THE D3 GROUP

ISSUE #14 JUNE 2020

D3G DISPATCH

News about Developmental Dental Defects (D3s), The D3 Group, and the Chalky Teeth Campaign.

COMMENT FROM THE CUSP:

Ducks in a row

So COVID-19 is still with us – regrettably but not unsurprisingly. While pleased that life is stabilising Down Under, I sympathise with those of you more-severely compromised still. A pleasing upside has been widespread publicity for science and the need for effective translation (bleach anyone?). We can only hope this newfound popularity gets carried through to climate science.

Countering the pandemic's doom and gloom, we have some wonderful things to report including a science breakthrough, a translational advance, and a surprising D3 centenary. Even the necessitated rejigging of our October symposium turns out to be a blessing in disguise. This progress takes me to the underpinning logic of "**getting one's ducks in a row**" *(**interesting etymology**)* when pursuing high social impact, as we are. If you'll pardon the **anatid** metaphor, D3G has been labouring to overcome historic weaknesses by raising not one but **three D3 duck families**, all happily living together *(i.e. integrated Research, Education and Translation)*. At last Research ducks can be given more attention, now the others are lined up and running. In this regard we can look to **Isaac Newton** who, in a year of self-isolation during the **Great Plague**, came up with **three momentous discoveries** – a masterclass in duck management!

D3-Mike | Mike Hubbard
D3G Founder-Director

IN THIS ISSUE

NEWS: Trumpeting and ducks

Three happenings merit special mention and, at risk of "**blowing our own trumpet**", we think there's strong reason for D3ers to take pride in the way D3G's ducks are congregating. First up *(Research ducks)* is a **breakthrough study** into the pathological origins of "chalky enamel" published this month by D3G's lead biomedical researchers in Melbourne – for a gentle introduction and free download, follow the orange "Science Breakthrough" button on **D3G's homepage**. This rather complex biochemical investigation is simplified in the ***Clinical Feature*** summary below. It remains to explain the **hiatus** since the **initial discovery** was **published in 2010**. Unsurprisingly, scientific responsibility mandates that, having discovered what appears to be an exciting new path, one should follow it some distance before popping corks and tooting horns. And from a social-good perspective, ideally one should've prepared a "translational nest in which to lay the scientific egg". The latter goal has led to D3G's cross-sector **online education resource** and **international network**, which together provide visible reason and a 'willing army' to pursue this and other scientific advances. Meanwhile, out of sight, the research journey has involved three postgrad projects, one of which inspired novel molecular diagnostics for chalky enamel *(now patented)*. So – if you haven't already put two and two together – the new pathological path looks to hold much promise for **Molar Hypomin prevention** and more.

Secondly *(Translation ducks)*, **Indigenous Reconciliation Week** **in Australia** triggered consideration of the **culture and values** D3G may wish to pursue as an international community. Recent progress with **Black Lives Matter** provides further impetus. A draft statement, which combines retrospective acknowledgement with prospective thoughts on collaborative future-building, is **now online** and we'll highly your **feedback please**. **Thirdly** *(Education ducks)*, we're thrilled to report that last issue's "cautious toe into the murky waters of research publication quality" led to totally positive feedback and agreement that D3G should take a lead in developing **publication standards** *(and providing reviewers)* for the D3 field. Thanks to all concerned, and particularly D3er **Kevin Donly** (***AAPD*** *president)* and **Pediatric Dentistry Journal** editor **Noel Childers** for encouraging this new development.

WEB UPDATES: Speak 'Chalky Teeth'

Previously we've outlined the ***'We Fight Chalky Teeth'*** *(WFCT)* initiative Down Under, which started with a **specialist practice network** and now embraces our first ***WFCT organisations*** (***ASO*** *and* ***NZAO***, ***in progress***). Lurking behind the scenes were thoughts of an allied **'translational language'** (***lingo***) venture – available to everyone in the healthcare community – that welcomes and facilitates discussion of D3 matters in plain language. To make it work, 'chalky terminology' first had to be legitimised from a clinico-scientific perspective, knowing for example that some practitioners view "chalky teeth" as a wrongful excuse for poor plaque control. Hence we developed **academic and social histories** for "chalky terms" *(teeth, spots, enamel)* which to our surprise extend back 100 years *(see **here** and CENTENARY, below)*. Now, with science and history onside, it was opportune to launch a **Speak 'Chalky Teeth'** pilot – again, your **feedback** and thoughts about allied branding/revenue opportunities are welcomed.

