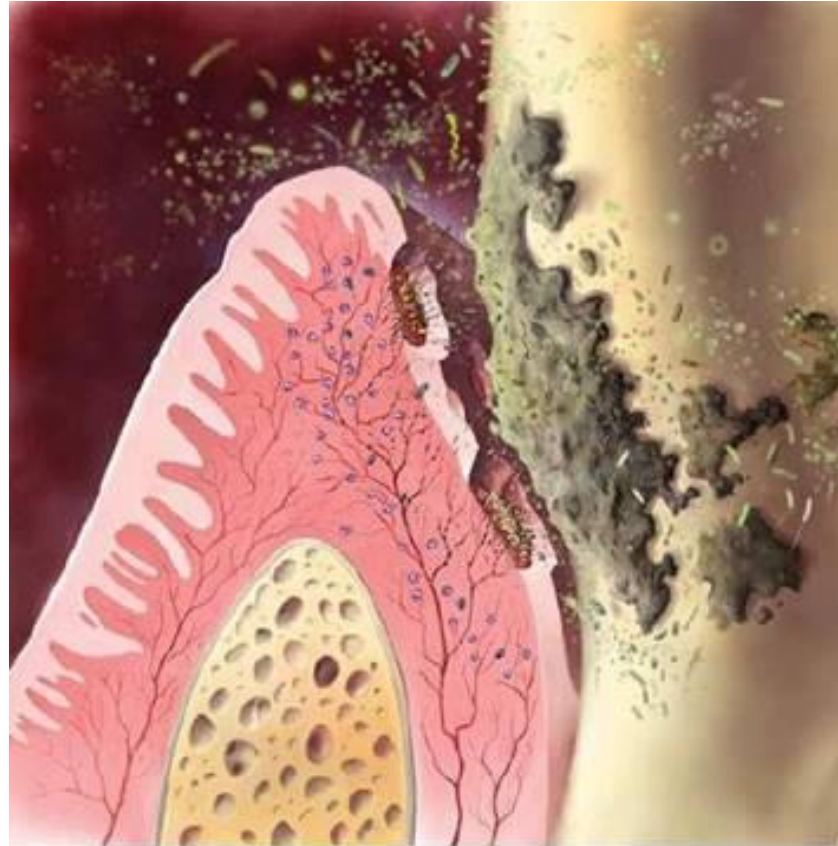
biofilm = **plak**



Gingivitis = vnetje

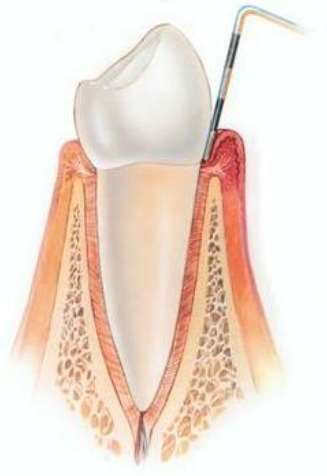


Gingivitis



vnetje in bakterije v ravnovesju

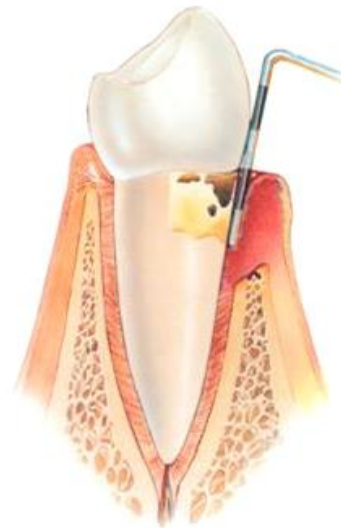
Gingivitis (vnetje)



Začetna stopnja



Zmerna stopnja

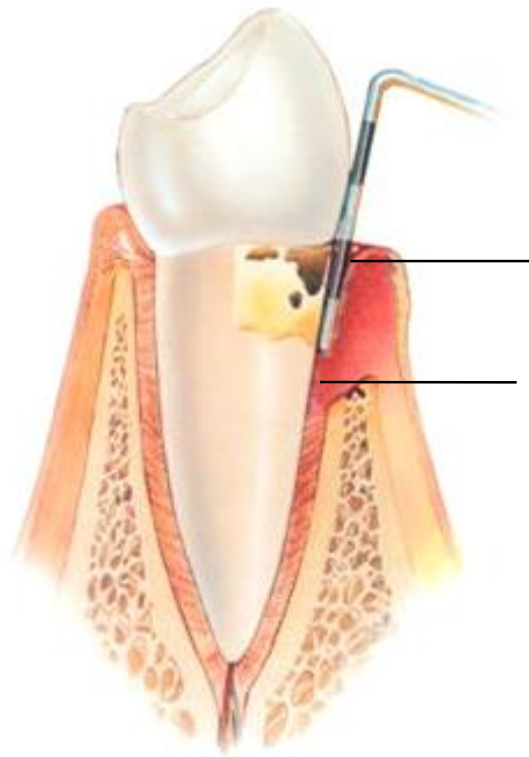


Napredovana stopnja



Parodontitis (vnetje in razgradnja)

