Journal of Dental Sciences 17 (2022) 1387–1400

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-jds.com

Review article

Risk factors for and prevention of caries and dental erosion in children and adolescents with asthma

Ulla Moberg Sköld [a], Dowen Birkhed [b], Jian-Zhi Xu [c], Kai-Hua Lien [c], Malin Stensson [d], Jeng-Fen Liu [c,e*]

[a] Department of Cariology, University of Gothenburg, Göteborg, Sweden
[b] Former: Department of Cariology, University of Gothenburg, Göteborg, Sweden
[c] Pediatric Dentistry, Taichung Veterans General Hospital, Taichung, Taiwan
[d] Centre of Oral Health, School of Health Sciences, Jönköping University, Jönköping, Sweden
[e] School of Dentistry, National Yang Ming Chiao Tung University, Taipei, Taiwan

Received 19 February 2022; Final revision received 16 March 2022
Available online 9 April 2022

KEYWORDS
Children;
Adolescents;
Asthma;
Caries;
Dental erosion;
Prevention

Abstract There are many studies and reviews of the relationship between the asthma disease in young individuals on the one hand and caries and dental erosion on the other. The causes of caries and dental erosion might be related to the asthmatic drugs, low pH and the sweeteners that the inhaled drug contains and perhaps even the lifestyle of children and adolescents with asthma. The main focus of this review is therefore to describe various preventive strategies, based on long experience of preventive dental care in Sweden. Two fact boxes are presented, one on fluoride toothpaste as a population-based intervention for different ages and one on diet counselling in children and adolescents with asthma. The most important thing is to introduce fluoride toothpaste early in the child's life and that the parents brush the child's teeth twice a day, in the morning after breakfast and at night before bedtime, up to the age of 10. Moreover, a high-risk approach with an additional fluoride supply at home is presented, together with the application of fluoride varnish at the clinic. Regarding diet counselling, it is important to make sure that the child has regular meals during the day, maximum five to six times a day, to allow the teeth to rest between meals and restrict sweets and soft drinks to once a week. It is important to identify children and adolescents with asthma as early as possible and to refer them to a dental team for preventive treatment.

* Corresponding author. Taichung Veterans General Hospital, 1650 Sec. 4, Taiwan Boulevard, Taichung, 40705, Taiwan. Fax: +886 4 22087126.
E-mail addresses: jengliu@vghtc.gov.tw, jengfen1124@yahoo.com.tw (J.-F. Liu).

https://doi.org/10.1016/j.jds.2022.03.007

Introduction

It is well known that the asthma disease can affect and impair oral health in children and adolescents; the present review addresses various aspects of this issue.

When searching for literature in PubMed, more than 1000 publications were found with the MeSH terms < asthma + oral health + children> and more than 100 on < asthma + dental caries + children>. This indicates that there is great interest in these aspects around the world. Some of the studies were published more than 50 years ago, but the majority were published during the last two decades, in parallel with improvements in the early diagnosis of the disease and in modern medication against asthma.

Earlier reviews illustrate the relationship between asthma on the one hand and caries and dental erosion on the other among children and adolescents. Most of these studies show an association, but very few take up prevention from caries and dental erosion in their reviews.[1,2] Harrington et al., however, describe different strategies to keep the teeth healthy in children with asthma.[3]

Since there are few studies of caries prevention in children and adolescents with asthma, we believe it is important to take advantage of the extensive knowledge that is available for general populations.[4] To our knowledge, no longitudinal studies of the prevention of dental erosion in children and adolescents with asthma have been published. However, there are several reviews of preventive strategies, where dietary counselling, the use of fluorides, tooth brushing and saliva stimulants play an important role in the prevention of dental erosion.[5] The interventions to prevent caries and dental erosion should be implemented at an early stage in the asthma disease when the teeth are still free from disease.

Against this background, the aim of the present review was to focus on both aetiological factors and ways of preventing caries and dental erosion in children and adolescents with asthma.

Asthma in children and adolescents

Definition

Asthma has been defined as a common chronic disorder of the airways that is complex and characterised by variable and recurring symptoms, airflow obstruction, bronchial hyper-responsiveness and an underlying inflammation.[6]

Epidemiology

Asthma is one of the most common chronic and non-communicable diseases affecting all age groups and it is a serious global health problem. Moreover, it is the most common chronic disease among children and adolescents according to the World Health Organisation (WHO).[7] They report that more than 262 million people were affected by asthma globally in 2019 and that asthma caused 461,000 deaths[7,8] The global prevalence of self-reported, physician-diagnosed asthma in adults is 4.3%, with wide variations between countries.[9] Prevalence is higher in developed countries and lower in developing countries.[10] Greater variations are seen for asthma symptoms in children, ranging from 2.8% to 37.6% in children aged six to seven years and from 3.4% to 31.2% in children aged 13—14 years.[9,11] Among children, asthma prevalence is higher in boys than in girls; however, prevalence is around 20% higher in women than men, indicating a switch during puberty.[9,12] Higher prevalence in boys is partly due to their smaller airways relative to lung size compared with young girls and this pattern reverses during adolescence.[9] Many infants wheeze early in life, but three in four school-aged children outgrow asthma by adulthood.[13]

Symptoms

Asthma symptoms are non-specific. The classic signs and symptoms of asthma include a cough, wheeze, shortness of breath and chest tightness, which are intermittent and usually progress at night or during exercise. Triggers differ from person to person and can include viral infections, dust, smoke, fumes, changes in the weather, grass and tree pollen, animal fur and feathers, strong soaps and perfume.[7] Symptoms may resolve spontaneously or as a good response to medication and they may sometimes be absent for weeks or months. On the other hand, patients can experience episodic flare-ups, exacerbations, of asthma which can be life-threatening and impose a significant burden on patients and the community. The status of airway inflammation usually persists, even when symptoms are absent or lung function is normal, but it may normalise with treatment.[4]

Diagnosis

Tools for diagnosing asthma include history-taking, physical examination, pulmonary function testing and laboratory evaluations. The diagnosis of asthma is based primarily on identifying both a characteristic pattern of respiratory symptoms, such as wheezing, dyspnea, chest tightness or cough, and variable expiratory airflow limitation.[4,14] In children aged five years and younger, reduced activity and past or family history are additional features that can help to diagnose asthma.[4] In children, tiredness, irritability and difficulty concentrating are typical of poorly controlled asthma.[15] The Global Initiative for Asthma (GINA) and the National Asthma Education and Prevention Program (NAEPP) base initial therapy on an assessment of asthma symptoms, respiratory impairment and the risk of poor asthma outcomes.[4,6] The pattern of symptoms is important, as respiratory symptoms may be due to acute or chronic conditions other than asthma. It is often more difficult to confirm a diagnosis of asthma once the patient has been started on control treatment.[4] Recurrent wheezing occurs in a large proportion of children aged five years and younger, typically with viral upper respiratory tract infections. Deciding when this is the initial presentation of asthma is difficult.[4]

Phenotype

Asthma is a heterogeneous disease, with different underlying disease processes. Recognisable clusters of demographic, clinical and/or pathophysiological characteristics are often

called "asthma phenotypes".[4,16–18] Some of the most common phenotypes are allergic asthma, non-allergic asthma, adult-onset (late-onset) asthma, asthma with persistent airflow limitation and asthma with obesity.[4] New-onset asthma in adulthood sometimes originates from undiagnosed childhood asthma.