CHALKY TEETH

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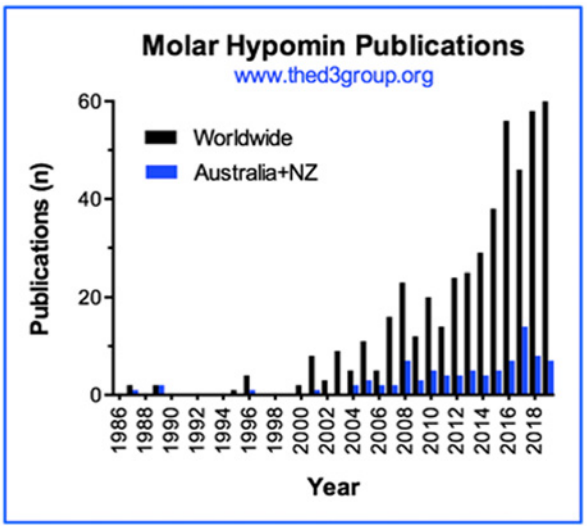
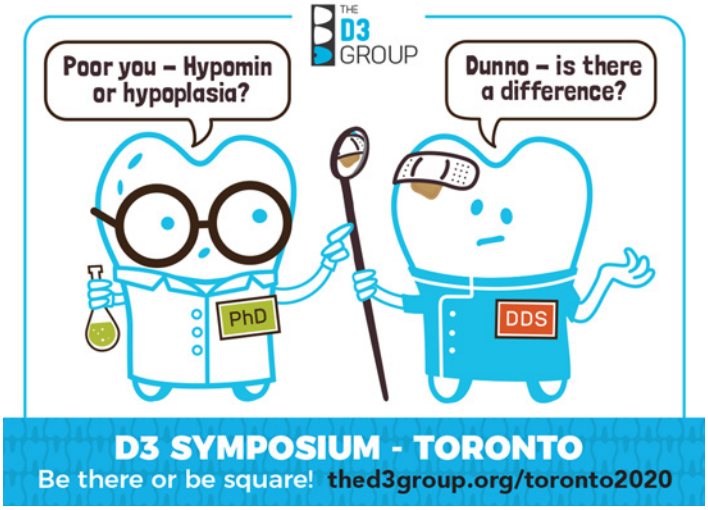
Second, the Molar Hypomin **bibliography** and **prevalence** pages have had their annual updates – this takes some patience but it's great to see the answers! About 60 peer-reviewed papers appeared in 2019 which, although only a minor increase on 2018, cements an impressive **doubling of publication rate over 5 years** (***graph***). Whereas previously only papers listed in **PubMed** were included, increasingly we're seeing robust articles in new journals yet to be accredited. In such cases, the onus to set a quality threshold currently lies with **D3-Mike**, but hopefully the **Publication Standards Project** *(see NEWS)* will lead to transparent guidelines and multiple adjudicators. And regards MH prevalence, we're now up to **20 studies across 11 countries for 2-year molars**, and **121 studies from 47 countries for 6-year molars** – giving **average prevalences of 9% and 15%**, respectively. Pleasingly, a growing number of authors are citing our **prevalence page**, recognising several advantages over traditional review articles.



ROAD TO TORONTO: A happy detour

Due to COVID-19, there isn't much concrete progress to report other than what was flagged as a possibility in March is now reality – i.e. our symposium advertised for **October 22-24** in Toronto will now be an **online pre-symposium workshop** (***same dates***). In turn, the symposium is **rescheduled for May 6-9, 2021 in Toronto**. Based on members' reactions and our own musings, this unexpected detour actually has much going for it. Most notably, our "**translational roadmap matrix**" – embracing identification of key questions across the sector and ensuing development of global collaborative projects to tackle them – has attracted numerous expressions of interest from D3ers and others wanting to be involved *(yay, thanks all!)*. Whereas initially we thought that frameworking for the live symposium could be done by a select few, now we see major advantage in embracing broader inputs from the outset. By this reckoning, when the 2021 symposium eventuates, rough ideas will already have been improved by numerous D3ers, making for stronger live discourse. So current thoughts are to **(1)** assemble a core "brain trust" covering all elements of the **matrix**, who then **(2)** recruit volunteers for working groups, that