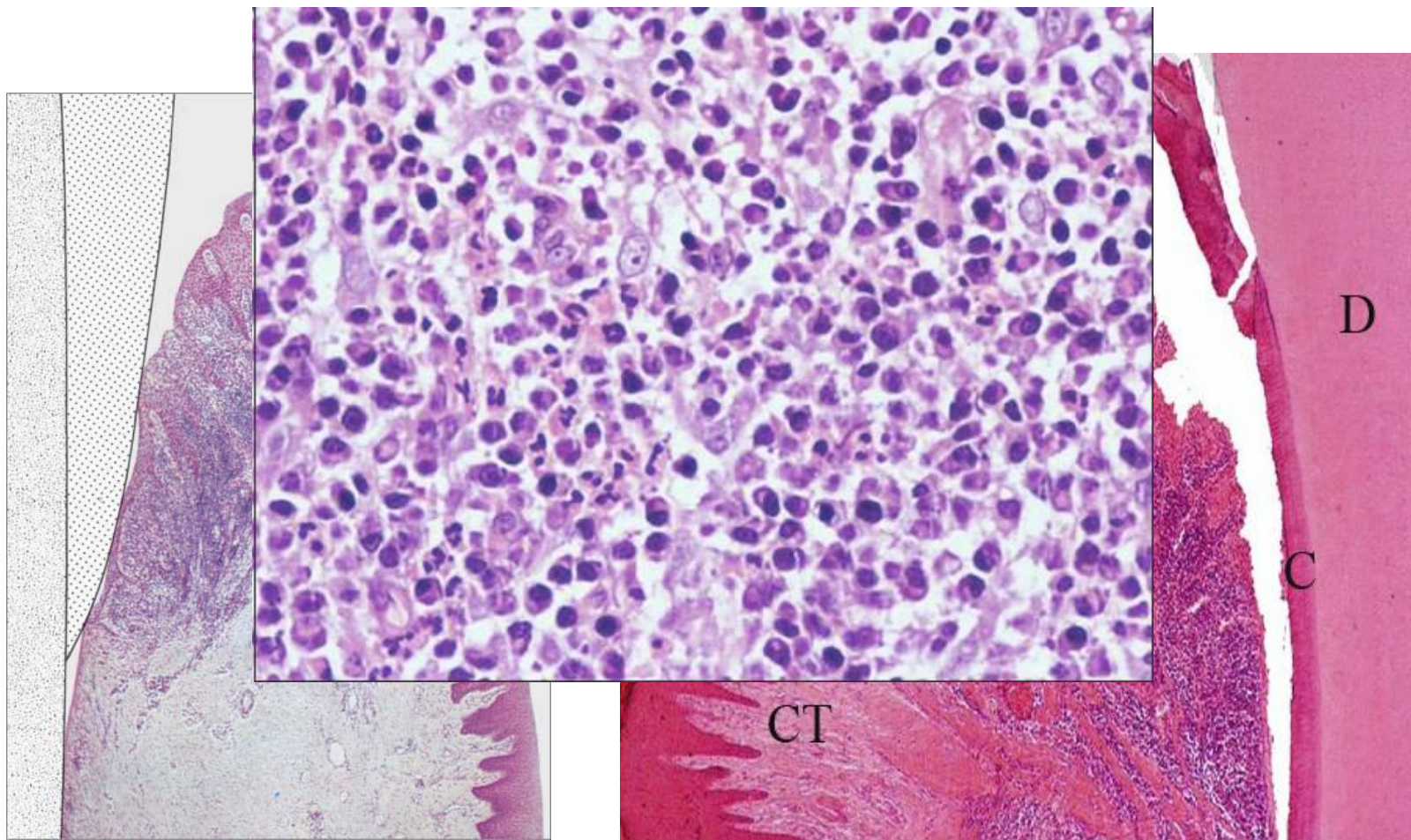




žep

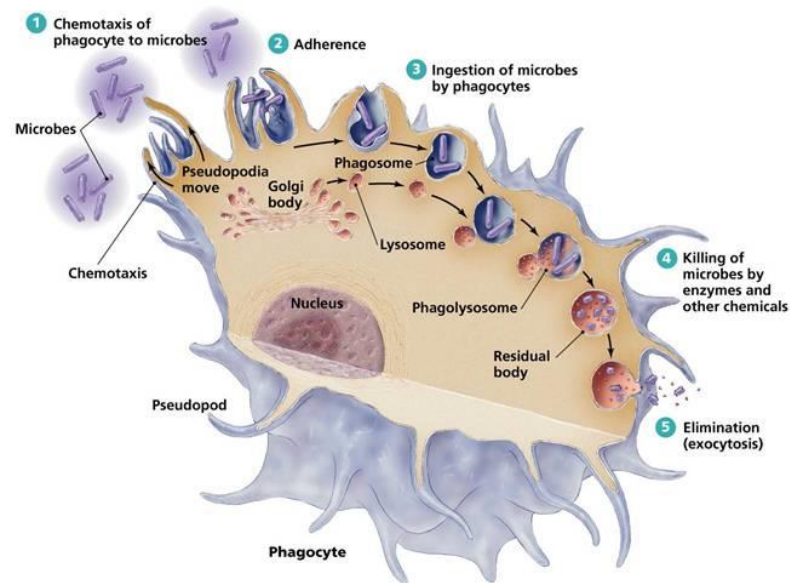
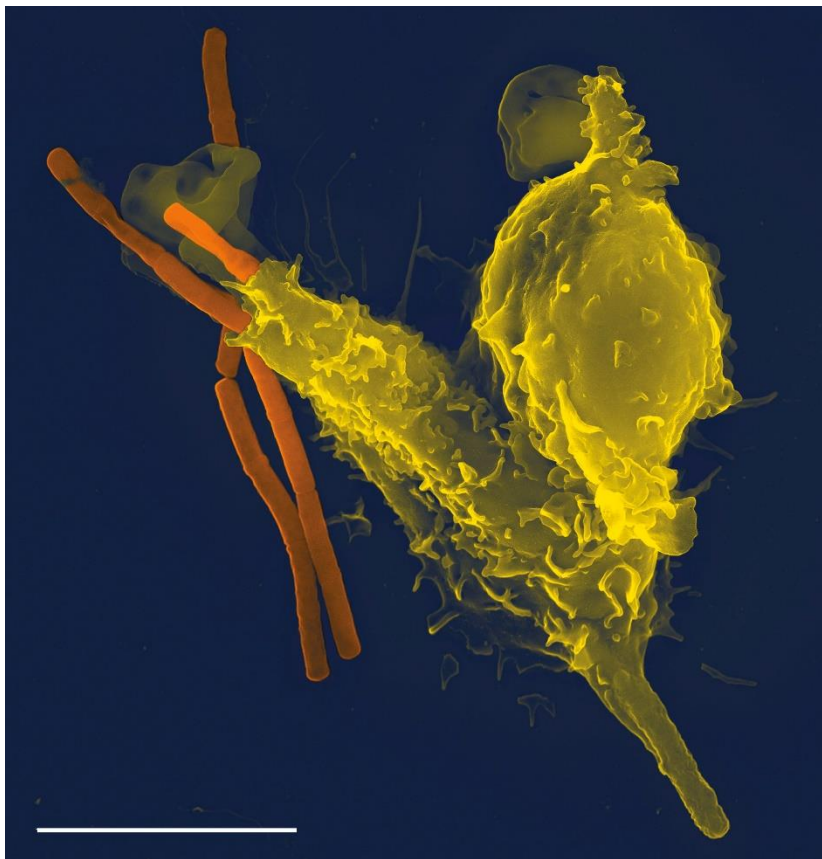


razgradnja kosti



Spremenjen vnetno imunološki odziv

Fagociti – znotrajcelična presnova (gingivitis)



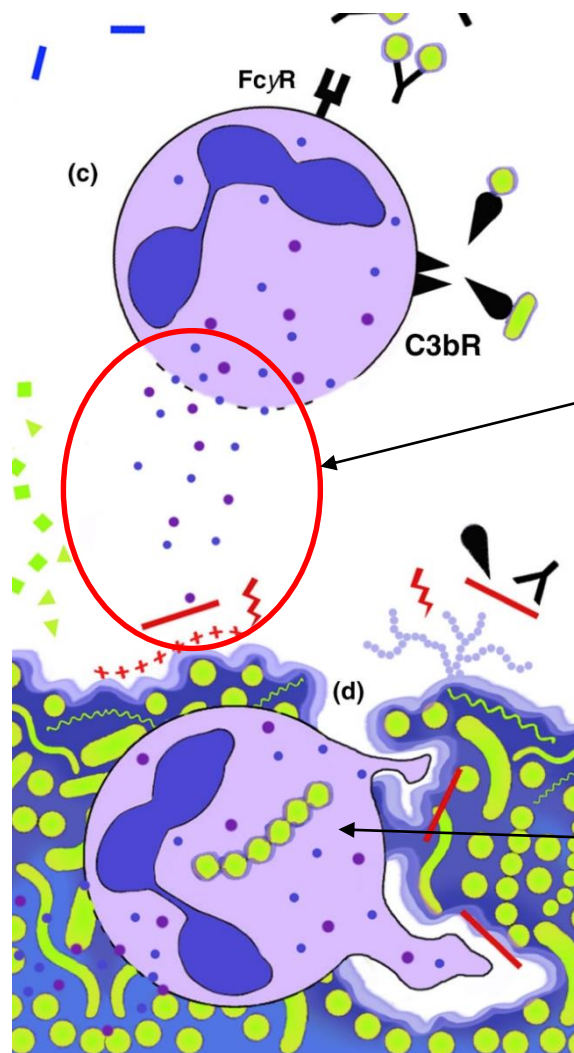
Fagociti – zunajcelična presnova (parodontitis)