Medical treatment of children and adolescents with asthma

The main goals of asthma management in children and adolescents are effectively controlling the symptoms and preventing and minimising the risk of asthma exacerbations.[4,6] Avoiding asthma triggers can also help to reduce asthma symptoms.[7] Pharmacological treatment is the mainstay of management in most patients with asthma.[19] The choice of medication is based on the age of the patient (e.g. ≥12 years, 5–11 years, 0–4 years), symptoms, lung function, risk factors for exacerbations, patient preference and practical issues such as the ability to use the medication delivery device, or the accessibility of medication. National and international guidelines advise initiating pharmacological therapy based on the frequency and severity of symptoms and then adjusting therapy up or down, as needed, according to a "stepwise approach", although some of the details differ between guidelines.[4,6] The most commonly used control medications for children younger than 12 years of age are inhaled glucocorticoids (also called inhaled corticosteroids [ICSs]), plus inhaled long-acting beta agonists (LABAs) or oral leukotriene receptor antagonists (LTRAs) in combination with ICSs. Long-acting anticholinergic agents (or long-acting muscarinic antagonists [LAMAs]; tiotropium, for children ≥6 years of age) and biological agents (monoclonal antibodies against immunoglobulin E [IgE] and interleukin [IL] 5, for children ≥6 years of age) are used as step-up therapy in patients whose asthma is not effectively controlled on other medications. Oral glucocorticoids; inhaled chromones; and sustained-release oral theophylline are rarely used for daily asthma control.[4] In adults and adolescents, GINA no longer recommends short-acting beta-agonist (SABA)-only treatment for Step 1 and recommends that all adults and adolescents with asthma should receive ICS-containing control treatment, to reduce the risk of serious exacerbations.[20] The ICS can be delivered by regular daily treatment or, in mild asthma, by as-needed low-dose ICS formoterol.[20] The GINA 2021 treatment figure for adults and adolescents shows two "tracks", based on evidence relating to outcomes with the two reliever choices across asthma severity.[4] Track 1 is the preferred approach, which means using ICS formoterol as the reliever, and can reduce the risk of exacerbations. Track 2, with SABA as the reliever, is an alternative approach which is used when Track 1 is not possible, or is not preferred by a patient with no exacerbations on their current control therapy.[4] Maintenance and reliever therapy (MART) in Steps 3–5 with an ICS-formoterol reliever reduces the risk of severe exacerbations compared with regimens with a SABA reliever.[4] Patients with the phenotype of allergic asthma usually respond well to inhaled corticosteroid (ICS) treatment, while patients with non-allergic asthma often demonstrate a poorer short-term response to ICS.[4] Severe asthma is asthma that remains uncontrolled despite optimised treatment with high-dose ICS-LABA, or that requires high-dose ICS-LABA to prevent it from becoming uncontrolled.[4] Treatment may be stepped up or down within a track using the same reliever at each step, or switched between tracks, according to the patient's needs and preferences.[4]

Caries and dental erosion in primary and permanent teeth

In Taiwan, the prevalence of caries in children under nine years of age with asthma was significantly higher than that in children without asthma.[21] According to the results of the meta-analyses, the risk of caries was approximately 1.5–2 times higher in relation to asthma in both the primary and permanent dentition.[1,22] However, it revealed a wide age range among these participants who were mainly around 0–19 years of age As we all know, the aetiology of caries mainly involves factors of tooth susceptibility, bacterial plaque, refined carbohydrates and time. Other variables, such as oral sugar clearance, salivary flow and pH and immune factors, add to the complexity of this process. Some studies have shown that DMFT was not significantly higher in patients with asthma.[23] Another study revealed that, regardless of asthma type and severity, only the use of salbutamol, a type of β2-agonist, increases caries.[24] Children and adolescents with asthma also run a higher risk of dental erosion in both the primary and permanent dentitions. Statistically significant higher values in the primary dentition are presented, especially in children with severe asthma, although the definition of severe asthma was not given.[25] Dental erosion is the loss of dental hard tissue caused by acids, including intrinsic factors such as acid reflux and excessive vomiting and/or extrinsic factors such as diet and carbonated soft drinks. Those who are diagnosed with gastro-esophageal reflux are also predicted to have greater degrees of dental erosion.[2,26] Interestingly, recent studies have shown that inhalers which contain β-agonists lead to the dilation of the lower esophageal sphincter, which in turn causes gastro-esophageal reflux.[2] Furthermore, some powdered asthmatic drugs create a pH of less than 5.5.[27] However, several studies have shown that there was no statistically significant difference between the type and pH of inhaler used and the degree of dental erosion. Further, no association was found between the duration of the medication that was taken and the severity of dental erosion.[24,26] It may probably be due to the other aetiological factors of dental erosion, including lifestyle habits, such as the consumption of acidic food or drinks. One common symptom of dental erosion is dentine hypersensitivity and it is also considered significant in patients with asthma in their permanent teeth. Nor was there any association between the severity of dental erosion and gender, type and the duration of medication.[26] However, some studies showed that there was no significant difference in dentine hypersensitivity between the two groups.[28]

Risk factors for caries and dental erosion in children and adolescents with asthma

There are multiple factors that can put children and adolescents with asthma at risk of caries. The causes might be

related to the mechanism of the asthmatic drugs, low pH and the sweeteners that the inhaled asthmatic drug contains, as well as the lifestyle of children and adolescents with asthma.

Mechanism of the asthmatic drug

Asthmatic drugs indirectly play a significant role in caries through the adverse effect of beta-2 agonist anti-asthmatics in reducing the salivary flow rate.[29] Saliva has a beneficial effect on reducing caries due to four main actions: physical cleansing, antibacterial effect, buffering capacity and super-saturation with calcium phosphate.[3] Ryberg et al.[30] reported that overall salivary flow decreased by 26% and parotid flow was reduced by 36% in the group with asthma compared with the control group. Moreover, patients with asthma who take beta-2 agonist anti-asthmatics also show a modification in stimulated salivary components, such as a decrease in total protein, amylase, hexosamine, salivary peroxidase, lysozyme and secretory IgA.[31] Taken together, reducing the quantity and quality of saliva may therefore significantly increase the risk of caries. From a microbial point of view, children and adolescents with asthma undergoing treatment with short-acting β2-agonists may influence their caries susceptibility, with significantly higher *S. mutans* and lactobacilli colonies in saliva testing.[32] Children and adolescents with asthma were also found to have a significantly low salivary flow rate, pH and buffering capacity, as well as high mutans streptococci and lactobacilli levels, compared with adolescents without asthma.[33] These findings may contribute to the higher risk of caries rate in children and adolescents with asthma. The beta-2 agonist anti-asthmatics used as bronchodilators to reverse the airway obstruction and act as smooth-muscle relaxants could induce the significant relaxation of other smooth muscles, such as the lower esophageal sphincter. This relaxation is associated with gastro-esophageal reflux, which is considered to be a factor in the aetiology of dental erosion.[25]

The low pH and the sweeteners that inhaled asthmatic drugs contain

Children and adolescents with asthma are more susceptible to caries progression, since anti-asthmatic drugs have a relatively low pH and also contain sweeteners and fermentable carbohydrate.[34,35] In order to mask the bitter medication taste and improve patient tolerance, 60% of the powder inhaled drugs contain fermentable carbohydrates in the form of lactose. Although lactose is one of the least cariogenic sugars used to deliver beta-2 agonists, the frequent oral inhalation of sugar, combined with the decrease in salivary flow rate, may contribute to an increase in caries experience.[36] Moreover, Tootla et al.[37] found that a dry powder inhaler consistently produces a pH below 5.5, indicating its cariogenic potential. Kargul et al.[38] concluded that, during the first 30 min of inhalation, the pH of saliva decreases significantly. The pH of plaque (pH = 5.5) dropped to a pH lower than that required for enamel demineralisation. The prolonged use of inhaled drugs lowers pH and reduces salivary flow, leading to the increased colonisation of streptococcus and lactobacillus, which plays a significant role in caries.[39] Furthermore, the inhaled therapy is often taken at night, before going to bed. Owing to low patient and parent awareness, no oral hygiene measures were usually taken after the medication. The diminution of salivation and the lack of masticatory movements during the night might have further increased the cariogenic potential of the medicines.[40]

The lifestyle of asthmatic children

Children with asthma often lead restricted lifestyles, missing many school days, not being able to play sports and participate in normal activities, so the family may tend to indulge them with the frequent consumption of sweets that leads to an increase in caries.[40] In addition, these children usually develop mouth-breathing habits due to the frequent airway obstruction, which in turn results in the dehydration of the oral mucosa and creates a feeling of thirst.[25] To compensate for this oral drying, patients with asthma may regularly consume liquids. The continual masking of the bitter medication taste, thirst quenching with carbohydrate drinks, combined with reduced salivary protection may be a major contributor to caries among these patients.[41]

Others

In patients with asthma, due to the reduced oxygen supply to activate ameloblasts, enamel formation is often impaired, which results in enamel defects, leading to the decreased tolerance of acid in the tooth.[38] Respiratory disease in the early years of life can affect tooth formation and contribute to the development of hypomineralised enamel lesions that affect DMFS.[38,42,43] Further, in the exhaled breath of people with inflammatory airway disease, the concentration of nitric oxide increases.[39] In water, nitrous oxide transforms into nitric acid and, as the oral cavity is fairly moist, the risk of the demineralisation of dental hard tissues increases.[44] Saliva has a beneficial effect on reducing caries due to four main actions: physical cleansing, antibacterial effect, buffering capacity and super-saturation with calcium phosphate.

Preventive strategies against caries and dental erosion among children and adolescents with asthma

Since there are few longitudinal studies of caries prevention, it is important to take advantage of the extensive knowledge that is available in the literature for general populations.[45] To our knowledge, no longitudinal studies of the prevention of dental erosion in children and adolescents with asthma have been published, although there are several reviews of preventive strategies in general.