then **(3)** develop framework documents to be discussed at the online workshop. It's hoped volunteer and workshop registration will be available shortly. Meanwhile we're grateful for free advertising provided by IADR, AAPD, NZDA and others, and ask that members do their bit locally too – a range of content is **available**, including the humorous new take on an old terminological trap shown above.

CENTENARY: 100 years of chalky enamel research

For some academics at least, COVID-19 lockdown has helped clear the backlog of work-related reading. With media reflecting on the Spanish flu pandemic whose **4th wave** was lingering 100 years ago, imagine the excitement of discovering a D3 centenary – being a seminal **1920 research article** describing **"chalky enamel"** at length. The author was **Bernhard Gottlieb**, an eminent medical scientist then in Vienna, who later

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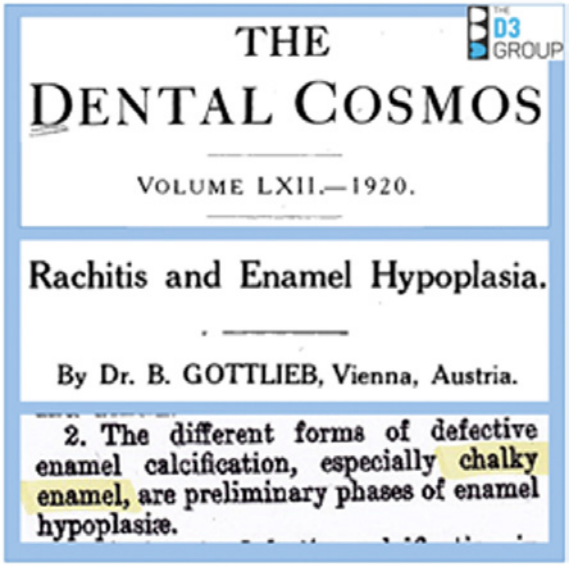
became regarded as the founder of biological thinking in dentistry having instigated the field of oral histopathology (***read more***). His study addressed what was loosely described as "**enamel hypoplasia**", and the *(post-mortem)* dental specimens came from young children overcome by various contemporary diseases including rickets, measles, enteritis and syphilis. The results combined histological and clinical observations, and his two-part report was published in the fabled **Dental Cosmos** *(forerunner to **JADA**)*. Remarkably from the translational perspective of our ***Chalky Teeth Campaign*** – which was developed without knowledge of this historic paper – Gottlieb refers to "**chalky enamel**" and "**chalky spots**" that "**crumble**" easily. Moreover, it's evident the enamel lesions he examined were a mixture of *(true)* hypoplasias and hypomineralised opacities. So in other words, he used our **chalky teeth lingo** to describe **today's clinico-scientific terms** (***demarcated opacities, post-eruptive breakdown***) exactly 100 years ago. Making this **serendipity** even better, Gottlieb introduced two key questions about pathomechanism that persist today – in essence, why are lesions scattered amongst normal enamel, and do they reflect cellular or extracellular disruption? Having found instances of chalky enamel overlaid by normal-looking enamel cells (***ameloblasts***), he concluded the primary disruption must occur extracellularly – and in the case of rickets, presumably due to "defective deposition of lime" *(i.e. mineralisation)*. While realising the field has made significant progress since 1920, we do hope the next century will see a stronger pace and outcomes! (read more **here** and **here**)


THE DENTAL COSMOS

VOLUME LXII.—1920.

Rachitis and Enamel Hypoplasia.

By Dr. B. GOTTLIEB, Vienna, Austria.

2. The different forms of defective enamel calcification, especially chalky enamel, are preliminary phases of enamel hypoplasiæ.

