

## Gosti uredništva

### Guests Editorial

## Novi svijet dentalne medicine i onkologije

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Već se dugo zna da visoke doze konvencionalne onkološke terapije, kao što su kemoterapija i zračenje glave i vrata, uzrokuju klinički značajne akutne i kronične oralne komplikacije (1, 2). No prevencija i liječenje, zasnovano na mehanizmu nastanka, ograničeno je samo na dio njih. Tako je uporaba radioterapije moduliranog intenziteta, kako bi se zaštitila zdrava oralna tkiva kao što su slinovnice i sluznica, pokazala smanjenje akutnih i dugoročnih oralnih komplikacija kod bolesnika s karcinomima glave i vrata. No za druge oblike oralne toksičnosti ili nam nije dovoljno poznat patobiološki model, ili nemamo na raspolaganju tehnologiju zasnovanu na molekularnoj ciljanoj terapiji kojom bismo ublažili oralne lezije.

Razvijanjem novoga, molekularno usmjerenog biološkog liječenja malignih bolesti, trajno se približavamo našem cilju – djelotvornijem lijeku s manjim neželjenim učincima na zdrava tkiva. Ali i ti su lijekovi u određenim skupinama onkoloških bolesnika uzrokovali neočekivane toksične nuspojave koje su rezultirale nužnim smanjenjem doze. Na primjer, stomatitis povezan s inhibitorom ciljane molekule rapamicina kod sisavaca (prema engl. *the mammalian target of rapamycin inhibitor-associated stomatitis* (mIAS)) prepoznat je kao proces nalik na afte čija se patogeneza očito u osnovi razlikuje od nastanka uobičajenih mukozitisa zbog/tijekom liječenja malignih bolesti. Ova, vjerojatno jedinstvena patogeneza mIAS-a, ima jednu prednost kad je riječ o kliničarima i bolesnicima – za razliku od uobičajenih mukozitisa pokazalo se da se mIAS do određene mjere može liječiti topikalnim ili sistemskim steroidima.

Ovaj primjer nedavno uočene klinički važne oralne komplikacije, podcrtava značenje interdisciplinarnе suradnje i dijeljenja znanja, s obzirom na to da će idućih godina područje oralne onkologije napredovati. Interprofesionalno modeliranje omogućilo bi brže prepoznavanje oralnih toksičnih nuspojava u kliničkom okruženju i promicalo razvoj sučelja između laboratorijskog i kliničkog istraživanja te liječenja. Takav dinamički model mogao bi maligne bolesnike manje toksično opterećivati te povećati postotak izlječenja i dugotrajnije remisije (2,3).

## The New World of Dental Medicine and Oncology

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It has long been known that conventional high dose cancer treatments such as cancer chemotherapy and head and neck radiation can result in clinically important acute and chronic oral complications (1, 2). However, mechanism-based prevention and treatment have been limited to only some of these complications. For example, utilization of intensity-modulated head and neck radiation to protect normal oral tissues such as salivary glands and oral mucosa has been shown to result in reduced acute and long-term oral sequelae in head and neck cancer patients. For many other oral toxicities, however, either the pathobiologic model is not well established and/or the technology is not clinically available such that the lesions can be ameliorated based on molecular targeting.

With the ongoing development of novel, molecularly directed biological cancer therapies, the goal of enhanced cancer treatment efficacy with less adverse effects on normal tissues continues to evolve. However, these treatments have in selected oncology patient cohorts caused unexpected profiles of dose-limiting oral toxicities. For example, the mammalian target of rapamycin inhibitor-associated stomatitis (mIAS) is recognized as an aphthous-like pathogenesis that seemingly differs in fundamental ways from that of conventional cancer therapy-induced mucositis. This apparent unique pathogenesis for mIAS has worked to the advantage of clinicians and their patients; unlike conventional mucositis, mIAS has to some extent been shown to be treatable by topical or systemic steroids.