Even now, in the 21st century, caries remains a global health problem, as 573 million children worldwide have untreated caries in their primary teeth and untreated caries in permanent teeth affects 2.5 billion people.[46] In its early stages, caries is a reversible process and, even in its more advanced stages, it can be arrested.[47] Sugar is undoubtedly

the most important dietary factor for caries development and has been described as the arch-criminal.[48,49] The relationship between sugar consumption and caries has been known since the 1950s. Factors that influence this relationship are the availability of fermentable carbohydrates, such as sugar and starch, acidogenic bacteria, fluoride and the amount and quality of saliva. Fluoride plays a key role in successful caries prevention by reducing demineralisation, promoting remineralisation and the widespread use of fluoride has dramatically reduced the prevalence of caries and the rate of the progression of caries lesions.[50,51] These changes enable dentists and dental hygienists to adopt more conservative management strategies directed at the prevention and cure of caries. Fluoride, and especially the daily use of fluoride toothpaste, is the single factor that has the greatest importance for the improvement in dental health among children and adolescents in the last 40 years.[52–54] Fluoride prevention is even more important today, owing to the frequent intake of sweet drinks, sweets and easily fermentable carbohydrates.[55]

The prevalence of dental erosion is growing steadily and is becoming an increasingly important factor when considering the long-term health of the dentition.[56] Today, erosive dental tooth wear in children is a common condition.[57] Extrinsic or intrinsic acids are the main causes of dental erosion. The potential risk factors are changes in lifestyle and the frequent consumption of acidic beverages and foods.[58] In dental erosion, the effects of fluoride supply differ from those of caries because of the missing biofilm in the erosive process, as well as the lower pH of the acids compared with bacterial acids. In order to achieve a preventive effect, it is necessary to use products with a higher fluoride concentration and to increase the frequency of application. Furthermore, the fluoride compound plays a role; fluoride combined with stannous or titanium ions and stannous ions are found on the surface but are also incorporated in the enamel and dentine, making the tooth surface more resistant to acid demineralisation.[59] Early diagnosis, correct intervention and prevention are key factors when it comes to minimising the risk of developing caries and dental erosion among children and adolescents with asthma, with the ultimate goal of preserving healthy teeth. To achieve this, children and adolescents must follow basic prevention rules relating to diet, drug administration, fluoride and oral hygiene. Since these patients also run a high risk of caries and dental erosion, there is a need for a high-risk approach and it is therefore important to educate children and their parents and adolescents about the increased susceptibility to oral diseases and to encourage regular dental check-ups with extended fluoride supply with a frequency of three to six months, depending on the severity of the asthma disease and follow recommendations relating to diet and supplementary fluoride products.

Population-based fluoride prevention

Fluoride toothpaste

Toothbrushing with fluoride toothpaste is inexpensive, culturally approved and widespread and it is therefore a convenient way for population-based prevention for all ages to control caries and dental erosion. Moreover, its correct use is important for children and adolescents with asthma.[60] Many systematic reviews have confirmed its efficacy in preventing caries in children and adolescents, with an average reduction of 24% in decayed, missing and filled tooth surfaces (DMFS).[53,61–65] The caries-preventive effect depends on several determining factors and, to achieve the maximum effect, it is important to take advantage of all these factors. There is a dose–response effect related to fluoride concentration which means that toothpaste with a higher fluoride concentration, 1500 ppm fluoride, yields a better effect than toothpaste with 1000 ppm and the caries-preventive effect is only statistically significant for concentrations of 1000 ppm fluoride and above.[65,66] Brushing twice a day improves caries protection versus brushing once a day, or less frequently.[67,68] Brushing with 1.5 g toothpaste compared with 0.5 g more than doubled the fluoride recovered in saliva after brushing.[69] A Swedish study reported a 47% increase in fluoride concentration interproximally when the amount of toothpaste is increased from 1 to 2 cm.[70] A longer brushing time firstly progressively reduces the retention of dentifrice on the brush, thereby increasing the amount delivered into the mouth, and secondly increases the fluoride concentration in saliva for at least 2 h after the end of brushing.[69] Increasing the brushing time to 2 min instead of 1 min produces a 27% higher interproximal fluoride concentration.[70] Less rinsing or not rinsing at all with water during and after brushing confers a greater caries reduction than rinsing with a great deal of water.[67,68,71,72] Reducing the amount of water from 20 to 10 ml results in a 41% higher fluoride concentration interproximally.[70] Furthermore, rinsing with the toothpaste slurry afterwards is even better.[73,74] Supervised brushing yields a better effect than unsupervised brushing, probably because of greater compliance.[53] The fluoride compounds most commonly used are sodium fluoride NaF and sodium monofluorophosphate SMFP, with the same documented effect on caries. On the other hand, the use of tin-containing fluoride toothpaste, such as stannous fluoride SnF_2, might provide the best approach for the effective prevention of dental erosion, probably because of the content of tin.[75]

As basic prevention, all children and adolescents with asthma should use fluoride toothpaste in an appropriate way twice daily against caries and dental erosion. It is important to give clear-cut advice and encourage parents to start tooth-brushing with fluoride toothpaste as soon as the first deciduous tooth erupts and then use a "rice-sized" amount of very mild 1000 ppm fluoride toothpaste up to two years of age. From the age of two years, the amount of toothpaste should increases to "pea size" and, from six years of age, the routine should be 1450 or 1500 ppm fluoride toothpaste on the full brush length.[53,55,69] The use of toothpastes with candy-like flavours in children less than six years of age should not be encouraged.[51] It is important to emphasise that the appropriate amount of toothpaste is used, the benefit of brushing twice daily and that parents assist children with tooth-brushing up to the age of 10 years. Good habits established at an early stage maintain lifelong protection. For children under the age of four years, care must be taken to ensure that there is a balance between maximising the preventive effect against caries and dental erosion and minimising the risk of dental

fluorosis, since children at these ages swallow a large amount of the toothpaste.[55] After the age of six years, only the third molars are subject to mineralisation and this explains why the risk of dental fluorosis is minimised. For detailed information about the age-adjusted concentration and amount of fluoride toothpaste see Fig. 1.

High-risk approach with additional fluoride supply at home

High fluoride toothpaste

Toothpastes containing up to 5000 ppm fluoride are available on prescription or free over the counter in many countries and can be used as an additional fluoride supply for individuals running a high risk of caries or of dental erosion, especially when addressing the burden of disease in hard-to-reach groups such as adolescents of caries risk ages, 12—16 years. During these years, adolescents often change their way of living and consume a great deal of junk food and sweets and are careless about optimal toothbrushing. There is a well-established dose—response relationship between the concentration of fluoride present in toothpaste and caries prevention.[76] The highest probability of caries-preventive benefits was found in those toothpastes containing higher fluoride concentrations, which are also of great value in reducing dental erosion.[65] A high content of fluoride in toothpaste increases the fluoride retention in both saliva and plaque and without water rinsing after toothbrushing. The fluoride concentration in approximal saliva was more than twice as high compared with no water rinsing after toothbrushing with 1450 ppm fluoride toothpaste in adolescents.[77] A forty per cent lower caries progression was found among caries-active 14—16 year olds using 5000 ppm fluoride toothpaste compared with those of the same ages using 1450 ppm fluoride toothpaste.[78] Scientific data may indicate that 5000 ppm toothpaste has a greater impact on individuals who do not use toothpaste regularly or do not brush twice a day.[79]