INTRODUCING: Rebecca Williams, D3G's superstar student

At long last, we're thrilled to introduce **Rebecca *(Bec)* Williams** as D3G's superstar student of website and laboratory fame. Bec's research *(see **Lab Feature** below)* adds a key piece to an apparent breakthrough in understanding the long-elusive **pathogenesis of demarcated opacities** – and hence Molar Hypomin. Looking back, it still seems amazing that, as a busy postgrad specialising in paediatric dentistry, Bec not only learned how to do some complex biochemistry but also helped with its **translation into a story** that kids *(and maybe dental professionals too?)* can understand. And on top of that mammoth task, she applied her clinical knowledge to developing reams of other content for the pioneering website D3G **launched in 2013**. Once again, as part of allied translational activities, she went beyond the call of duty by adeptly handling an **interview on national radio**. While Bec's website contributions were duly acknowledged at the time *(does that cheery face on **D3G's homepage** look familiar now?)*, her annointment as a **published author** had to await completion of several follow-on activities. Unsurprisingly, Bec pressed on with her clinical career and keeps super busy in specialist private and hospital practice. And on top of these two day jobs, somehow she finds energy to play leadership roles in two professional organisations and serve as D3G's representative in Western Australia. But wait, there's more – a husband, two young kids and a dog also have the pleasure of having Bec central to their lives. We gratefully take our hats off to a superstar student and person. For more info, **contact Bec**.

QUICK QUIZ: Delving into D3s

QUESTION 1 *(easy)*
Historically, did researchers apply the term "chalky spots" to both enamel opacities and early decay?

QUESTION 2 *(harder)*
It's often stated that "tooth decay is mostly preventable". Is this valid for children?

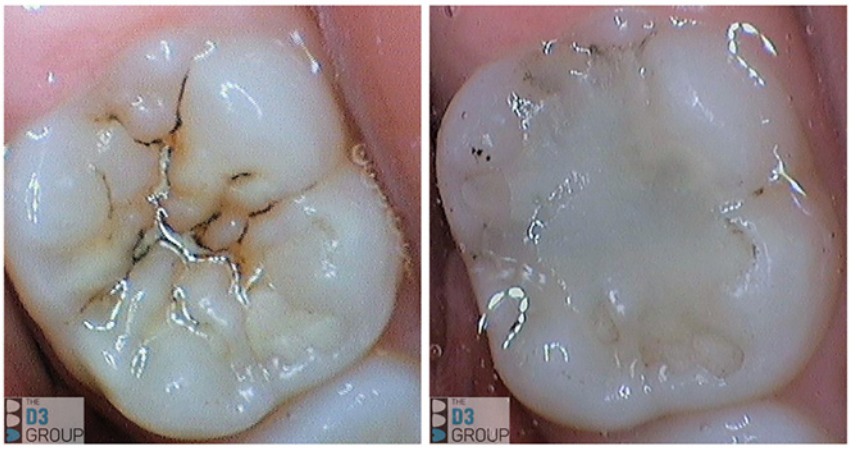
Answers: *see* ***Suggestions Box*** *on pg 7.*

WOW FACTOR: Soothing silver fluoride

Last issue we covered two sides of the silver fluoride (AgF) debate – being a review article reflecting the paucity of research regarding Molar Hypomin, and then quite the opposite from AgF expert ***Cathy Boyce*** *whom we introduced as D3G's 200th member. We're grateful to Cathy for providing today's informative case.*

The issue

Frequently, hypomineralised molars are painful leading to challenges for child *(eating, cleaning)* and dental professional *(super-squirmy patient, treatment selection)* alike. Particularly problematic are teeth with annoying sensitivity despite appearing only mildly hypomineralised, and for which standard preventive treatments *(fluorides, resin sealants)* have proven ineffective. Although AgF is known to desensitise and arrest decay – often eliminating the need for fillings – the black staining it leaves behind can be a downside.



The wow

The ***left picture*** above shows a 6-year molar – diagnosed as mildly hypomineralised yet annoyingly sensitive – one week after applying AgF/SnF_2 solution to all exposed enamel *(CSDS x 3 min)*. Complete desensitisation had been achieved within 12 hours, leading to a happy kid who was then comfortable to have a protective white sealant *(GIC)* placed *(right picture, taken 6 months later)*. Note the black staining was limited to the most hypomineralised areas *(grooves)*, and this was largely hidden by the GIC.