This example of a recently emergent, clinically important oral complication highlights the importance of interdisciplinary collaboration and sharing of knowledge as the field of oral oncology advances in the years ahead. This interprofessional modeling would facilitate both the recognition of oral toxicity in the clinical setting, as well as foster the interface between laboratory and clinical research with clinical management. This dynamic model could then lead to reduction in the toxicity burden to cancer patients while enhancing their cure rates and durability of remissions (2, 3).

There is thus now a strategic new opportunity to address the complex science and clinical care that is essential to ef-

Za to danas postoji nova strateška mogućnost, a to je uključivanje kompleksne znanosti i kliničke skrbi nužne za učinkovito i sigurno liječenje oralnih komplikacija kod malignih bolesnika. Ta je nova mogućnost nastala u mnogobrojnim sektorima u kojima specijalisti iz područja dentalne medicine imaju ključne zadaće, uključujući:

- međunarodne organizacije zdravstvenih djelatnika, kao što je Multinacionalno udruženje za potpurnu skrb u slučaju karcinoma (*Multinational Association for Supportive Care in Cancer*) u suradnji s Međunarodnim društvom za oralnu onkologiju (*International Society of Oral Oncology*) (MASCC/ISOO); misija tih dviju organizacija usmjerena je na liječenje onkoloških bolesnika na temelju dokaza, uključujući i interprofesionalni model potreban za održavanje oralnog zdravlja (4–8);
- Američko društvo za kliničku onkologiju (*American Society of Clinical Oncology*, ASCO) koje sve više ističe potpurnu njegovu onkoloških bolesnika;
- iscrtavanje novih granica u znanosti koje obuhvaćaju oštećenje oralne sluznice malignih bolesnika; u lipnju 2013. prva takva Gordonova istraživačka konferencija pod nazivom *Zdravlje i bolest sluznice* (*Gordon Research Conference "Mucosal Health & Disease"*) odličan je primjer komponente opisanog modeliranja (9);
- pojačano uključivanje oralne onkologije u nastavno gradivo zdravstvenih djelatnika na različitim razinama, uključujući dodiplomsku izobrazbu liječnika i stomatologa te trajnu izobrazbu.

Znanstvenici i stomatolozi-kliničari iz cijeloga svijeta pridonijeli su stvaranju okvira za ovakvo kolektivno znanstveno i kliničko modeliranje. Oni, zajedno s ostalim ključnim pojedincima iz naše struke, danas sudjeluju u ulozi voditelja i suradnika kako bi se poboljšala oralna skrb malignih bolesnika. Nadamo se da bi dugoročan uspjeh u pomicanju sadašnjih granica pridonio novim i učinkovitim načinima skrbi o onkološkim bolesnicima. Ako je nedavna prošlost ikakav pokazatelj budućnosti, oralna skrb malignih bolesnika vrlo je svijetla.

fective and safe management of oral complications in cancer patients. This new opportunity has emerged from a number of sectors in which dental medicine specialist contributes key roles, including:

- international health professional organizations such as the *Multinational Association for Supportive Care in Cancer*, in collaboration with the *International Society of Oral Oncology* (MASCC/ISOO). The mission of these two organizations is centered in evidence-based management of the oncology patient, including the interprofessional model needed for maintenance of oral health (4–8)
- *American Society of Clinical Oncology* (ASCO), in which supportive care in cancer is becoming increasingly highlighted
- delineation of new frontiers in science that includes oral mucosal injury in cancer patients. The June 2013 first-in-kind Gordon Research Conference "*Mucosal Health & Disease*" is an excellent recent example of this component of the modeling (9)
- increased incorporation of oral oncology into health professional curricula at multiple levels, including predoctoral medical and dental education as well in continuing education.

Dental scientists and clinicians from around the world have contributed to setting the stage for this collective scientific and clinical modeling. These and other key individuals from our profession are now contributing at leadership and collaborative roles to advance the mission of oral management of the cancer patient. Continued success in these new frontiers will hopefully contribute to novel and impactful new ways to manage oncology patients in the future. If the recent past is any predictor of the future, oral care of the cancer patient has very bright promise.

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