Fluoride mouth rinse

Fluoride mouth rinse was introduced at schools in Sweden in the 1960s, every week or every second week for all schoolchildren, with a documented caries decline of 20—50%.[80] After two decades, this school-based programme was abandoned, as the daily use of fluoride toothpaste became routine in society. A review by Marinho et al.[81] of 34 studies involving 14,600 children and adolescents concluded that the regular and supervised use of fluoride mouth rinse by children was associated with a clear reduction in caries increment, with a reduction in D(M)FS of 27%, if the effect of fluoride toothpaste was excluded. The combined effect of fluoride toothpaste and fluoride mouth rinse produced an additional 10% effect compared with fluoride toothpaste alone.[82] Most of the evaluated studies used supervised school-based rinsing, but the findings may be applicable to children in other settings with supervised or unsupervised daily rinsing at home.[83,84] The caries levels in these reviews were defined as being clinically or radiographically recorded at dentine level, thus excluding caries lesions in enamel. If the diagnostic threshold was enamel lesions on approximal surfaces, rinsing with a 0.2% sodium fluoride solution on the first three and the last three schooldays of every term yielded a prevented fraction of 59% among 13—16 year olds.[85] The effect of rinsing depends on several factors, such as fluoride concentration, frequency of application, timing of rinsing, rinsing volume, rinsing time, supervised rinsing or not, fluoride mouth rinsing after fluoride toothpaste or not.[86] Today, daily rinsing is applied compared with the previous weekly or fortnightly rinsing. Ten ml of the solution should be swished around the mouth for 1 min and the patient should not eat or drink for 20—30 min after application. Dry-mouth children and adolescents obtain a much higher fluoride concentration in the saliva and the rinsing time can therefore be reduced to 30 s.[87] Supervised use by parents is more efficacious than unsupervised.[81,84] Behaviour after rinsing has the potential to either reduce or enhance the effectiveness of fluoride toothpaste. Using a fluoride rinse with too low a fluoride concentration after brushing with 1450 ppm fluoride toothpaste will result in a wash-out effect on fluoride and it is therefore important to have a fluoride concentration that is high enough in the solution.[88] This study showed that a 0.2% sodium fluoride solution with 900 ppm fluoride produced the highest fluoride retention in saliva compared with solutions with lower fluoride concentrations and is the concentration that should be used in order to take advantage of the additional effect of fluoride after brushing with 1450 ppm fluoride toothpaste. Another study showed that a 500 ppm fluoride mouth rinse provided a significant increase in fluoride retention compared with the 225 ppm fluoride rinse after brushing with 1450 ppm fluoride toothpaste.[89] With the support of the scientific literature, the use of a daily fluoride mouth rinse at home is recommended from the age of six years for children and adolescents with asthma, supplementary to the appropriate use of fluoride toothpaste. Between the age of six and 10 years, the fluoride concentration should be 225 ppm fluoride in a 0.05% sodium fluoride solution and, from 10 years of age, 900 ppm fluoride in a 0.2% sodium fluoride solution. Fluoride mouth rinse is not generally recommended for children below the age of six years, because most young children lack the ability to spit out effectively.

Fluoride tablets and chewing gums

Fluoride tablets and lozenges could be regarded as a supplement to the appropriate use of fluoride toothpaste, as children and adolescents with asthma suffer from dry mouth because of their medication. It is better to suck on a fluoride tablet than on a sugar-containing tablet in order to stimulate the salivary flow rate. The first option is, however, to improve the quality of tooth brushing with fluoride toothpaste or use a higher concentration of fluoride toothpaste. Two systematic reviews of fluoride tablets and lozenges concluded that there might be an effect on caries in the permanent dentition, but there was no clarity in terms of the effect on the primary dentition and both reviews examined older studies, conducted at a time when topical fluorides were not widely used.[90,91] To control the amount of fluoride children less than six years of age ingest, fluoride tablets should not be recommended for children below this age. It is much better to ensure that tooth brushing with the correct amount of fluoride toothpaste is performed by parents at least twice a day. To compensate

<table>
<tr><th colspan="3">Fluoride toothpaste as a population-based intervention for different ages</th></tr>
<tr><th>Children 0-2 years</th><th>Children 2-6 years</th><th>From 6 years of age</th></tr>
<tr><td>Parents introduce brushing once the first tooth erupts

Hold the child on the lap during brushing

Use 1000 ppm F toothpaste with a very mild taste

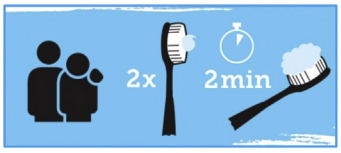
Brush twice a day, in the morning after breakfast and at night before bedtime

Do not rinse with water after brushing</td><td>Parents brush the child´s teeth twice a day, in the morning after breakfast and at night before bedtime

Use 1000 ppm F toothpaste with a very mild taste

The child should spit out the excess of toothpaste

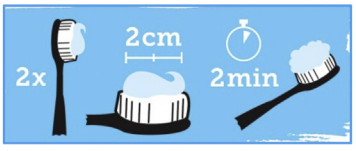
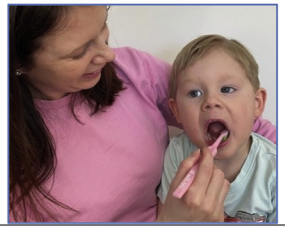
Do not rinse with water after brushing

  </td><td>Parents help the child up to 10 years of age to brush the teeth twice a day, in the morning after breakfast and at night before bedtime

Use 1450 ppm F toothpaste with a mild taste

Brush for at least 2 minutes

Rinse with the toothpaste slurry and spit out carefully

  </td></tr>
<tr><td> 
  </td><td>  </td><td> 
  </td></tr>
<tr><td>Use F toothpaste with a size of a rice grain

  </td><td>Use F toothpaste with a size of a pea

  </td><td>Use toothpaste on the full length of the toothbrush (2 cm)
Apply toothpaste twice on the electric brush

  </td></tr>
</table>

Figure 1 Fluoride toothpaste as a population-based intervention for different ages.

for dry mouth, there is consistent evidence to support the use of xylitol- and sorbitol-containing chewing gum as part of normal oral hygiene to prevent caries and dental erosion, rather than using sugar-containing chewing gums.[92]

Drug administration and fluoride supply

To minimise the negative effects of medication and help prevent caries and dental erosion, the inhaled asthma therapy must be followed by some sort of fluoride supply. The patients must be encouraged to use fluoride products for this purpose. The ultimate method is for inhalation to be performed before breakfast in the morning, that breakfast should end with tooth brushing with fluoride toothpaste and that inhalation should take place one or 2 h before the evening tooth brushing with fluoride toothpaste, but that this inhalation should then be followed by rinsing with tap water. During the daytime, the inhalation should, if possible, be followed by a fluoride mouth rinse in order to neutralise oral pH among children older than six years who can manage to spit out the solution. Under the age of six, the inhalation should be followed by rinsing the mouth with tap water.

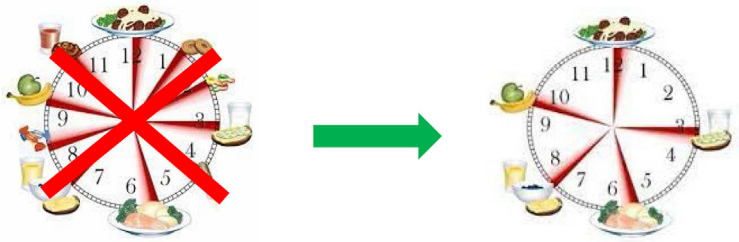
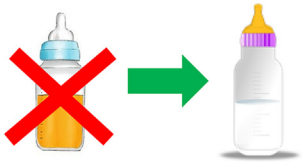
Professionally applied topical fluoride at the dental clinic

Fluoride varnish

Several different fluoride varnishes for professional use are available on the market of which the most used is Duraphat®. Their advantages as compared with other fluoride products are the high fluoride concentration and the prolonged contact time of fluoride on the tooth surface, allowing slow release and remaining for a long time on the tooth surface. Duraphat® contains 22,600 ppm fluoride, which enables the formation of intraoral fluoride due to the formation of calcium fluoride CaF_2, which serves as a pH-regulating reservoir. When the pH drops, free fluoride ions can act and, at a higher pH, they are bound to calcium.[93,94] A preventive effect on caries has been shown when treatment is repeated at least twice a year in children and adolescents, together with the concurrent use of fluoride toothpaste and, because of the high content of fluoride, it is also suitable for protection from dental erosion. Fluoride varnish has been identified as the first choice for dental erosion, as it is able effectively to reduce wear progression due to erosion and combined erosion and brushing abrasion, mainly related to the formation of this calcium fluoride layer.[95–98] Fluoride varnish is recommended for all ages and is the only appropriate topical fluoride product apart from fluoride toothpaste for preschool children.[99] Its effectiveness, ease of application, safety, not being time consuming, less patient discomfort and great patient acceptability offer significant advantages over other topical fluoride treatments.[100–102] Many reviews and meta-analyses support fluoride varnish for caries prevention in both the primary and the permanent dentition.[101,103–107] An updated Cochrane review of 22 trials found that fluoride varnish, applied two to four times a year, was associated with a reduction of 43% in caries in the permanent teeth and 37% in the primary teeth of children and adolescents, compared with placebo or no treatment, and that evidence of the caries-preventive effect is greater in terms of quality and quantity for permanent rather than primary teeth.[84,108] This substantial caries-inhibiting effect of varnish was not influenced by the caries level of the population or by exposure to other sources of fluoride. A recent review of preschool children stated that it is uncertain that fluoride varnish at low ages is cost effective.[109] Among high-risk preschool children, caries increases with age, as does excessive exposure to sugar, and this is the reason for more caries, not the lack of fluoride. This explains why sugar restriction among small children is urgently needed.[110] Fluoride varnish supplementary to fluoride toothpaste should be targeted at children and adolescents running a high risk of caries and dental erosion, such as those suffering from asthma.[107] A single 0.25 ml application of fluoride varnish with 22,600 ppm fluoride contains 5.65 mg of fluoride ion, which is well below the probable toxic dose of fluoride of 5 mg/kg body weight, even if all the dispensed varnish is swallowed. This has contributed to its being widely recommended as the main professional fluoride therapy for caries prevention in preschool children.[55] Use a syringe or a brush with varnish and apply it in a thin film on caries predilection sites and on initial caries lesions. The effect produced by fluoride is greatest on smooth tooth surfaces where the proximal surfaces are of the greatest interest, as caries on these surfaces accounts for most of the treatment needed in adulthood. Recently, some studies have reported the effect of fluoride varnish even on the occlusal surfaces where fissure sealants were previously the predominant treatment.[111–114] Advise the patient not to eat or drink for 30 min following the procedure and not to brush their teeth that day in order to leave the varnish on the teeth surfaces for as long as possible to enable a slow release. Repeat the application two to four times a year, depending on the individual risk of caries and dental erosion. In children with asthma, check any medical history with the parents, checking specifically for allergies to sticking plaster or severe allergy or asthma that has required hospitalisation. The only substance in Duraphat that might cause allergy is the resin, cholophony. If so, there are other fluoride varnishes without this substance.