Fagociti v tkivu

Izločeni encimi

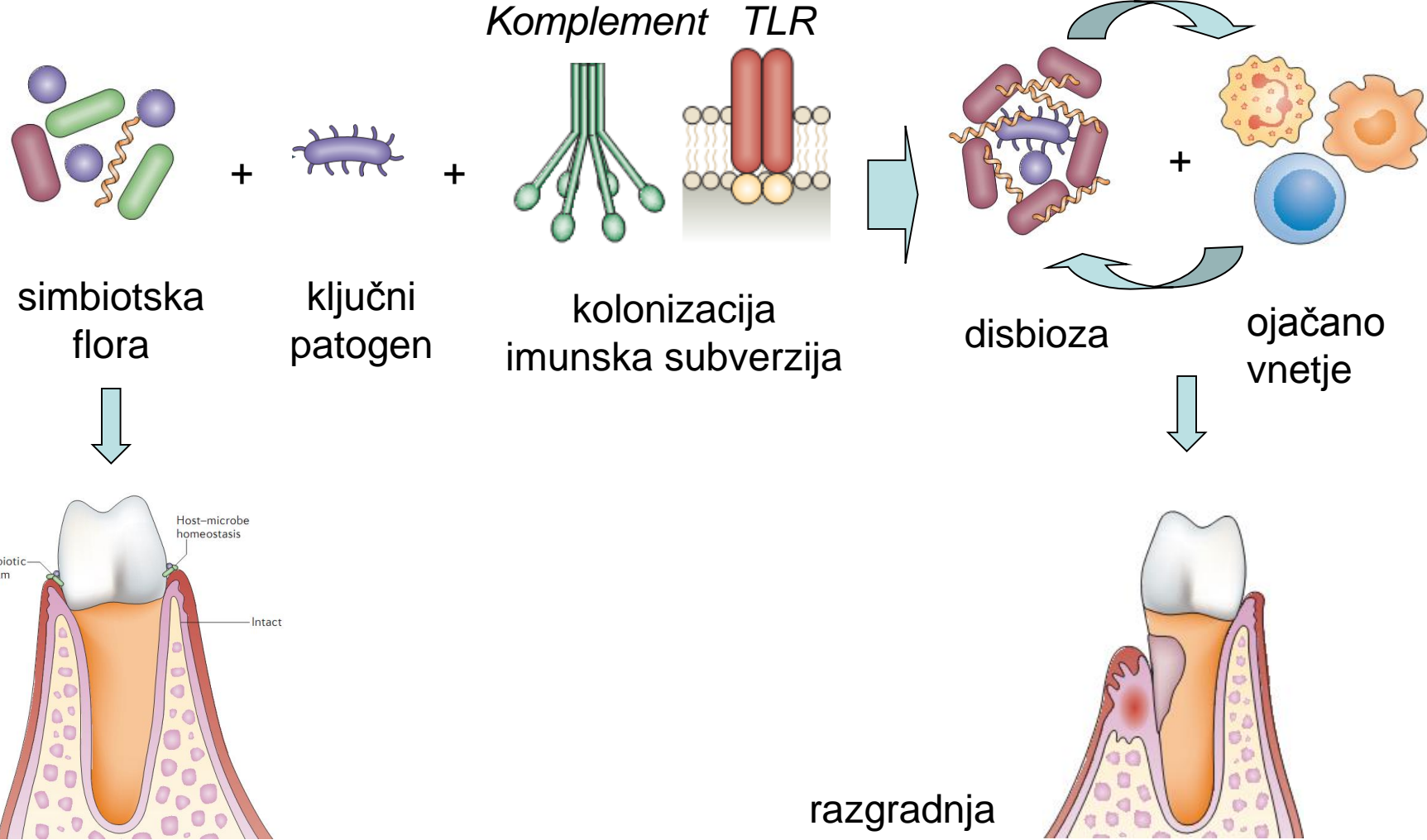
Biofilm bakterij

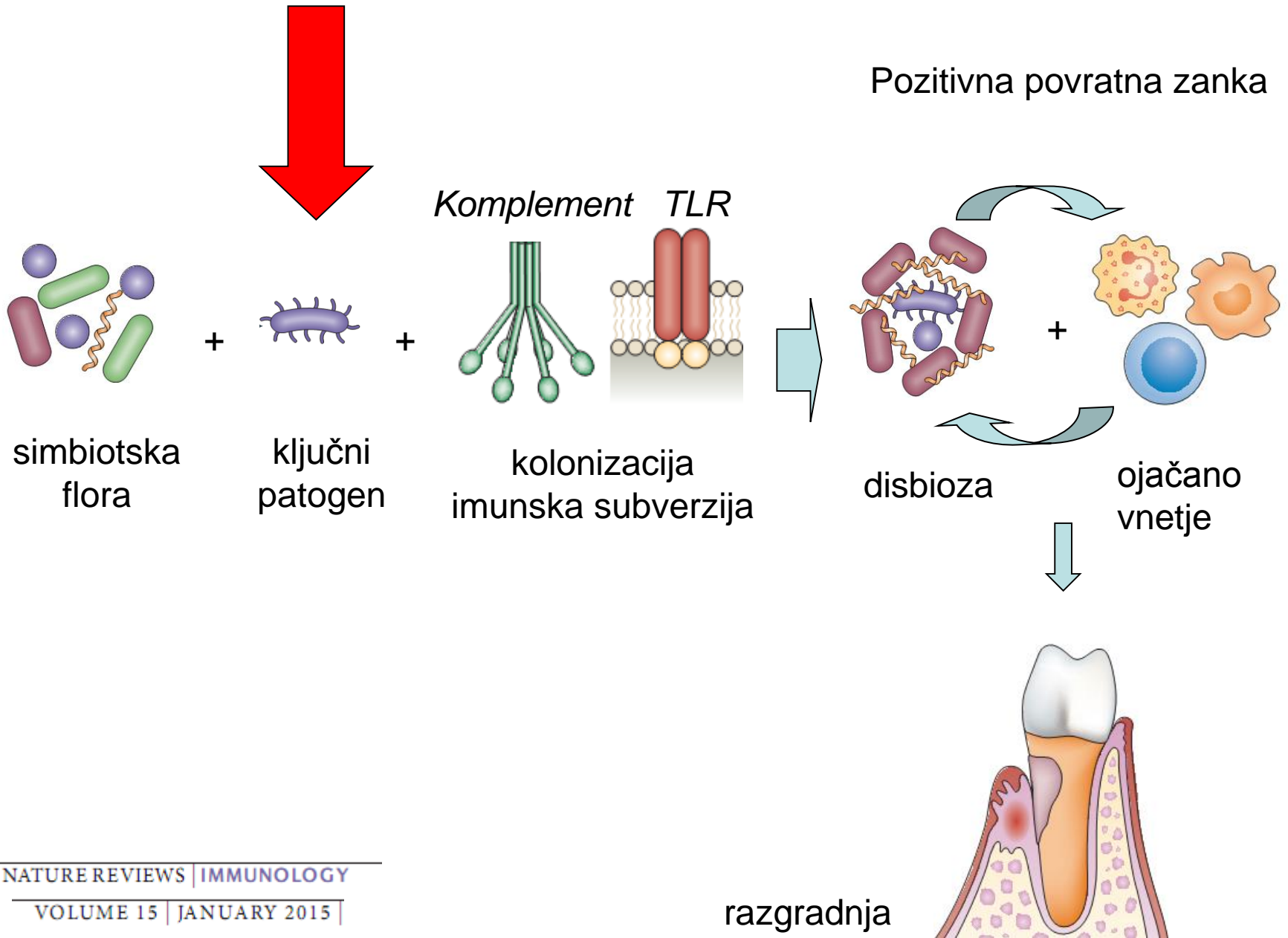
Bakterije preživijo znotraj fagocitov

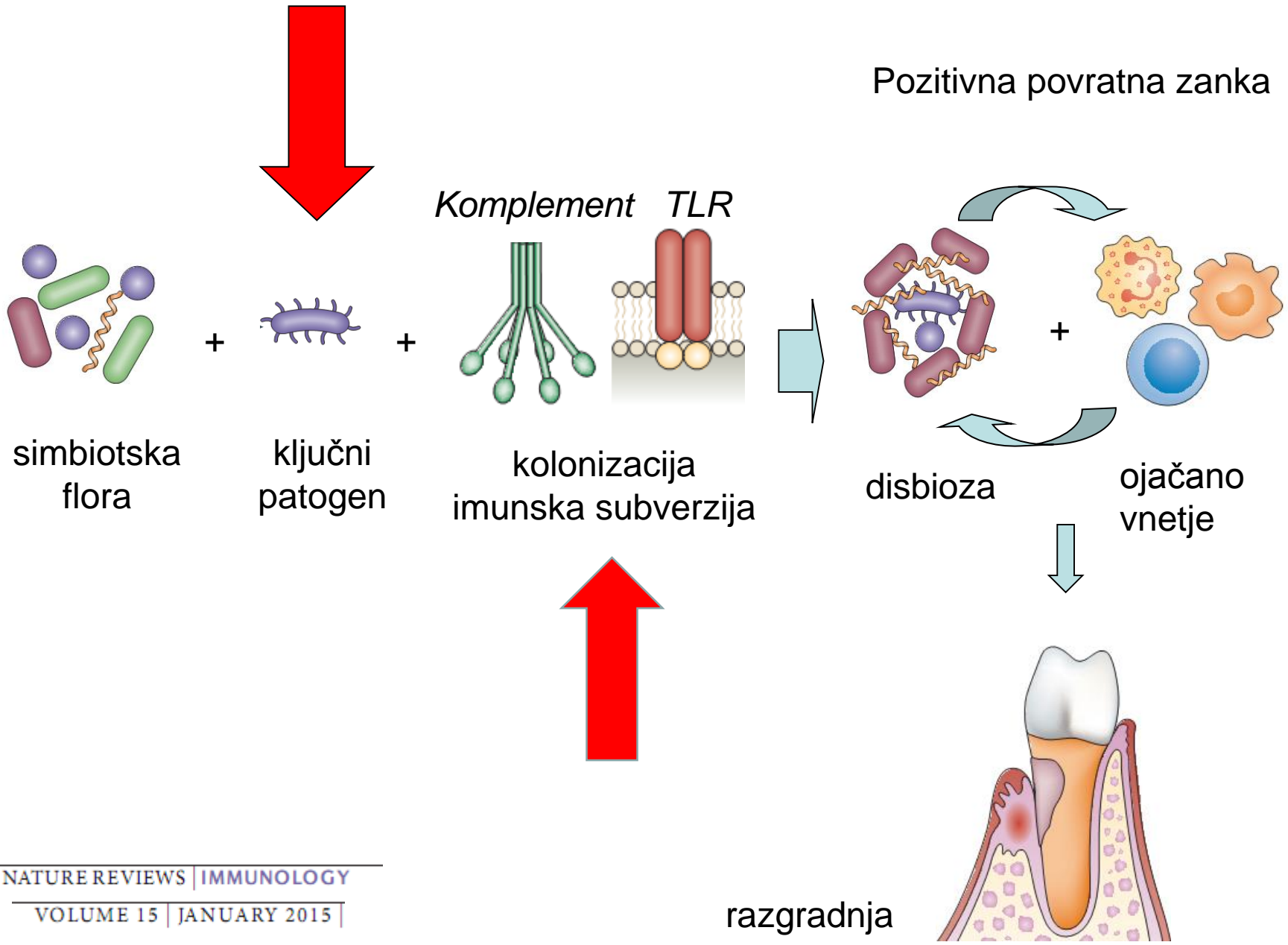


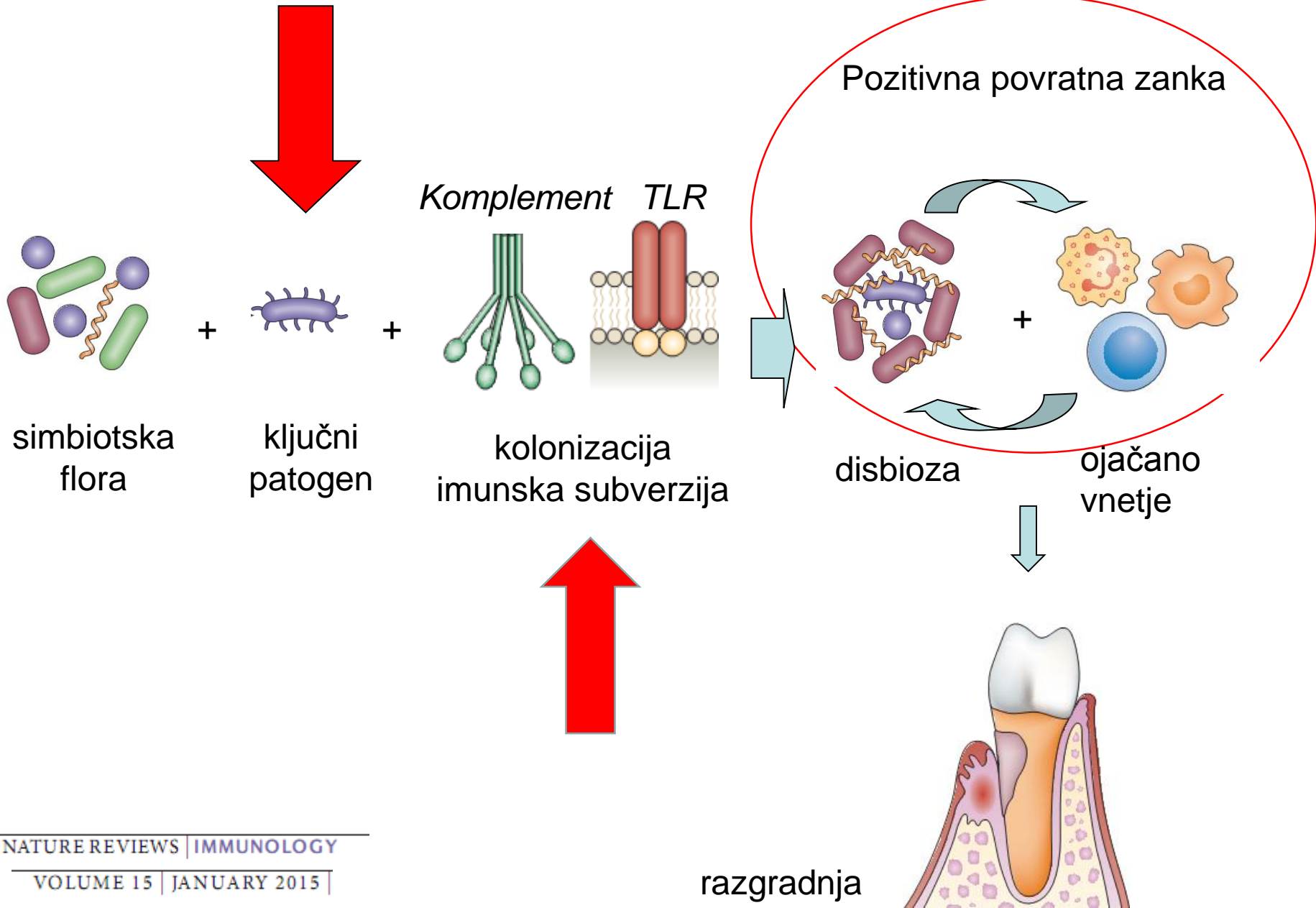


Pozitivna povratna zanka





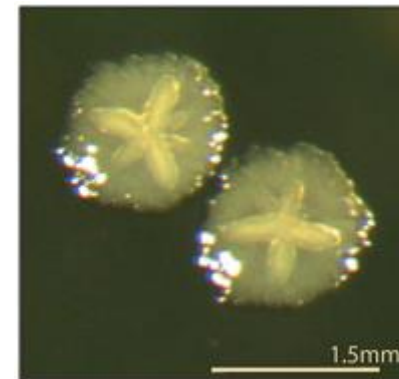
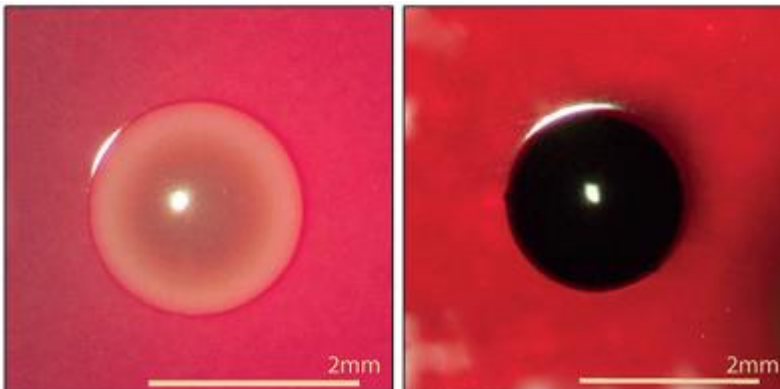




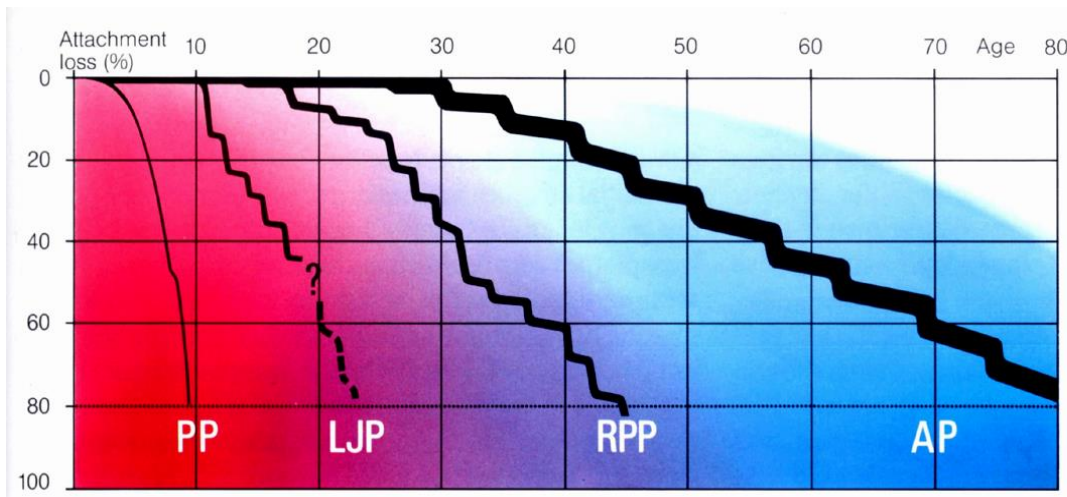
Ključni parodontalni patogeni

– *Porphyromonas gingivalis*
(PG)

• *Aggregatibacter
actinomycetemcomitans*
(AA)



Različna hitrost napredovanja



171 Forms of periodontitis – Clinical course