Questions arising and Cathy's answers

(1) was any injection or drilling involved? – none; **(2)** did this "low impact" treatment last? – yes, still pain-free a year later; **(3)** is it a permanent solution? – the GIC may need maintenance/replacement; **(4)** is this a great way to "buy time" until the child is more resilient? – absolutely, and so conservative! **(5)** what's different with severer cases of hypomin? – a second application is often required for complete desensitisation, and removal of unstable enamel may be indicated before sealing. As usual, readers are invited to comment and to send other educational cases for future issues – please contact **D3-Mike**.

D3 LITERATURE: Keeping you current!

Lab Feature: Breakthrough – what makes enamel chalky?

Medical scientist **Bernhard Gottlieb** first addressed what makes enamel chalky 100 years ago *(see above)*. Until now, this question and the allied mystery of why "chalky spots" are **sporadic** *(i.e. limited to some regions in some teeth)* have remained an enigma. With growing evidence that chalky enamel is the **principal risk factor for childhood tooth decay**, medical prevention of chalky opacities has become an arguable **research priority** with potential to benefit global health. Although Gottlieb thought disruption started with immature enamel rather

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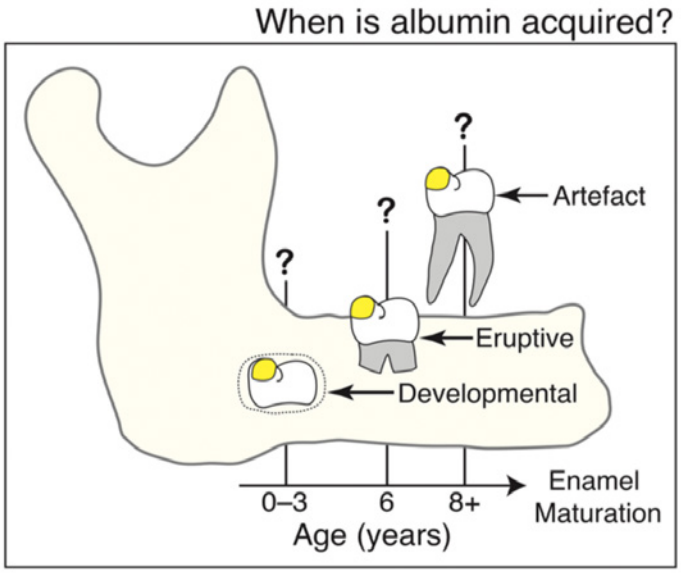
than its formative cells (***ameloblasts***), subsequent researchers including D3 guru **Grace Suckling** favoured the opposite. Consequently, a **40-year dogma** has centred on the notion of **injured ameloblasts** triggering hypomineralisation. With traumatic injuries *(e.g. front teeth of a fallen toddler)*, it's easy to envisage localised patches of ameloblasts being damaged. But for the **idiopathic** demarcated opacities that define **Molar Hypomin**, a logical connection to presumed systemic causes *(e.g. illness or medicines)* has been sorely lacking. Strong hints of "**barking up the wrong tree**" came from a **2010 D3G study** showing that chalky enamel was predominated by a blood protein, **serum albumin**. However, before accepting this alternative idea, it was necessary to prove that albumin actually ***caused*** the chalkiness *(porosity)*, rather than later sticking **adventitiously** *(e.g. blood contamination during extraction)* to existing porosity caused by something else. **Rebecca Williams** and fellow D3ers have addressed this tricky question by developing a new biochemical test and showing that chalky enamel from 6-year molars contains traces of **alpha-fetoprotein**, a "**baby albumin**" which disappears from blood during early infancy.



This breakthrough finding **directly links albumin to the medical onset of MH in babies** and shifts attention to **enamel mineralisation being "poisoned"** by localised exposure to tissue fluid or blood. However, before leaping to medical significance, some additional questions need to be answered – read more **here**, and watch this space!