Fluoride gel

Fluoride gel is a highly concentrated topical fluoride agent which contains up to 12,300 ppm fluoride based on sodium fluoride, acidulated phosphate fluoride APF or amine fluoride. The most frequently used are APF gels which are acidulated and buffered with phosphate with a fluoride content of 1.23%, corresponding to 12,300 ppm fluoride. In the USA, this was the most widely used professionally applied topical agent from the late 1960s until the 2000s, when it was gradually replaced by fluoride varnishes.[115] Fluoride gel shows a preventive fraction of 21% compared with placebo and the effect is greater in terms of quality and quantity on the permanent teeth than on the primary teeth.[84,116] The effect on the tooth surface is the same as for fluoride varnish, forming a fluoride reservoir on the tooth surface that slowly releases fluoride over time. It is usually administered professionally at the dental clinic using a plastic tray two to four times a year and the recommended application time is 4 min, after which the

<table>
<tr><th colspan="3">Diet counselling in children and adolescents with asthma</th></tr>
<tr><th>Children 0-2 years</th><th>Children 2-6 years</th><th>From 6 years of age</th></tr>
<tr><td colspan="3">Questions to the parents, child and adolecents at the regular dental check-ups
- What does your child or what do you drink when you are thirsty?
- Does your child or do you eat sweets and, if yes, how often?</td></tr>
<tr><td colspan="3">- Make sure that the child has regular meals during the day, maximum five to six times a day.
- Let the teeth rest between meals.
  </td></tr>
<tr><td colspan="3">- When thirsty, encourage children to drink water
  </td></tr>
<tr><td colspan="2">No sugar at all
- Avoid sweet drinks in baby bottles or the child falling asleep with a baby bottle
 
-Avoid starch products between meals, like maize pop and shortbread.
  </td><td>-Try to avoid soft drinks and sugar/starch-containing products between meals and restrict sweets and soft drinks to once a week.
 

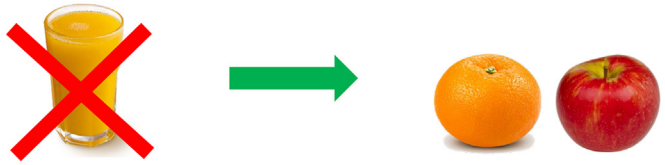
-To minimise the risk of dental erosion, avoid acidic foods and soft drinks, eat whole fruit instead of juice.
 
-Products such as milk, sugar-free yoghurt and cheese can neutralise the acid in the mouth. If sugar-containing products can not be avoided, the recommendation is to use sucrose substitutes like sorbitol and xylitol.
  </td></tr>
</table>

Figure 2 Diet counselling in children and adolescents with asthma.

patient should expectorate the gel.[117] There is little information on the effectiveness in the primary dentition of young children and, because a relatively large amount of fluoride is present in the gel, there is a risk of excessive ingestion by young children.[118] Since fluoride varnish application takes less time, is more convenient for the patient and contains a smaller quantity of fluoride, it is more frequently used today, especially in children younger than six years of age.[119]

Population-based dietary prevention

Frequency of sugar intake

The strongest evidence relating to the role of the frequency of sugar intake comes from the Vipeholm study.[120] Over a period of five years, patients at a mental hospital were given different sugars and carbohydrate products at meals or in between. The group of patients who developed most caries had 24 sticky candy toffees between ordinary meals and those who had sugar in connection with meals developed almost no new caries lesions. The results showed clearly that, the more frequently sugar is consumed, the greater the risk and sugar consumed between meals has much greater caries potential than when it is consumed during a meal.[120] Children run a higher risk of caries and newly erupted teeth are more susceptible to caries when sucrose-containing food is eaten frequently.[121] The frequent consumption of sugar-containing products during the first years of life is associated with caries development later in life.[122] When sugars are eaten less frequently, it may take a higher level of sucrose to cause caries. This also applies if the teeth have been in the mouth for a longer time. The same effect is achieved by frequently applied topical fluoride, which means that the safe level of sugars increases.[123] Diet also has an essential impact on dental erosion, where the frequent intake of acidic products such as soft drinks and food has been reported to be the most important extrinsic factor.[56,124] The availability of acidic products and active marketing have increased in recent years worldwide and this is contributing to an increased risk of dental erosion among children and adolescents.[125]

At regular dental check-ups, it is important in motivational interviewing to ask children, their parents and adolescents about their intake pattern. Some relevant questions can be found in Fig. 2. The advice in order to minimise the risk of caries and dental erosion should be: maximum five to six intakes a day, let the teeth rest between meals and, when thirsty, drink water.

High-risk approach relating to diet

The amount of sugar and other important factors

Many studies report on the role of sucrose in the caries process. During World War II, caries decreased because of sugar restriction and, after the war, caries increased when sugar consumption increased. Tristan da Cunha is a remote island with no sugar consumption and, after a modern diet including sugar and refined carbohydrates was introduced, the caries prevalence increased significantly.[49] There is strong dose—response relationship between the intake of sugars and caries, which means that, in order to reduce caries, a reduction in the amount of sugar is necessary and that the frequency of sugar intake should not only be examined in children and adolescents with asthma.[123,126] The level of intake of free sugar that the World Health Organisation suggests for a safe intake should be less than 10% of the total energy intake and preferably below 5%, calculated on a daily energy intake of 2000 kcal.[127] In the Netherlands, the average daily intake of free sugars among children and adolescents is as high as 20% of the total daily intake.[128] According to these authors, sugar-sweetened beverages and fruit drinks, sweets, candy and dairy products account for 80% of the sugar intake. The extrinsic causes of dental erosion are dietary acids, such as fruit acids, ascorbic and phosphoric acid, fruit juices, sport drinks and carbonated beverages, and all these products should be avoided in order to avoid dental erosion.[129] Focusing on the amount of sugars is also consistent with the guidelines in order to reduce the risk of other diseases related to excess sugar.[127] Dietary counselling is very important at regular dental check-ups, as the diet of children with asthma can be a risk factor for both caries and dental erosion.[56,130,131] The parents of children with long-term diseases may overindulge their children by allowing the frequent consumption of sweets and sugary drinks.[132] It is not the disease per se that causes higher caries prevalence but the high consumption of sugary drinks in combination with a lower salivary secretion rate and frequent mouthbreathing.[133,134] The aim of dietary counselling with children, parents and adolescents is to find tools to change and improve the dietary intake. This can include dietary history, where all dietary intakes are recorded with special emphasis on the source, amount and frequency of the meals during the last 24 h or during a longer period of three to five days.[135] It is important to consider overall health, with special emphasis on the asthma disease, the family situation and the child's and parents' motivation to change. The dietary intakes can be recorded on the dental charts and reviewed together with the child and the parent at the dental check-ups. To encourage a low sugar intake as recommended by the WHO, children should not consume any sugar-sweetened beverages at all before two years of age and water and milk are suggested as the healthiest beverages.[136] Suitable alternatives for caries prevention and dental erosion prevention can be seen in Fig. 2 and are milk, cheese products and sugar-free yoghurt, which can reduce the effect of metabolic acids and promote remineralisation by casein, calcium and phosphorus components, thereby increasing buffering and salivary stimulation.[137,138]