AP – Adult Periodontitis, slowly progressive periodontitis of adults

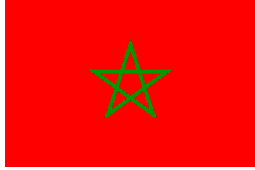
RPP – Rapidly Progressive Periodontitis, aggressive form of periodontitis seen in young adults

LJP – Localized Juvenile Periodontitis, a highly localized and rapidly progressing form of disease in young persons

PP – Pre-pubertal Periodontitis, rapidly progressing periodontitis in pre-pubertal individuals

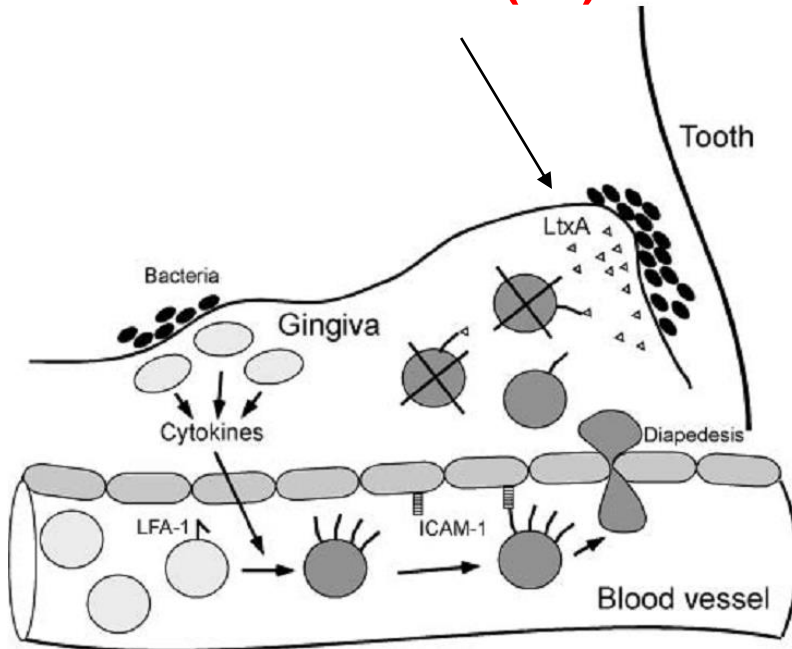
Agresivne oblike

Kronične oblike

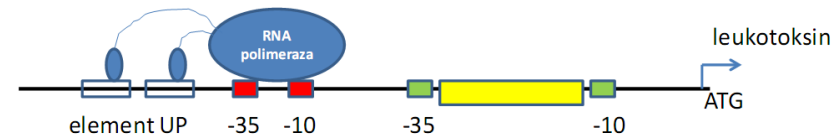


AA in agresivni parodontitis

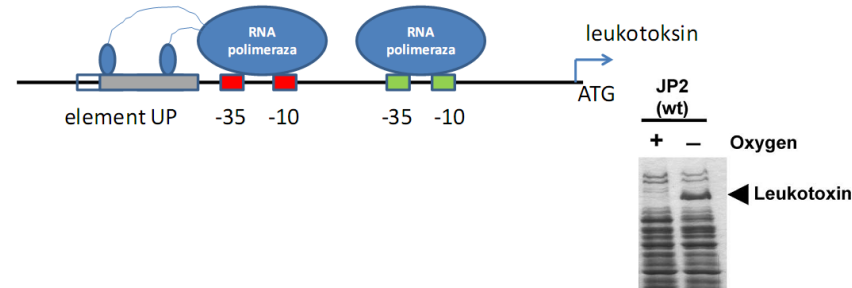
LEVKOTOKSIN (ltx)