Clinical Feature: *Does childhood asthma cause MH?*

A potential association between asthma and demarcated opacities – and hence Molar Hypomin – was first investigated by **Grace Suckling** **33 years ago**. No strong link was found and multiple studies since have been inconclusive. To many, a causal link seems attractive because both conditions are common in children, and some maintain MH prevalence is increasing like that of asthma. A contrarian view notes that asthma *(and allied medication use)* usually manifests later in childhood than infancy when the developing 2-year and 6-year molars become malformed – hence a hypothesis about disease mechanism seems lacking. In 2010, D3 friend **Dorte Haubek** reported a possible link with severe cases of MH – **that study** benefited from using medical records to verify exposure to asthma medications but the results didn't reach statistical significance. In a new study, the group has bolstered their approach by using older children *(i.e. longer exposures to asthma drugs)*, a larger group of subjects, and several medical variables to assess aetiological confounding. Moreover, this follow-up tested the hypothesis that corticosteroids *(as used to treat asthma, with known side effects on bone growth)* might affect enamel formation. Remarkably, 37% of the 9-year old children had used asthma drugs, but no overall link was found to MH – even in those children hospitalised due to asthma. Initially, the relatively few kids treated with corticosteroid were found to have a 1.5-fold higher risk for MH but this disappeared after confounding factors

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were considered. Several other aetiological factors *(e.g. premature birth, neonatal asphyxia and/or hospitalisation, antibiotics, maternal smoking)* were also ruled out. We think this approach, combining the convenience of a cross-sectional population study with the strength of comprehensive medical records, stands to provide further insights to MH – all that's needed are some well-focussed and substantiated hypotheses to test. Read more **here**.

Other New Reports: *Spotlighting Molar Hypomin*

Aesthetic perception in children with molar incisor hypomineralization. Fragelli C, Barbosa TS, Bussaneli DG, Restrepo M, Cordeiro RCL, Santos-Pinto L. *Eur Arch Paediatr Dent.* 2020; Epub ahead of print. **PMID: 32524329**

Distribution and morphology of enamel hypomineralisation defects in second primary molars. Vlachou C, Arhakis A, Kotsanos N. *Eur Arch Paediatr Dent.* 2020; Epub ahead of print. **PMID: 32524328**

Esthetic Management of Incisors with Diffuse and Demarcated Opacities: 24 Month Follow-up Case Report. Athayde GS, Jorge RC, Americano G, Barja-Fidalgo F, Soviero VM. *Oper Dent.* 2020; **PMID: 32516394**

Transillumination-aided infiltration: A diagnostic concept for treating enamel opacities. Marouane O, Chtioui F. *J Esthet Restor Dent.* 2020; Epub ahead of print. **PMID: 32497384**

Molar incisor hypomineralization and celiac disease. Kuklik HH, Cruz ITSA, Celli A, Fraiz FC, Assunção LRDS. *Arq Gastroenterol.* 2020; Epub ahead of print. **PMID: 32490904**

Determinants of children's oral health-related quality of life following aesthetic treatment of enamel opacities. Hasmun N, Vettore MV, Lawson JA, Elcock C, Zaitoun H, Rodd HD. *J Dent.* 2020; 98:103372. **PMID: 32437856**

Saliva proteomic patterns in patients with molar incisor hypomineralization. Bekes K, Mitulović G, Meißner N, Resch U, Gruber R. *Sci Rep.* 2020; 10(1):7560. **PMID: 32371984**

Esthetic rehabilitation of anterior teeth with molar-incisor hypomineralization and dental fluorosis: a case report. Cavalheiro JP, Souza MIAV, Duque CCO, Bussaneli DG, Zuanon CC, Jeremias F. *Gen Dent.* 2020; 68(3):34-39. **PMID: 32348241**

Use of asthma drugs and prevalence of molar incisor hypomineralization. Wogelius P, Viuff JH, Haubek D. *Int J Paediatr Dent.* 2020; Epub ahead of print. **PMID: 32294280**

Estimating molar-incisor-hypomineralization among 8-year- olds based on 15-year public oral health practice-based data. Tseveenjav B, Furuholm J, Mulic A, Valen H, Maisala T, Turunen S, Varsio S, Auero M, Tjäderhane L. *Acta Odontol Scand.* 2020; Epub ahead of print. **PMID: 32293217**

