



Dental care of the pediatric patient with splenic dysfunction

Marcio A. da Fonseca, DDS, MS Alexander Hirsch, Dr. Med. Dent.

Dr. da Fonseca is assistant clinical professor, Department of Orthodontics and Pediatric Dentistry, University of Michigan School of Dentistry, Ann Arbor, Mich; Dr. Hirsch is in private practice, Sindelfingen, Germany. Correspond with Dr. da Fonseca at marcio@umich.edu

Abstract

The spleen is strategically situated in the vascular tree to filtrate the circulating blood, therefore it is of paramount importance in the defense against pathogenic organisms. Sepsis in individuals who have splenic dysfunction or have had a splenectomy is a life-long risk, thus patients, caretakers and health professionals should prevent infections and recognize them promptly so that treatment can be instituted immediately. This manuscript reviews the consequences of splenic dysfunction and provides recommendations for dental care of the pediatric patient. (*Pediatr Dent* 24:57-63, 2002)

KEYWORDS: SPLENIC DYSFUNCTION, SPECIAL CARE PATIENT

Received October 23, 2001 Accepted December 18, 2001

The spleen comprises approximately 25% of the body's lymphoid tissues, receiving 5% of the blood volume per minute and pooling around 30% of the circulating platelets.¹⁻⁵ Hematopoiesis is a major splenic function from 3 to 6 months of intrauterine life.^{5,6} The neonatal spleen is functionally and histologically immature with few lymphoid follicles and little or no germ centers, which raises questions about its humoral capabilities to respond to antigenic stimulation at a young age.⁷ In the first years of life, before specific immunity has developed, phagocytosis of encapsulated organisms occurs almost exclusively in the spleen.^{1,8}

The spleen has a unique circulatory arrangement. On entering the organ, the splenic artery divides into smaller trabecular arteries which branch into vessels that penetrate the adjacent parenchima.⁹ Surrounding them is a reticular framework (white pulp) with a population of lymphoid cells which, in the presence of antigenic material, undergo a functional transformation and secondary differentiation to form cells that will produce antibodies.^{9,10} The parenchimal arteries leave the white pulp branching into penicillar arteries that enter a filtering system (red pulp), which consists of anastomosing sinuses bound by plates called splenic cords, a reticular scaffolding for macrophages.^{5,9,10}

Small branches of the penicillar arteries enter into a maze where circulating blood cells must eventually pass through small openings in the cords to enter the sinuses to finally arrive in the splenic vein and then on to the hepatic portal vein.^{4,9-11} These openings to the sinuses permit the removal

of normal and pathologic blood cells from the circulation, a process known as culling.^{3,5,6,9,10} The spleen also presents a unique function called pitting which is the ability to clear intraerythrocyte inclusions (particulate matters, denatured hemoglobin, parasites) while maintaining the integrity of the cell.^{2,5,6,9}

The spleen plays an important role in the generation of immune mediators involved in clearing bacteria (opsonins) and other soluble mediators of phagocytosis (tuftsin, properdin) as well as in the defense against infection caused by encapsulated organisms such as *S. pneumoniae*, *H. influenzae* type B and *N. meningitidis*.^{1,2,6,11,12} It also recycles the iron released by the breakdown of red blood cells, sending it back to the bone marrow to be used in the production of new cells.⁶ In summary, the spleen has an "administrative" role to bring together different cell types to a place they can interact constructively for maximal anticapsular antibody production.¹¹ Therefore, asplenic and hyposplenic patients present a high risk for infection because of their decreased ability to clear damaged red cells and intraerythrocyte inclusion bodies, higher level of circulating immune complexes, defective recognition of carbohydrate antigens, defective production of IgM early in infection, defective removal of lightly opsonized particles, and lower concentration of tuftsin and properdin.^{5,6}

This manuscript reviews the risks of splenic dysfunction and its implications for dental care delivery for pediatric patients.

Splenic dysfunction: treatment and risks

Hypersplenism is characterized by an increased splenic function with destruction of circulating cells, leading to peripheral blood cytopenias, increased bone marrow activity and splenomegaly.^{5,10} It is usually secondary to another disease, such as chronic leukemia or lymphoma, and may be cured by treatment of the underlying condition or by splenectomy.^{5,10} Congenital absence of the spleen can be observed in children who have severe organ malformation such as complex cyanotic cardiac defects, dextrocardia and heterotopic abdominal organs.^{5,6,13} Functional hyposplenism may be normal in neonates, particularly premature infants but it is most commonly part of a wide variety of gastrointestinal, immunologic, inflammatory, infiltrative and hematologic diseases.^{5,6,9,10,13-15}

Functional hyposplenism may also occur in malaria, after irradiation to the left upper quadrant, and when the reticuloendothelial function of the spleen is overwhelmed.⁵ Traumatic rupture of the spleen, with consequent life-threatening hemorrhage, is the most common reason for splenectomy.^{5,9,10,13,15} However, splenic injuries may be seen without incurring a higher morbidity or mortality rate as well as a higher rate of blood transfusion.¹⁶ Treatment may include careful observation of the patient with attention to changes in vital signs or abdominal findings, and serial hemoglobin evaluations with prompt surgical intervention if deterioration occurs.⁵ Healthy patients who had a splenectomy due to trauma carry the least risk of overwhelming infections, possibly due to the preservation of some function as a result of implanted splenic remnants in the peritoneum or the presence of an accessory spleen.¹⁵ Table 1 summarizes the most common causes of splenic dysfunction and possible indications for splenectomy.

Because of the spleen's importance in the defense against infections, considerable attention has been paid to developing therapeutic alternatives such as laparoscopic splenectomy, partial splenectomy, splenic artery ligation or embolization, partial splenic embolization, autologous splenic transplantation and close observation with no surgical intervention.^{1,5,11,12} The choice of an alternative varies with each patient and which of them is effective is still a matter of debate.¹¹

Partial splenectomy has been particularly advocated for children younger than 2 years in whom complete removal of the organ causes the greatest risk of post-operative sepsis due to their reduced ability to mount an antibody response.^{1,6,13} