Objectives: The aims of this study were as follows: (1) to review the learning impact of The Oral Cavity: Portal to Health and Disease (TOC), a massive open online course in oral medicine developed by Penn Dental Medicine using the Coursera platform; and (2) to analyze course enrollment to determine worldwide interest in accessible, high-quality oral medicine education.

Methods: The authors analyzed Coursera learner statistics to critically evaluate learner traits and course engagement for TOC, which launched on September 17, 2017, and covers topics relevant to oral medicine and the interprofessional relationship between dentistry and medicine.

Results: To date, TOC has garnered 16,653 visitors, 4,318 of whom have enrolled and demonstrate approximately steady continued monthly and daily engagement. Most learners are between 25 and 34 years of age, and 54% are female, reflecting interest in acquiring oral medicine–related knowledge in this demographic. TOC includes more participants than Coursera averages who have obtained professional and doctoral degrees. TOC participants also include more individuals who are unemployed, employed part time, and self-employed, demonstrating a broad range of participants. Some participants have successfully applied to and enrolled in dental schools and oral medicine residency programs, including at the University of Pennsylvania. Enrollees are from 6 continents, with higher proportions of learners than other courses on the platform being from Africa and Asia. The countries with the highest proportions of participants include the United States, India, Egypt, the United Kingdom, and Brazil, demonstrating a geographically wide interest among these participants. One hundred twenty-six learners have rated the course with 4.9 of 5 stars; 95% of participants have given the course a "thumbs up"; and many submit positive reviews, including one individual who remarked, "It is a great course for dental students who want to know how systemic diseases or conditions may affect in [sic] the Oral Cavity."

Conclusions: Coursera is a worldwide technology platform that hosts free courses spanning various levels and disciplines. TOC presents an opportunity to learn oral medicine and interprofessional health care concepts for individuals with interests in dental, medical, and allied health professions. High learner engagement with wide global distribution demonstrates interest in oral medicine–related education worldwide.

OPTIMIZING OVERNIGHT ORAL APPLIANCE FOR SUSTAINED-RELEASE VARNISH DELIVERY SYSTEM OF SIROLIMUS

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Objectives: Intraoral trays can be used to deliver treatment materials and medications for dental or mucosal conditions. Maintaining appropriate salivary levels of the active ingredient is challenging when using local application. We have previously analyzed salivary levels and local effects of slow-release varnishes (with clotrimazole or sirolimus as the active ingredient) during the daytime. The aims of the present study were as follows: (1) to optimize overnight appliances for slow-release medications by measuring saliva and blood levels and (2) to evaluate the safety of overnight use.

Methods: An acrylic tray containing 0.5 mg of sirolimus in a sustained-release varnish was applied to 6 anterior teeth for 12 hours in 10 healthy volunteers. Whole unstimulated saliva was collected 1, 2, 10, and 12 hours after application, and a blood sample was taken after 12 hours. Drug levels were analyzed. Results from slow- and fast-release formulations, varnish application position on the tray (buccal, palatal, or lingual), and tray placement (mandibular vs maxillary) were compared. The volunteers evaluated the varnish and tray. The study was approved the hospital ethics committee.

Results: Salivary sirolimus was undetected with use of the slow formulation. The faster formulation produced salivary concentrations of 0.3-45 ng/mL. The highest salivary levels were observed with a mandibular tray with lingual varnish application (up to 178 ng/mL). The sialometry of all participants was within normal range (0.2-2 mL/min), and the highest drug levels were found when salivary flow was lowest. The medication was undetected in the blood. No local reactions or side effects were reported.

Conclusions: Salivary concentrations of medications delivered using an oral tray can be affected by the release rate of formulation and, more important, by the position of the tray and the varnish within it and salivary flow rate. Overnight oral trays can be used to deliver medications especially when 24-hour drug exposure is desired. Further studies regarding local factors affecting drug release and salivary levels are required.

THALIDOMIDE THERAPY FOR REFRACTORY MUCOSAL DISEASE: BENEFIT AND RISKS OVER 10 YEARS

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Background: The immunomodulatory and antiangiogenic effects of thalidomide have been demonstrated in a number of refractory ulcerative oromucosal conditions, including recurrent aphthous stomatitis (RAS), Behçet disease, erythema multiforme (EM), erosive lichen planus, and orofacial granulomatosis (OFG). Thalidomide acts by modulating the inflammatory cascade, interacting with various cytokines, including tumor necrosis factor-α, interleukin 10, and cyclooxygenase 2. Despite its efficacy, thalidomide is associated with a number of risks, including peripheral neuropathy, thromboembolic disease, and embryofetal toxicity, which limit its clinical use.

Methods: A retrospective review of the clinical database of the Oral Medicine Department at the Royal National ENT and Eastman Dental Hospitals, UCLH, London, UK, was undertaken to identify patients prescribed thalidomide between 2009 and 2019.