Factors Associated with Molar-Incisor Hypomineralization: A Population-Based Case-Control Study. Lee DW, Kim YJ, Oh Kim S, Choi SC, Kim J, Lee JH, Kim HJ, Shin J, Lee NY, Kim SM, Ra J, Kim J, Yang YM. *Pediatr Dent.* 2020; 42(2):134-140. **PMID: 32276681**

Prevalence of hypomineralised second primary molars (HSPM) in Syrian preschool children. Halal F, Raslan N. *Eur Arch Paediatr Dent.* 2020; Epub ahead of print. **PMID: 32266665**

The relationship between molar incisor hypomineralization, dental caries, socioeconomic factors, and polymorphisms in the vitamin D receptor gene: a population-based study. Fatturi AL, Menoncin BL, Reyes MT, Meger M, Scariot R, Brancher JA, Küchler EC, Feltrin-Souza J. *Clin Oral Investig.* 2020; Epub ahead of print. **PMID: 32236726**

Quantitative evaluation of masking effect of resin infiltration on developmental defects of enamel. Khanna R, Chandra A, Singh RK. *Quintessence Int.* 2020; 51(6):448-455 **PMID: 32368763**

Developmental Enamel Defects (DDE) and Their Association with Oral Health, Preventive Procedures, and Children's Psychosocial Attitudes towards Home Oral Hygiene: A Cross-Sectional Study. Nota A, Palumbo L, Pantaleo G, Gherlone EF, Tecco S. *Int J Environ Res Public Health.* 2020; 17(11):E4025. **PMID: 32516977**

Microbiology of molar-incisor hypomineralization lesions. A pilot study. Hernandez M, Planells P, Martinez E, Mira A, Carda-Dieguez M. *J Oral Microbiol.* 2020; **Open access**

Assessment of enamel permeability using scanning electron microscopy in permanent teeth with and without Molar Incisor Hypomineralisation – an in vivo study. Krishnan R, Al Wadei MM, Al Qahthani MT, Albeshri E, Ramesh M, Assiri YH, Sabarinathan J. *J Clin Diag Res.* 2020; 14(2):18-22 **Open access**

Prevalence and Treatment Need of Molar Incisor Hypomineralisation in 8-12 Year Old School Going Children of Cuttack, Odisha. Ray P, Mohanty UK, Sethi D, Mahakur M, Sharma G. *J Clin Diag Res.* 2020; 14(3):5-9 **Open access**

Dental Caries, Developmental Defects of Enamel and Enamel Microhardness Associated with Genetic Polymorphisms in the RANK/RANKL/OPG System. Calvano Küchler E, Maschietto Pucinelli C, Carpio Horta K, Assed Bezerra da Silva R, de Castro Costa M, Rezende Vieira A, Nelson-Filho P, Assed Bezerra da Silva L, Santos Antunes L, Azeredo Antunes L. *J Clin Pediatr Dent.* 2020; 44(1):35-40. **PMID: 31995419**

Decline in Dental Fluorosis Severity during Adolescence: A Cohort Study. Curtis AM, Levy SM, Cavanaugh JE, Warren JJ, Kolker JL, Weber-Gasparoni K. *J Dent Res.* 2020; 99(4):388-394. **PMID: 32091961**

Fluoride exposure alters Ca^{2+} signaling and mitochondrial function in enamel cells. Aulestia FJ, Groeling J, Bomfim GHS, Costiniti V, Manikandan V, Chaloemtoem A, Concepcion AR, Li Y, Wagner LE 2nd, Idaghdour Y, Yule DI, Lacruz RS. *Sci Signal.* 2020; 13(619):eaay0086. **PMID: 32071168**

For more Molar Hypomin reports see 2020 editions of D3G Dispatch and also go here >

SUGGESTIONS BOX

In D3 family spirit, please **contact us** to share your thoughts on how we might improve this newsletter and other communications.

Answers to quiz:
Q1: Yes *(see **here**)*

Q2: Only subject to dental intervention given Molar Hypomin is the principal risk factor *(see **here**)*

Towards better understanding and care of people with D3s.