Sev 652 – minimalno levkotoksičen



Sev JP2 - hiperlevkotoksičen





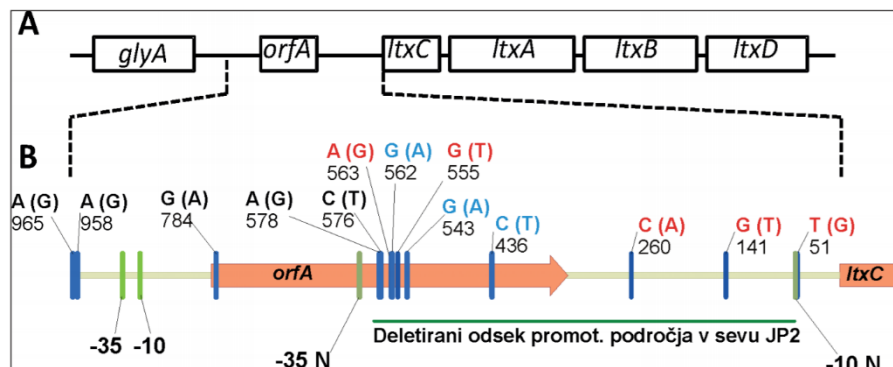
Prisotnost genov, pomembnih za virulenco AAC

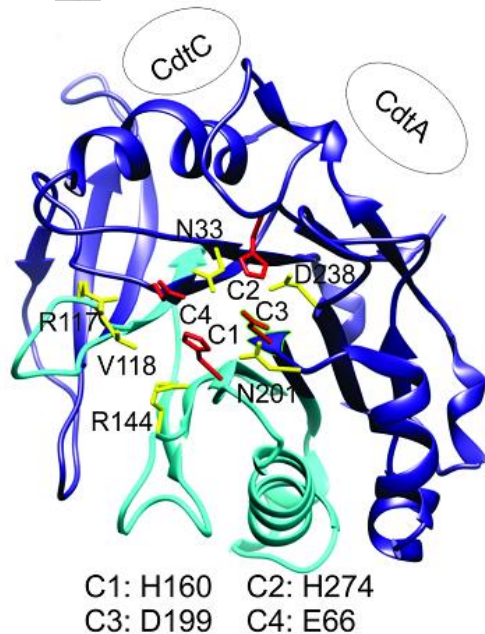
Preglednica 1: Serotipizacija in prisotnost testiranih genov, pomembnih za virulenco *A. actinomycetem-comitans*, pri izolatih slovenskih bolnikov z zmernim ali napredujočim kroničnim parodontitisom.

Bolnik	Serotip	<i>ltxA</i>	<i>apaH</i>	<i>flp-1</i>	<i>cdtA</i>	<i>cdtB</i>	<i>cdtC</i>
1	B	+	+	+	+	+	+
2	C	+	+	+	+	+	+
3	C	+	+	+	+	+	+
4	C	+	+	+	+	+a	+
9	C	+	-	+	+	+	+
16	C	+	-	+	+	+a	+
18	B	+	+	+	+	+	+
20	C	+	+	+	+	+	+
22	C	+	+	+	+	+	+
25	B	+	+	+	+	+	+
31	C	+	+	+	+	+	+
32	C	+	+	+	+	+	+
34	A	+	+	+	+	+	+
35	B	+	+	+	+	+	+
36	Nd	+	+	+	+	+	+

ltxA: levkotoksin A, *apaH*: protein za invazijo, *flp-1*: poglavitni protein fimbrij, *cdtA*, *cdtB*, *cdtC*: podenota A, B in C toksina

Genetska karakterizacija levkotoksinskega gena sevov AA





RESEARCH ARTICLE

A Cytolethal Distending Toxin Variant from *Aggregatibacter actinomycetemcomitans* with an Aberrant CdtB That Lacks the Conserved Catalytic Histidine 160

Davor Obradović¹, Rok Gašperšič², Simon Caserman³, Adrijana Leonardi⁴, Maja Jamnik³, Zdravko Podlesek¹, Katja Seme⁵, Gregor Anderluh³, Igor Križaj^{4,6}, Peter Maček^{1*}, Matej Butala^{1*}

1 Department of Biology, Biotechnical Faculty, University of Ljubljana, Ljubljana, Slovenia, 2 Department of Oral Medicine and Periodontology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, 3 Laboratory for Molecular Biology and Nanobiotechnology, National Institute of Chemistry, Ljubljana, Slovenia, 4 Department of Molecular and Biomedical Sciences, Jožef Stefan Institute, Ljubljana, Slovenia, 5 Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, 6 Department of Chemistry and Biochemistry, Faculty of Chemistry and Chemical Technology, University of Ljubljana, Ljubljana, Slovenia



Bakterije ↔ Vnetno-imunološki odziv

Različna hitrost napredovanja

Kajenje



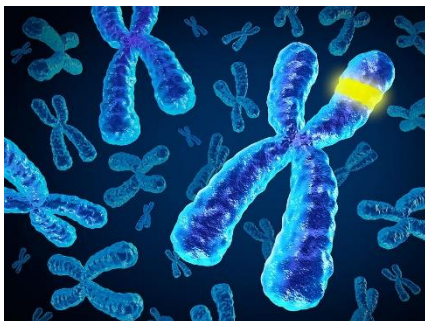
Stres



Bakterije



Vnetno-immunološki odziv



Genetski faktorji



Sistemske faktorji

Povezava s sistemskim zdravjem

1. Spremembe v telesu, ki vplivajo na obzobna tkiva (nosečnost, diabetes, zdravila)
2. Dejavniki, ki sočasno vplivajo na ustno votlino in druga področja telesa (kajenje, starost)
3. PB vpliva na potek bolezni na drugih področjih

Povezava s sistemskim zdravjem

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3. PB vpliva na potek bolezni na drugih področjih