Results: Sixteen patients (9 men and 7 women) with a mean age of 46 years (range, 20-66 years) were identified in this cohort. Clinical diagnoses included RAS (n = 10), human immunodeficiency virus (HIV)-related oral ulceration (n = 3), EM (n = 2), and OFG (n = 1). All patients, with the exception of HIV-related cases, had proved refractory to systemic corticosteroids and/or immunosuppressive therapy. Patients were treated for a mean of 50 months (range, 1-120 months) with doses ranging

from 50 mg every 3 days to 100 mg daily. A complete remission (CR) rate of 56% was noted in this cohort, with CR defined as complete clearing of mucosal disease within 1 month of treatment onset and maintenance of this CR during the second month of treatment. All patients underwent a baseline sensory nerve action potential test before initiating thalidomide. Five of 16 patients subjectively reported transient peripheral neuropathy. There was objective evidence of mild length-dependent axonal sensory neuropathy in 2 of 16 patients, with treatment cessation occurring in an isolated case due to persistent neuropathy.

Conclusions: Within this cohort, thalidomide demonstrated a favorable efficacy/safety ratio with long-term use. It remains a viable treatment option for cases of refractory oral ulceration. Given the history of adverse effects associated with thalidomide, informed consent with regard to embryofetal toxicity and contraceptive counseling are pivotal to safe prescribing. Counseling with respect to other common adverse effects, including peripheral neuropathy and venous and arterial thromboembolism, is mandatory, and these adverse effects need to be understood.

XEROSTOMIA SYMPTOMS AND TREATMENT STRATEGIES ASSOCIATED WITH SALIVARY FLOWS

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Objectives: We sought to analyze the types and quantity of dry mouth products patients use as well as the reported dry mouth symptom severity and frequency in relation to salivary flows. We hypothesized that respondents with higher stimulated flow would report better responses to products that stimulate flow.

Methods: Patients with complaints of dry mouth who had documented unstimulated and stimulated whole salivary flows (UWS and SWS, respectively) completed a questionnaire to assess dry mouth products used, current symptoms, and response to therapy. Statistical analyses included descriptive analyses and associations between dichotomized (low/normal) salivary flow levels, and symptom severity was assessed using nonparametric Wilcoxon rank-sum tests.

Results: Eighty-seven patients completed the questionnaire; 38 patients had a diagnosis of Sjögren syndrome. More than half of patients (55%; n = 48) reported using 4 or more dry mouth products. The most common product used was water (n = 78), followed by rinses (n = 54) and lozenges (n = 48). Twenty-five patients (29%) reported use of parasympathomimetics. More than half (56%) of patients using parasympathomimetics reported that their mouth felt "much better" compared with less than one-third of patients using other methods: water (29%), gum (23%), lozenges (27%), candies (4%), rinse (26%), spray (24%), or gel (20%). Among parasympathomimetic users with normal SWS, 71% reported their mouth felt "much better" compared with 36% of those with low SWS. For water, gum, lozenges, candies, and sprays, greater than 50% of respondents reported improvement lasting less than 1 hour. Regarding rinses, gels, and parasympathomimetics, greater than 50% of respondents reported improvement lasting greater than or equal to 1 hour. The dichotomized level of UWS rate was not associated with any measures of symptom severity, whereas the low SWS rate was associated with the following measures: dryness of the mouth ($P = .004$), difficulty speaking due to dryness ($P = .03$), and difficulty swallowing due to dryness ($P = .004$).

Conclusions: Different treatment categories for dry mouth symptoms provided varying degrees of relief. Patients with normal vs low stimulated flow who used parasympathomimetics reported the greatest treatment response and longest relief of dry mouth symptoms. Assessment of salivary flow levels may be a useful guide for more targeted recommendations of dry mouth products.

COMPARISON OF THE IMMUNOLOGIC RESPONSE TO HERPES SIMPLEX VIRUS TYPE 1 ENTRY GLYCOPROTEINS INDUCED IN HUMANS AFTER PRIMARY INFECTION OF ORAL OR GENITAL SITES

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Objectives: We sought to determine potential differences in the humoral immune response to herpes simplex virus type 1 (HSV-1) in patients after primary infection in either oral or genital sites.

Methods: Serum samples from 20 patients with primary HSV-1 infection (10 oral, 10 genital) were compared. A neutralization assay categorized samples by their ability to inhibit virus entry into cells. An enzyme-linked immunosorbent assay determined the quantity of antibodies against each of the major HSV-1 glycoproteins (gD, gB, gC, gH/gL). Surface plasmon resonance imaging (SPRi) was used to estimate the quality of the response by determining the epitope specificity of antibodies against the receptor-binding glycoprotein gD. Information from these assays was combined to develop a comprehensive profile of immunologic response to HSV-1 infection.

Results: All 10 oral site serum samples contained significant levels of virus-specific antibodies to block virus entry and demonstrated excellent immune response to the major virion glycoproteins. In contrast, only 4 of the 10 genital site serum samples were able to block virus entry. The 6 genital site sera that failed to block entry had markedly reduced antiglycoprotein antibody levels, indicating a poor overall HSV-1 immunologic response. The quantity of antiglycoprotein antibodies in the 4 genital (protective) sera mirrored that induced by oral infection. Subsequently, SPRi was used to determine whether the qualitative response was equivalent between the oral and genital site sera. All 10 oral site sera targeted gD epitopes at levels significantly higher and more varied than those generated for the 4 protective genital site samples. Interestingly, the gD epitope profiles of the 6 nonprotective genital site samples were directed at a single non-neutralizing antigenic site on gD that is involved in cell-to-cell spread.

Conclusions: Based on a comprehensive profile of immunologic response to HSV-1 infection for individuals