Conclusion

Earlier reviews illustrate the relationship between asthma on the one hand and caries and dental erosion on the other among children and adolescents. Most of these studies show an association, but very few reviews take up prevention from caries and dental erosion. Therefore, in this review we highlight the importance to identify children and adolescents with asthma as early as possible and to refer them to a dental team for preventive treatment. Early diagnosis, correct intervention and prevention are key factors when it comes to minimising the risk of developing caries and dental erosion with the ultimate goal of preserving healthy

teeth. Children and adolescents must follow basic prevention rules relating to diet, drug administration, fluoride and oral hygiene. There is also a need for a high-risk approach and to educate children and their parents and adolescents about the increased susceptibility to oral diseases and to encourage regular dental check-ups with extended fluoride supply and follow recommendations relating to diet and supplementary fluoride products.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

References

1. Agostini BA, Collares KF, Costa FDS, Correa MB, Demarco FF. The role of asthma in caries occurrence - meta-analysis and meta-regression. *J Asthma* 2019;56:841—52.
2. Gani F, Caminati M, Bellavia F, et al. Oral health in asthmatic patients: a review: asthma and its therapy may impact on oral health. *Clin Mol Allergy* 2020;18:22.
3. Harrington N, Prado N, Barry S. Dental treatment in children with asthma — a review. *Br Dent J* 2016;220:299—302.
4. Global Initiative for Asthma (GINA). *Global strategy for asthma management and prevention*. 2021. Available from: ginasthma.org.
5. Milosevic A, O'Sullivan E. Royal College of Surgeons of England. Diagnosis, prevention and management of dental erosion: summary of an updated national guideline. *Prim Dent Care* 2008;15:11—20.
6. National Asthma Education and Prevention Program (NAEPP). *Third expert panel on the diagnosis and management of asthma. Expert panel report 3: guidelines for the diagnosis and management of asthma*. Bethesda (MD): National Heart, Lung, and Blood Institute (US); 2007 Aug. Available from: https://www.ncbi.nlm.nih.gov/books/NBK7232/.
7. World Health Organization (WHO). *Asthma*. Available at: https://www.who.int/news-room/fact-sheets/detail/asthma; 2021.
8. Vos T, Lim SS, Abbafati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990—2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020;396:1204—22.
9. Papi A, Brightling C, Pedersen SE, Reddel HK. Asthma. *Lancet* 2018;391:783—800.
10. To T, Stanojevic S, Moores G, et al. Global asthma prevalence in adults: findings from the cross-sectional world health survey. *BMC Publ Health* 2012;12:204.
11. Asher MI, Montefort S, Bjorksten B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 2006;368:733—43.
12. Leynaert B, Sunyer J, Garcia-Esteban R, et al. Gender differences in prevalence, diagnosis and incidence of allergic and non-allergic asthma: a population-based cohort. *Thorax* 2012;67:625—31.
13. Guilbert T, Krawiec M. Natural history of asthma. *Pediatr Clin* 2003;50:523—38.
14. Levy ML, Fletcher M, Price DB, Hausen T, Halbert RJ, Yawn BP. International primary care respiratory group (IPCRG) guidelines: diagnosis of respiratory diseases in primary care. *Prim Care Respir J* 2006;15:20—34.
15. van Maanen A, Wijga AH, Gehring U, et al. Sleep in children with asthma: results of the PIAMA study. *Eur Respir J* 2013;41:832—7.
16. Bel EH. Clinical phenotypes of asthma. *Curr Opin Pulm Med* 2004;10:44—50.
17. Moore WC, Meyers DA, Wenzel SE, et al. Identification of asthma phenotypes using cluster analysis in the Severe Asthma Research Program. *Am J Respir Crit Care Med* 2010;181:315—23.
18. Wenzel SE. Asthma phenotypes: the evolution from clinical to molecular approaches. *Nat Med* 2012;18:716—25.
19. Fanta CH. Asthma. *N Engl J Med* 2009;360:1002—14.
20. Global Initiative for Asthma (GINA). *Global strategy for asthma management and prevention*. 2019. Available from: ginasthma.org.
21. Wu FY, Liu JF. Asthma medication increases dental caries among children in Taiwan: an analysis using the National Health Insurance Research Database. *J Dent Sci* 2019;14:413—8.
22. Alavaikko S, Jaakkola MS, Tjaderhane L, Jaakkola JJ. Asthma and caries: a systematic review and meta-analysis. *Am J Epidemiol* 2011;174:631—41.
23. Ghapanchi J, Rezazadeh F, Kamali F, Rezaee M, Ghodrati M, Amanpour S. Oral manifestations of asthmatic patients. *J Pakistan Med Assoc* 2015;65:1226—7.
24. Rezende G, Dos Santos NML, Stein C, Hilgert JB, Faustino-Silva DD. Asthma and oral changes in children: associated factors in a community of southern Brazil. *Int J Paediatr Dent* 2019;29:456—63.
25. Arafa A, Aldahlawi S, Fathi A. Assessment of the oral health status of asthmatic children. *Eur J Dermatol* 2017;11:357—63.
26. Farag ZH, Awooda EM. Dental Erosion and dentin hypersensitivity among Adult asthmatics and non-asthmatics hospital-based: a preliminary study. *Open Dent J* 2016;10:587—93.
27. Widmer RP. Oral health of children with respiratory diseases. *Paediatr Respir Rev* 2010;11:226—32.
28. Sivasithamparam K, Young WG, Jirattanasopa V, et al. Dental erosion in asthma: a case-control study from south east Queensland. *Aust Dent J* 2002;47:298—303.
29. Vázquez EM, Vázquez F, Barrientos MC, et al. Association between asthma and dental caries in the primary dentition of Mexican children. *World J Pediatr* 2011;7:344—9.
30. Ryberg M, Möller C, Ericson T. Effect of beta 2-adrenoceptor agonists on saliva proteins and dental caries in asthmatic children. *J Dent Res* 1987;66:1404—6.
31. Thomas MS, Parolia A, Kundabala M, Vikram M. Asthma and oral health: a review. *Aust Dent J* 2010;55:128—33.
32. Khalifa MAAA, Abouelkheir HM, Khodiar SE-F, Mohamed GAM. Salivary composition and dental caries among children controlled asthmatics. *Egypt J Chest Dis Tuberc* 2014;63:777—88.
33. Bairappan S, Puranik MP, R Sk. Impact of asthma and its medication on salivary characteristics and oral health in adolescents: a cross-sectional comparative study. *Spec Care Dent* 2020;40:227—37.
34. Storhaug K. Caries experience in disabled pre-school children. *Acta Odontol Scand* 1985;43:241—8.
35. Meldrum AM, Thomson WM, Drummond BK, Sears MR. Is asthma a risk factor for dental caries? Finding from a cohort study. *Caries Res* 2001;35:235—9.
36. Mazzoleni S, Stellini E, Cavaleri E, Angelova Volponi A, Ferro R, Fochesato Colombani S. Dental caries in children with asthma undergoing treatment with short-acting beta2-agonists. *Eur J Paediatr Dent* 2008;9:132—8.
37. Tootla R, Toumba KJ, Duggal MS. An evaluation of the acidogenic potential of asthma inhalers. *Arch Oral Biol* 2004;49:275—83.