Bakterije

Vnetje

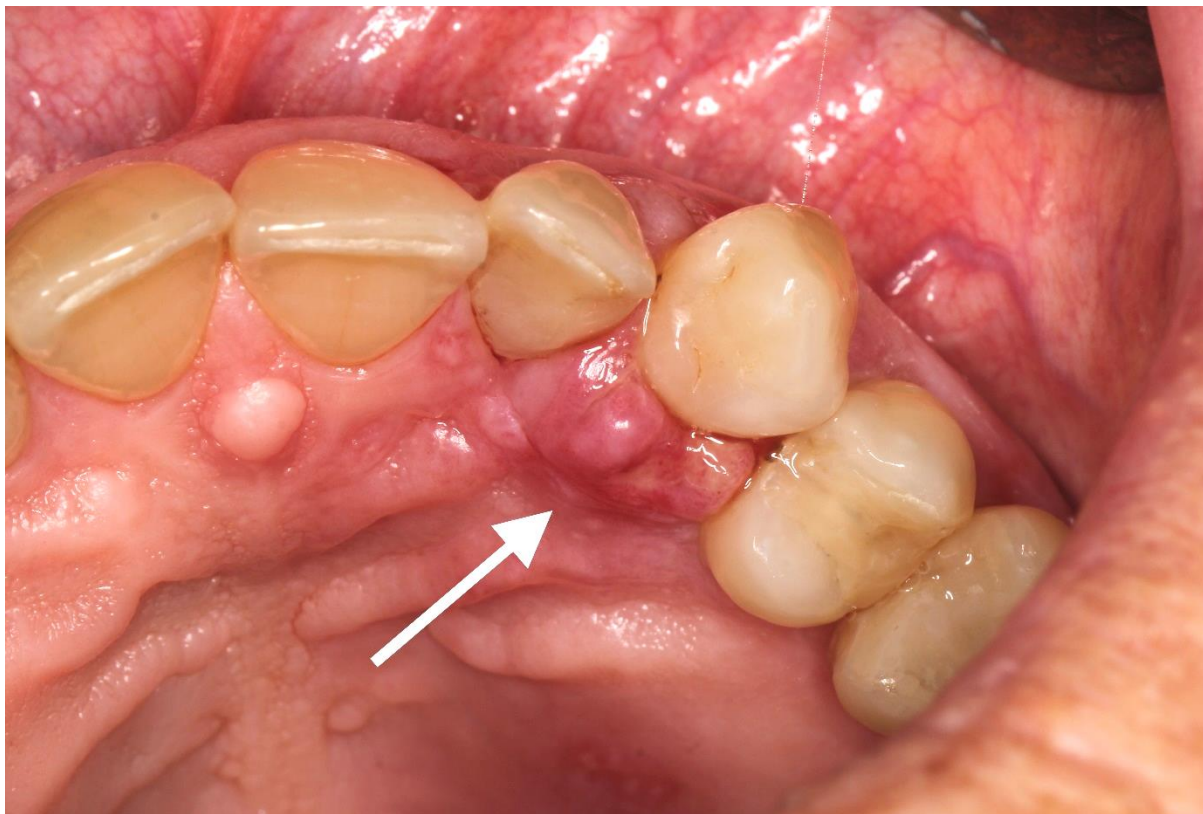


Spremembe v telesu, ki vplivajo na obzobna tkiva



Nosečnost

Spremembe v telesu, ki vplivajo na obzobna tkiva



**Nosečnost –
granulom dlesni**

Spremembe v telesu, ki vplivajo na obzobna tkiva



22 let

Diabetes

Spremembe v telesu, ki vplivajo na obzobna tkiva



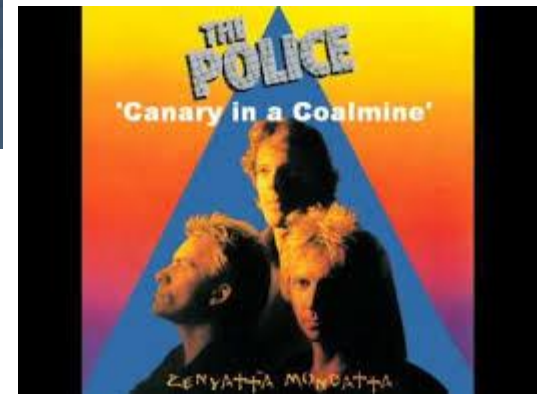
Jemanje zdravil

Spremembe v telesu, ki vplivajo na obzobna tkiva



Imunosupresija

Vloga ustne votline v telesu podobna vlogi kanarčka v rudniku



Povezava s sistemskim zdravjem

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3. PB vpliva na potek bolezni na drugih področjih

Sočasen vpliv



Kajenje

Sočasen vpliv



KAJENJE

Sočasen vpliv



Sočasn vpliv



Povezava s sistemskim zdravjem

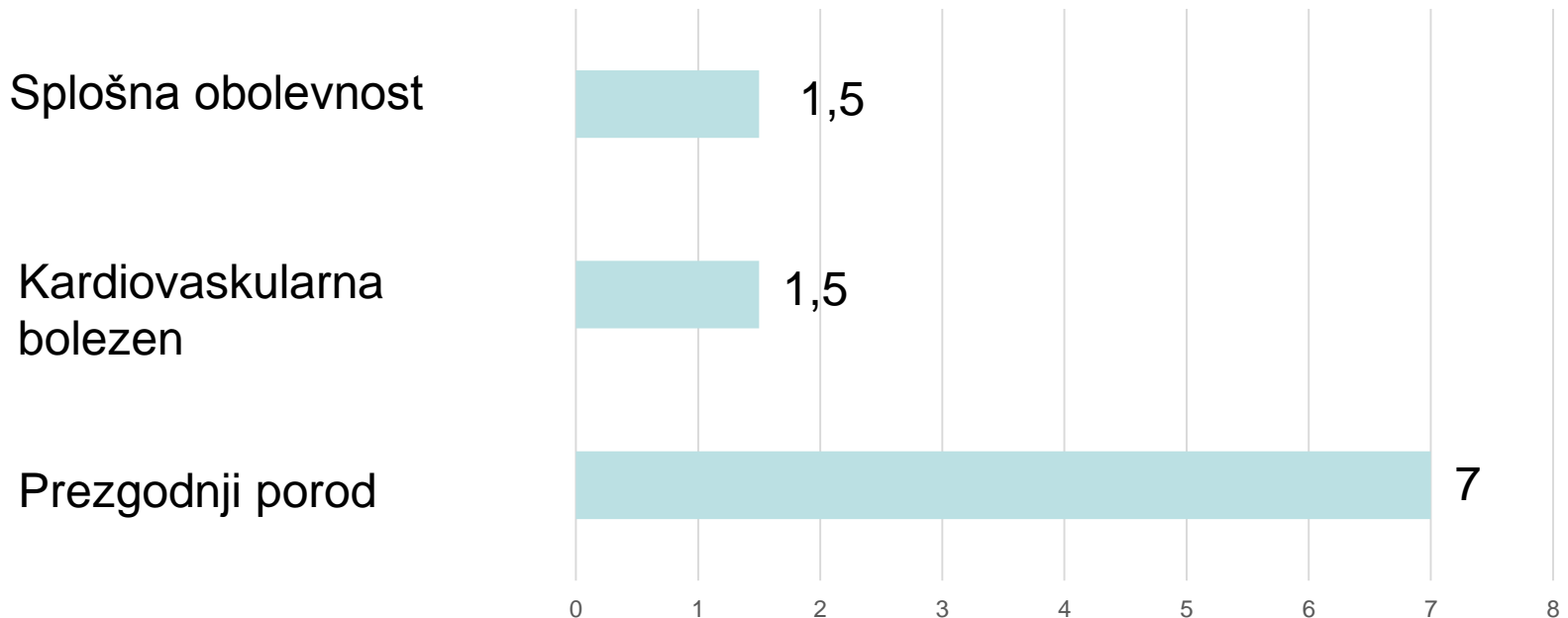
1. Spremembe v telesu, ki vplivajo na obzobna tkiva (prehrana, zdravila)
2. Dejavniki, ki sočasno vplivajo na ustno votlino in druga področja telesa (kajenje, starost)
3. **PB vpliva na potek bolezni na drugih področjih**

Povezava s sistemskim zdravjem

1. Spremembe v telesu, ki vplivajo na obzobna tkiva (prehrana, zdravila)
2. Dejavniki, ki sočasno vplivajo na ustno votlino in druga področja telesa (kajenje, starost)
3. **PB vpliva na potek bolezni na drugih področjih**
 1. Srčno-žilne bolezni
 2. Izid nosečnosti
 3. Diabetes
 4. Bolezni pljuč
 5. Nova področja raziskav (želodec, sklepi, živčevje,...)

Razmerje dogodkov

- Kakšno je razmerje neugodnih zdravstvenih dogodkov, če primerjamo ljudi z PB in z zdravo dlesnijo?





“tihi ubijalec”



?

Vs.



3 pogoji za dokaz vzročne povezanosti PB in sistemskih stanj

1. Povezava v smislu povečane verjetnosti dogodka
2. Biološki mehanizem
3. Preprečitev dogodka z zdravljenjem PB

PB in bolezni KVS



Ateroskleroza

PB in bolezni KVS

1. Povezava v smislu povečane verjetnosti dogodka

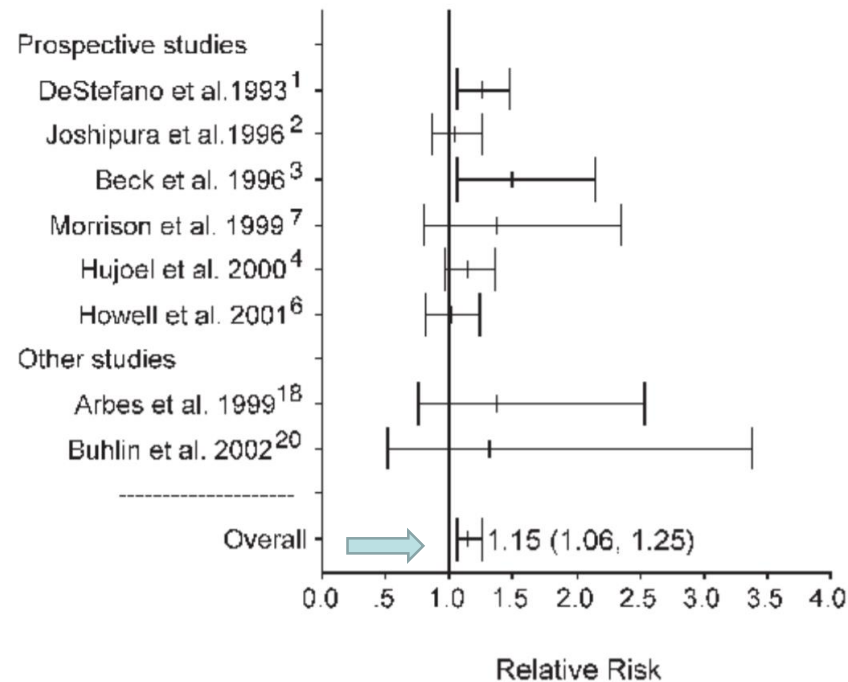
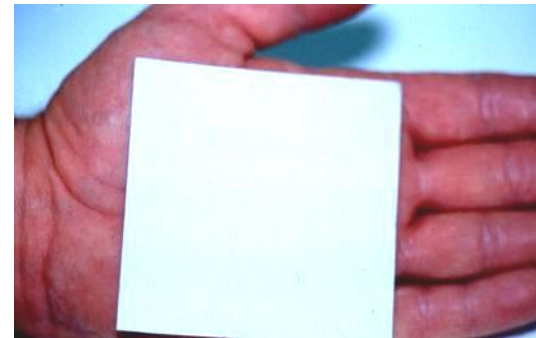
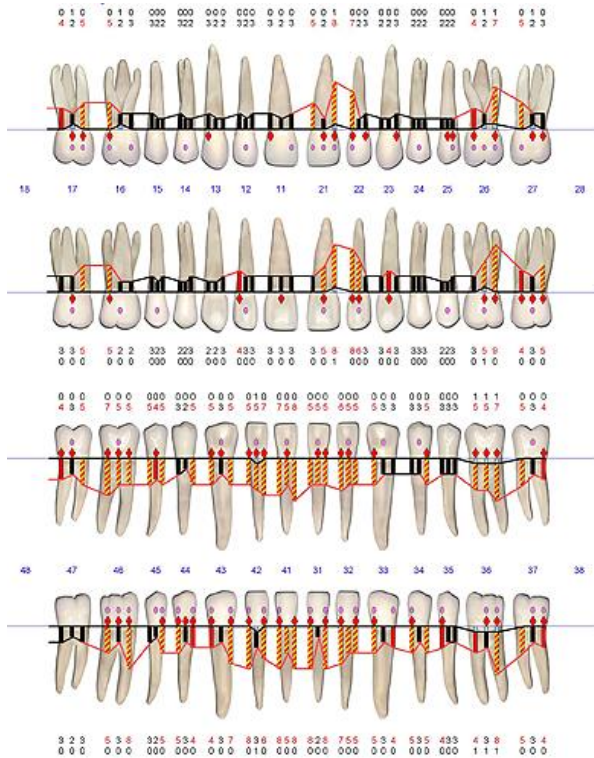