38. Kargul B, Tanboga I, Ergeneli S, Karakoc F, Dagli E. Inhaler medicament effects on saliva and plaque pH in asthmatic children. *J Clin Pediatr Dent* 1998;22:137—40.
39. Ersin NK, Gülen F, Eronat N, et al. Oral and dental manifestations of young asthmatics related to medication, severity and duration of condition. *Pediatr Int* 2006;48:549—54.
40. Reddy DK, Hegde AM, Munshi AK. Dental caries status of children with bronchial asthma. *J Clin Pediatr Dent* 2003;27:293—5.
41. Barry S, Fleming P, O'Connor M. Prescribing sugar-containing medicines for children–are we forgetting "primum non nocere"? *Ir Med J* 2009;102:298—300.
42. Lima LRS, Pereira AS, de Moura MS, et al. Pre-term birth and asthma is associated with hypomineralized second primary molars in pre-schoolers: a population-based study. *Int J Paediatr Dent* 2020;30:193—201.
43. Vejdani J, Zahiri Sorouri Z, Emami A. Survey the relationship between the type of delivery and enamel defects of the first permanent molars. *J Guilan Univ Med Sci* 2010;19:73—8.
44. Kharitonov SA, Yates D, Robbins RA, Logan-Sinclair R, Shinebourne EA, Barnes PJ. Increased nitric oxide in exhaled air of asthmatic patients. *Lancet* 1994;343:133—5.
45. SBU. *The Swedish Council on Technology Assessment in Health Care. Prevention of dental caries. Systematic review.* 2002. Report number 161.
46. Kassebaum NJ, Smith AGC, Bernabé E, et al. Global, regional, and national prevalence, incidence, and disability-adjusted life years for oral conditions for 195 Countries, 1990—2015: a systematic analysis for the global burden of diseases, injuries, and risk factors. *J Dent Res* 2017;96:380—7.
47. Zero DT. Dental caries process. *Dent Clin* 1999;43:635—64.
48. Newbrun E. Sucrose, the arch criminal of dental caries. *ASDC (Am Soc Dent Child) J Dent Child* 1969;36:239—48.
49. Zero DT. Sugars — the arch criminal? *Caries Res* 2004;38:277—85.
50. Marinho VCC. Cochrane reviews of randomized trials of fluoride therapies for preventing dental caries. *Eur Arch Paediatr Dent* 2009;10:183—91.
51. O'Mullane DM, Baez RJ, Jones S, et al. Fluoride and oral health. *Community Dent Health* 2016;33:69—99.
52. Bratthall D, Hänsel-Petersson G, Sundberg H. Reasons for the caries decline: what do the experts believe? *Eur J Oral Sci* 1996;104:416—22.
53. Marinho VCC, Higgins JPT, Logan S, Sheiham A. Fluoride toothpastes for preventing dental caries in children and adolescents (Review). *Cochrane Database Syst Rev* 2009;1:CD002278.
54. Pitts NB, Zero DT, Marsh PD, et al. Dental caries. *Nat Rev Dis Prim* 2017;25:17030.
55. Toumba KJ, Twetman S, Splieth C, Parnell C, van Loveren C, Lygidakis NA. Guidelines on the use of fluoride for caries prevention in children: an updated EAPD policy document. *Eur Arch Paediatr Dent* 2019;20:507—16.
56. Lussi A. Erosive tooth wear - a multifactorial condition of growing concern and increasing knowledge. *Monogr Oral Sci* 2006;20:1—8.
57. Lussi A, Schaffner M, Jaeggi T. Dental erosion — diagnosis and prevention in children and adults. *Int Dent J* 2007;57:385—98.
58. ten Cate JM, Imfeld T. Dental erosion, summary. *Eur J Oral Sci* 1996;104:241—4.
59. Lussi A, Buzalaf MAR, Duangthip D, et al. The use of fluoride for the prevention of dental erosion and erosive tooth wear in children and adolescents. *Eur Arch Paediatr Dent* 2019;20:517—27.
60. Burt BA. Prevention policies in the light of the changed distribution of dental caries. *Acta Odontol Scand* 2008;195:7—63.
61. Twetman S, Axelsson S, Dahlgren H, et al. Caries-preventive effect of fluoride toothpaste: a systematic review. *Acta Odontol Scand* 2003;61:347—55.
62. Twetman S. Caries prevention with fluoride toothpaste in children; an update. *Eur Arch Paediatr Dent* 2009;10:162—7.
63. Wong MCM, Clarkson J, Glenny AM, et al. Cochrane reviews on the benefits/risks of fluoride toothpastes. *J Dent Res* 2011;90:573—9.
64. Wright JT, Hanson N, Ristic H, Whall CW, Estrich CG, Zentz RR. Fluoride toothpaste efficacy and safety in children younger than 6 years: a systematic review. *J Am Dent Assoc* 2014;145:182—9.
65. Walsh T, Worthington HV, Glenny AM, Marinho VCC, Jeroncic A. Fluoride toothpastes of different concentrations for preventing dental caries in children and adolescents. *Cochrane Database Syst Rev* 2019;3:CD007868.
66. Ammari AB, Bloch-Zupan A, Ashley PF. Systematic review of studies comparing the anti-caries efficacy of children's toothpaste containing 600 ppm of fluoride or less with high fluoride toothpastes of 1,000 ppm or above. *Caries Res* 2003;37:85—92.
67. Chestnutt IG, Schafer F, Jacobsen APM, Stephen KW. The influence of toothbrushing frequency and post-brushing rinsing on caries experience in a caries clinical trial. *Community Dent Oral Epidemiol* 1998;26:406—11.
68. Ashley FP, Attrill DC, Ellwood RP, Worthington HV, Davies RM. Tooth brushing habits and caries experience. *Caries Res* 1999;33:401—2.
69. Zero DT, Creeth JE, Bosma ML, et al. The effect of brushing time and dentifrice quantity on fluoride delivery in vivo and enamel surface microhardness in situ. *Caries Res* 2010;44:90—100.
70. Ishizuka Y, Lehrkinder A, Nordström A, Lingström P. Effect of different toothbrushing routines on interproximal fluoride concentration. *Caries Res* 2020;54:343—9.
71. Chesters RK, Huntington E, Burchell CK, Stephen KW. Effect of oral care habits on caries in adolescents. *Caries Res* 1992;26:299—304.
72. Sjögren K, Birkhed D. Factors related to fluoride retention after toothbrushing and possible connection to caries activity. *Caries Res* 1993;27:474—7.
73. Sjögren K, Birkhed D. Effect of various post-brushing activities on salivary fluoride concentration after toothbrushing with sodium fluoride dentifrice. *Caries Res* 1994;28:127—31.
74. Seppä L, Salmenkivi S, Hausen H. Salivary fluoride concentration in adults after different fluoride procedures. *Acta Odontol Scand* 1997;55:84—7.
75. Magalhães AC, Wiegand A, Rios D, Buzalaf MAR, Lussi A. Fluoride in dental erosion. *Monogr Oral Sci* 2011;22:158—70.
76. Tavss EA, Mellberg JR, Joziak M, Gambogi RJ, Fisher SW. Relationship between dentifrice fluoride concentration and clinical caries reduction. *Am J Dent* 2003;16:369—74.
77. Nordström A, Birkhed D. Fluoride retention in proximal plaque and saliva using two NaF dentifrices containing 5,000 and 1,450 ppm F with and without water rinsing. *Caries Res* 2009;43:64—9.
78. Nordström A, Birkhed D. Preventive effect of a high-fluoride dentifrice (5,000 ppm) in caries-active adolescents — a 2-year clinical trial. *Caries Res* 2010;44:323—33.
79. Duane B. 5,000 ppm F dentifrice for caries prevention in adolescents. *Evid Base Dent* 2012;13:43—4.
80. Petersson LG, Reich E, Netuschil L, Brecx M. Mouth rinses and dental caries. *Int Dent J* 2002;52:337—45.
81. Marinho VC, Worthington Chong LY, Worthington HV, Walsh T. Fluoride mouth rinses for preventing dental caries in children and adolescents. *Cochrane Database Syst Rev* 2016;7:CD002284.