Figure 1.

Risk ratios of coronary heart disease associated with periodontitis from individual studies^{1-4,6,7,18,20} and overall.

PB in bolezni KVS

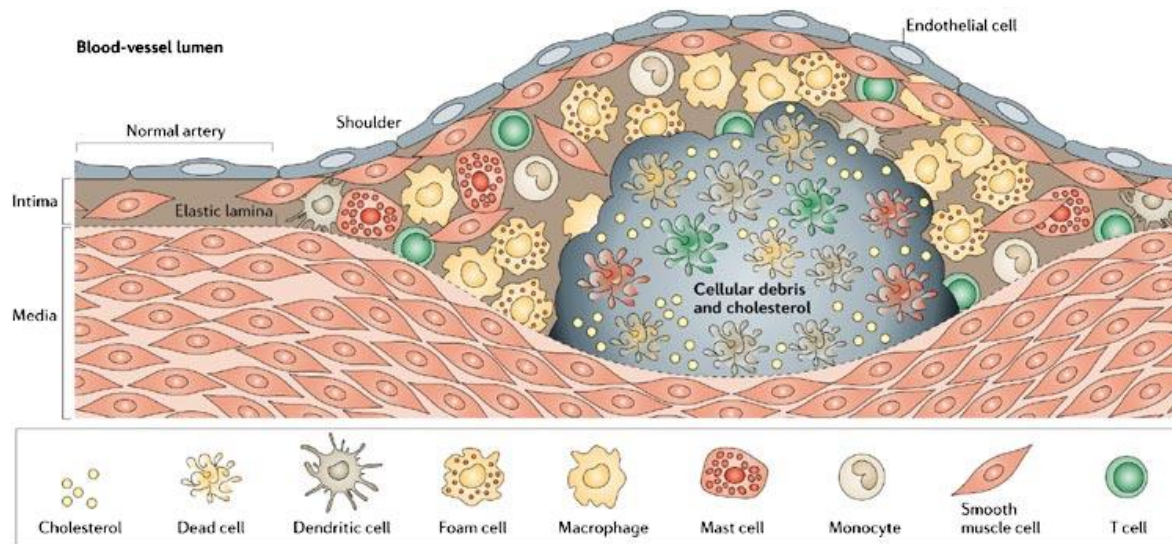
2. Biološki mehanizem



“Parodontalna rana”

PB in bolezni KVS

2. Biološki mehanizem



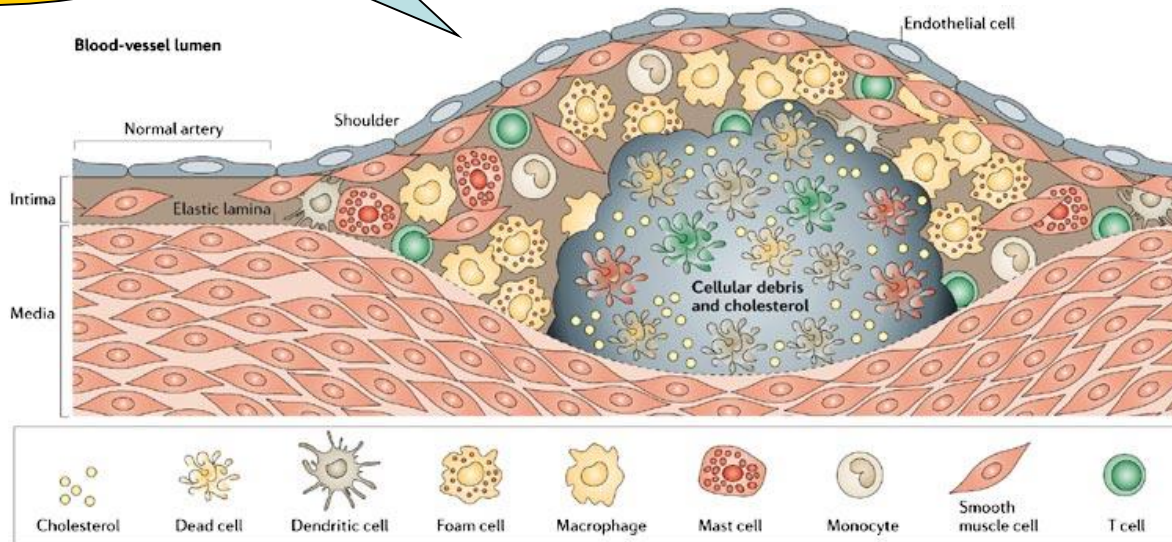
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Nature Reviews | Immunology

Hansson *et al.* *Nature Reviews Immunology* 6, 508-519 (July 2006) | doi:10.1038/nri1882

Vnetni mediatorji iz obzobnih tkiv

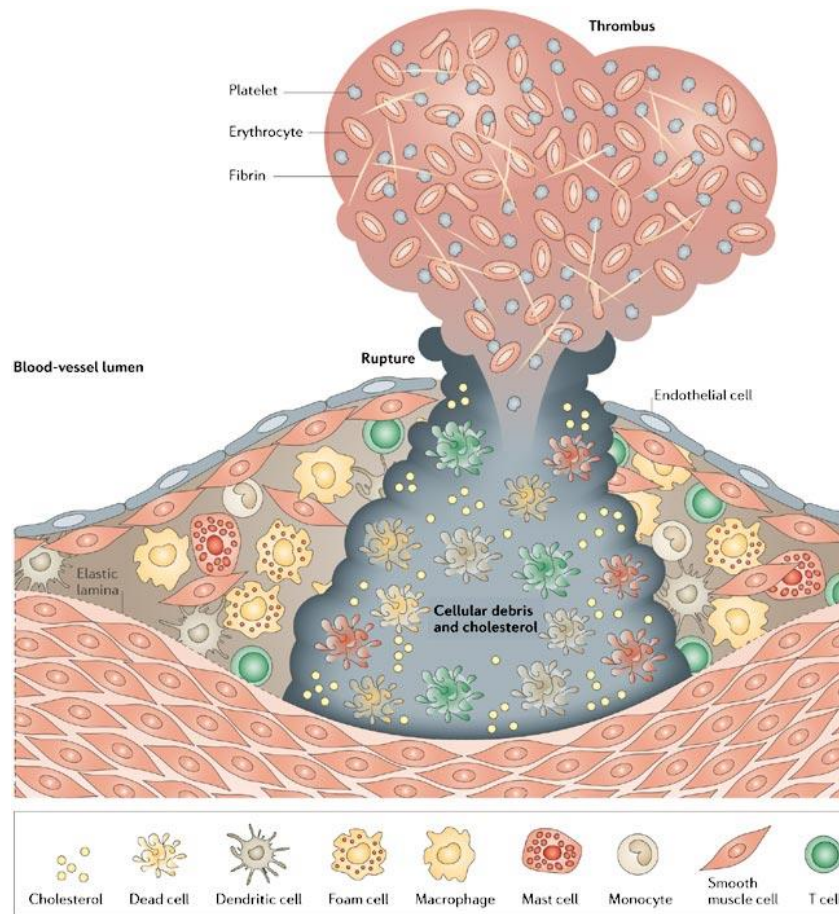
Bakterije zobnega plaka

Sistemski vnetni odziv



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Nature Reviews | Immunology

Hansson et al. *Nature Reviews Immunology* 6, 508-519 (July 2006) | doi:10.1038/nri1882



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Hansson *et al.* *Nature Reviews Immunology* **6**, 508-519 (July 2006) | doi:10.1038/nri1882

PB in bolezni KVS

3. Preprečitev dogodka z zdravljenjem PB

 The NEW ENGLAND
JOURNAL of MEDICINE

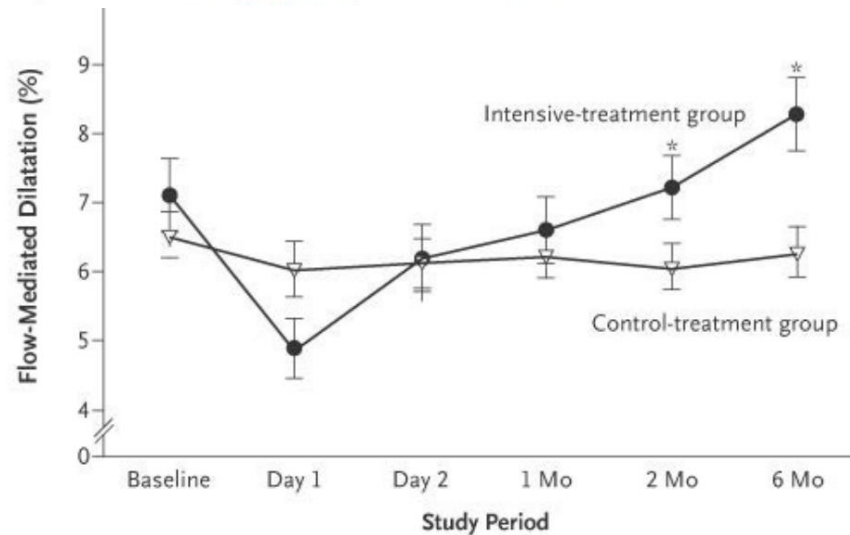
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ORIGINAL ARTICLE

Treatment of Periodontitis and Endothelial Function


Maurizio S. Tonetti, D.M.D., Ph.D., Francesco D'Aiuto, D.M.D., Ph.D., Luigi Nibali, D.M.D., Ph.D., Ann Donald, Clare Storry, B.Sc., Mohamed Parkar, M.Phil., Jean Suvan, M.Sc., Aroon D. Hingorani, Ph.D., Patrick Vallance, M.D., and John Deanfield, M.B., B.Chir.

N Engl J Med 2007; 356:911-920 | March 1, 2007 | DOI: 10.1056/NEJMoa063186



PB in bolezni KVS

3. Preprečitev dogodka z zdravljenjem PB



The NEW ENGLAND
JOURNAL of MEDICINE

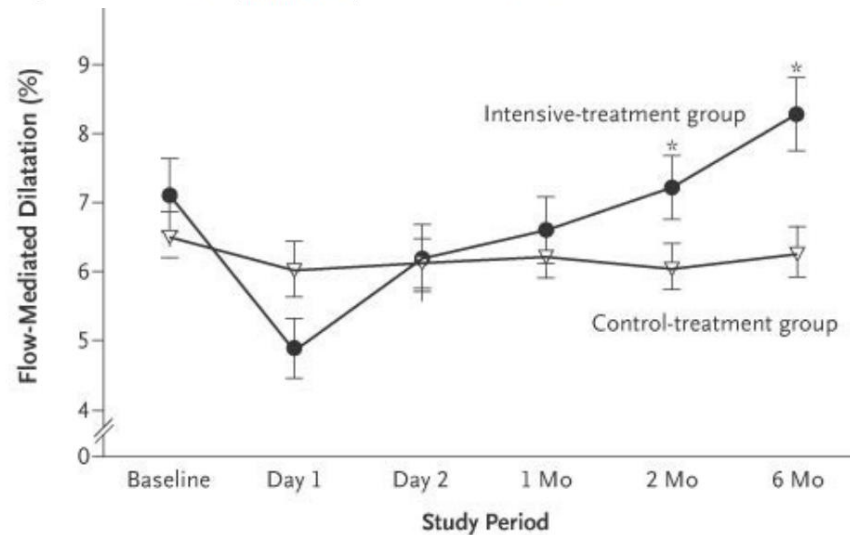
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ORIGINAL ARTICLE

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N Engl J Med 2007; 356:911-920 | March 1, 2007 | DOI: 10.1056/NEJMoa063186



PB in bolezni KVS

3. Preprečitev dogodka z zdravljenjem PB



- **Nadomestni izidi** (Surrogate endpoints) vs. **Pravi izidi** (True clinical endpoints)
 - P/ **Elastičnost žil** vs. **Infarkt**
 - P/ **Izguba prirastišča** vs. **Izguba zoba**

Obstet Gynecol. 2005 May;105(5 Pt 1):1114-8.

Surrogate end points in clinical research: hazardous to your health.

Grimes DA¹, Schulz KE.

AHA statement

AHA Scientific Statement

Periodontal Disease and Atherosclerotic Vascular Disease: Does the Evidence Support an Independent Association?

A Scientific Statement From the American Heart Association

Circulation 2012

- Observational studies **support the association** between PD and ASVD independent of the known co-founders
- They **do not**, however, **support causal relationship**
- Although periodontal interventions result in a reduction of systemic inflammation and endothelial dysfunction, there is **no evidence that they prevent ASVD or modify its outcomes**



Vs.



Področje intenzivnih raziskav

Acta Odontol Scand. 2012 Dec;70(6):520-8. doi: 10.3109/00016357.2011.640284. Epub 2012 Feb 14.

Periodontal inflammatory burden correlates with C-reactive protein serum level.

Skaleric E¹, Petelin M, Gaspirc B, Skaleric U.



Exp Lung Res. 2009 Sep;35(7):605-20.

Lack of soluble tumor necrosis factor alpha receptor 1 and 2 and interleukin-1beta compartmentalization in lungs of mice after a single intratracheal inoculation with live *Porphyromonas gingivalis*.

Nemec A¹, Pavlica Z, Svete AN, Erzen D, Crossley DA, Petelin M.

J Int Acad Periodontol. 2006 Apr;8(2):61-6.

Periodontal disease and diabetes metabolic control: a full-mouth disinfection approach.

Schara R¹, Medvescek M, Skaleric U.



J Dent Res. 2010 May;89(5):515-20. doi: 10.1177/0022034510363108. Epub 2010 Mar 3.

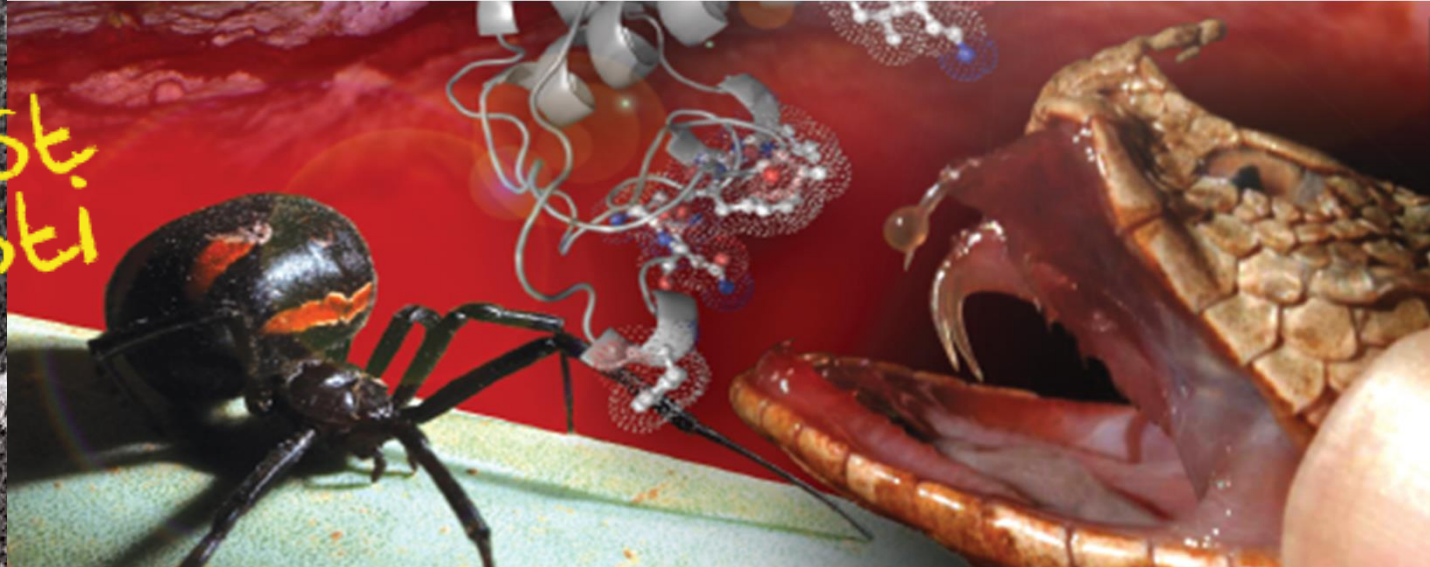
Anti-NGF treatment reduces bone resorption in periodontitis.

Gaspersic R¹, Kovacic U, Glisovic S, Cör A, Skaleric U.



Pripravljen na
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26. oktober 2016 ob 19h, Kavarna
Union

Zivalski strupi: od smrtonosnega k zdravilnemu

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Nataša Ivanuš Čuček, TV Slovenija



S A T E N A



Institut
"Jožef Stefan"
Ljubljana, Slovenija

Univerza v Ljubljani
Fakulteta za matematiko in fiziko



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