82. Marinho VCC, Higgins JPT, Sheiham A, Logan S. Combinations of topical fluoride (toothpastes, mouthrinses, gels, varnishes) versus single topical fluoride for preventing dental caries in children and adolescents. *Cochrane Database Syst Rev* 2004; 1:CD002281.
83. Weyant RJ. Seven systematic reviews confirm topical fluoride therapy is effective in preventing dental caries. *J Evid Base Dent Pract* 2004;3:129—35.
84. Twetman S, Keller MK. Fluoride rinses, gels and foams: an update of controlled clinical trials. *Caries Res* 2016;50:38—44.
85. Moberg Sköld U, Birkhed D, Borg E, Petersson LG. Approximal caries development in adolescents with low to moderate caries risk after different 3-year school-based supervised fluoride mouth rinsing programmes. *Caries Res* 2005;39: 529—35.
86. Pitts N, Duckworth RM, Marsh P, Mutti B, Parnell C, Zero D. Post-brushing rinsing for the control of dental caries: exploration of the available evidence to establish what advice we should give our patients. *Br Dent J* 2012;212:315—20.
87. Gabre P, Moberg Sköld U, Birkhed D. Simplified methods of topical fluoride administration: effects in individuals with hyposalivation. *Spec Care Dent* 2013;33:111—7.
88. Mystikos C, Yoshino T, Ramberg P, Birkhed D. Effect of post-brushing mouthrinse solutions on salivary fluoride retention. *Swed Dent J* 2011;35:17—24.
89. Moberg Sköld U, Birkhed D, Ellwood R. Effect of post-brushing mouthwash solutions on salivary fluoride retention - study 1. *J Clin Dent* 2012;23:97—100.
90. Tubert-Jeannin S, Auclair C, Amsallem E, et al. Fluoride supplements (tablets, drops, lozenges or chewing gums) for preventing dental caries in children. *Cochrane Database Syst Rev* 2011;12:CD007592.
91. Tomasin L, Pusinanti L, Zerman N. The role of fluoride tablets in the prophylaxis of dental caries. A literature review. *Ann Stomatol* 2015;6:1—5.
92. Twetman S. Consistent evidence to support the use of xylitol- and sorbitol-containing chewing gum to prevent dental caries. *Evid Base Dent* 2009;10:10—1.
93. Øgaard B, Seppa L, Rolla G. Professional topical fluoride applications—clinical efficacy and mechanism of action. *Adv Dent Res* 1994;8:190—201.
94. Cochrane NJ, Shen P, Yuan Y, Reynolds EC. Ion release from calcium and fluoride containing dental varnishes. *Aust Dent J* 2014;59:100—5.
95. Saxegaard E, Rolla G. Fluoride acquisition on and in human enamel during topical application in vitro. *Scand J Dent Res* 1988;96:523—35.
96. Vieira A, Jager DH, Ruben JL, Huysmans MC. Inhibition of erosive wear by fluoride varnish. *Caries Res* 2007;41:61—7.
97. Manarelli MM, Moretto MJ, Sassaki KT, Martinhon CC, Pessan JP, Delbem AC. Effect of fluoride varnish supplemented with sodium trimetaphosphate on enamel erosion and abrasion. *Am J Dent* 2013;26:307—12.
98. Sar Sancakli H, Austin RS, Al-Saqabi F, Moazzez R, Bartlett D. The influence of varnish and high fluoride on erosion and abrasion in a laboratory investigation. *Aust Dent J* 2015;60: 38—42.
99. dos Santos AP, Malta MC, de Marsillac MW, de Oliveira BH. Fluoride varnish applications in preschoolers and dental fluorosis in permanent incisors: results of a nested-cohort study within a clinical trial. *Pediatr Dent* 2016;38:414—8.
100. Seppä L, Leppanen T, Hausen H. Fluoride varnish versus acidulated phosphate fluoride gel: a 3-year clinical trial. *Caries Res* 1995;29:327—30.
101. Azarpazhooh A, Main PA. Fluoride varnish in the prevention of dental caries in children and adolescents: a systematic review. *J Can Dent Assoc* 2008;74:73—9.
102. Mascarenhas AK. Is fluoride varnish safe? Validating the safety of fluoride varnish. *J Am Dent Assoc* 2021;152:364—8.
103. Seppä L. Studies of fluoride varnishes in Finland. *Proc Finn Dent Soc* 1991;87:541—7.
104. Helfenstein U, Steiner M. Fluoride varnishes (Duraphat): a meta-analysis. *Community Dent Oral Epidemiol* 1994;22:1—5.
105. Petersson LG, Twetman S, Dahlgren H, et al. Professional fluoride varnish treatment for caries control: a systematic review of clinical trials. *Acta Odontol Scand* 2004;62:170—6.
106. Carvalho DM, Salazar M, Oliveira BH, Coutinho ES. Fluoride varnishes and decrease in caries incidence in preschool children: a systematic review. *Rev Bras Epidemiol* 2010;13: 139—49.
107. Weyant RJ, Tracy SL, Anselmo TT, et al. American dental association council on scientific affairs expert panel on topical fluoride caries preventive agents. Topical fluoride for caries prevention: executive summary of the updated clinical recommendations and supporting systematic review. *J Am Dent Assoc* 2013;144:1279—91.
108. Marinho VC, Worthington HV, Walsh T, Clarkson JE. Fluoride varnishes for preventing dental caries in children and adolescents. *Cochrane Database Syst Rev* 2013;7:CD002279.
109. de Sousaa FSO, dos Santos APP, Nadanovsky P, Hujoeld P, Cunha-Cruz J, de Oliveiraa BH. Fluoride varnish and dental caries in preschoolers: a systematic review and meta-analysis. *Caries Res* 2019;53:502—13.
110. Sheiham A, James WPT. Diet and Dental Caries: the pivotal role of free sugars reemphasized. *J Dent Res* 2015;94:1341—7.
111. Wright JT, Tampi MP, Graham L, et al. Sealants for preventing and arresting pit-and-fissure occlusal caries in primary and permanent molars. A systematic review of randomized controlled trials—a report of the American Dental Association and the American Academy of Pediatric Dentistry. *J Am Dent Assoc* 2016;147:631—45.
112. Ahovuo-Saloranta A, Forss H, Walsh T, Nordblad A, Mäkelä M, Worthington HV. Pit and fissure sealants for preventing dental decay in permanent teeth. *Cochrane Database Syst Rev* 2017; 7:CD001830.
113. Chestnutt IG, Playle R, Hutchings S, et al. Fissure seal or fluoride varnish? A randomized trial of relative effectiveness. *J Dent Res* 2017;96:754—61.
114. Li F, Jiang P, Yu F, Li C, Wu S, Zou J. Comparison between fissure sealant and fluoride varnish on caries prevention for first permanent molars: a systematic review and meta-analysis. *Sci Rep* 2020;10:2578.
115. Newbrun E. Finn Brudevold: discovery of acidulated phosphate fluoride in caries prevention. *J Dent Res* 2011;90:977—80.
116. Marinho VCC, Worthington HV, Walsh T, Chong L-Y. Fluoride gels for preventing dental caries in children and adolescents. *Cochrane Database Syst Rev* 2015;6:CD002280.
117. Hawkins R, Locker D, Noble J, Kay EJ. Prevention. Part 7: professionally applied topical fluorides for caries prevention. *Br Dent J* 2003;195:313—7.
118. Adair SM. Evidence-based use of fluoride in contemporary pediatric dental practice. *Pediatr Dent* 2006;28:133—42.
119. van Rijkom HM, Truin GJ, van't Hof MA. A meta-analysis of clinical studies on the caries-inhibiting effect of fluoride gel treatment. *Caries Res* 1998;32:83—92.
120. Gustafsson BE, Quensel CE, Lanke LS, et al. Vipeholm dental caries study; the effect of different levels of carbohydrate intake on caries activity in 436 individuals observed for five years. *Acta Odontol Scand* 1954;11:232—64.
121. Newbrun E. Sucrose in the dynamics of the carious process. *Int Dent J* 1982;32:13—23.
122. Alm A, Wendt LK, Koch G, Birkhed D, Nilsson M. Caries in adolescence—influence from early childhood. *Community Dent Oral Epidemiol* 2012;40:125—33.

123. Sheiham A. Dietary effects on dental diseases. *Publ Health Nutr* 2001;4:569—91.
124. Dugmore CR, Rock WP. A multifactorial analysis of factors associated with dental erosion. *Br Dent J* 2004;196:283—6.
125. Gambon DL, Brand HS, Veerman EC. Dental erosion in the 21st century: what is happening to nutritional habits and lifestyle in our society? *Br Dent J* 2012;213:55—7.
126. Bernabe;E, Vehkalahti MM, Sheiham A, Lundqvist A, Suominen AL. The shape of the dose-response relationship between sugars and caries in adults. *J Dent Res* 2016;95: 167—72.
127. World Health Organization. *Sugars intake for adults and children*. Geneva: WHO, 2015.
128. Sluik D, Van Lee L, Engelen AI, Feskens EJM. Total free and added sugar consumption and adherence to guidelines: the Dutch national food consumption survey 2007-2010. *Nutrients* 2016;8:70—84.
129. Meurman JH, ten Cate JM. Pathogenesis and modifying factors of dental erosion. *Eur J Oral Sci* 1996;104:199—206.
130. Stensson M, Wendt LK, Koch G, Nilsson M, Oldaeus G, Birkhed D. Oral health in pre-school children with asthma—followed from 3 to 6 years. *Int J Paediatr Dent* 2010; 20:165—72.
131. Dahllöf G, Jacobsen PE, Martens L. *Pediatric dentistry: a clinical approach*, 3rd ed. New Jersey: Wiley, 2016:316—7.
132. Children with chronic health conditions: implications for oral health, McDerra EJ, Pollard MA, Curzon ME. The dental status of asthmatic British school children. *Pediatr Dent* 1998;20: 281—7.
133. Venetikidou A. Incidence of malocclusion in asthmatic children. *J Clin Pediatr Dent* 1993;17:89—94.
134. Stensson M, Wendt LK, Koch G, Oldaeus G, Lingström P, Birkhed D. Caries prevalence, caries-related factors and plaque pH in adolescents with long-term asthma. *Caries Res* 2010b;44:540—6.
135. Feldens CA, Kramer PF, Vargas-Ferreira F. *Pediatric restorative dentistry*, 1st ed. Berlin: Springer, 2019:31—55.
136. Vos MB, Kaar JL, Welsh JA, et al. Added sugars and cardiovascular disease risk in children: a scientific statement from the American Heart Association. *Circulation* 2017;135: 1017—34.
137. Lussi A, Hellwig E, Zero D, Jaeggi T. Erosive tooth wear: diagnosis, risk factors and prevention. *Am J Dent* 2006;19:319.
138. van Loveren C, Broukal Z, Oganessian E. Functional foods/ingredients and dental caries. *Eur J Nutr* 2012;51:15—25.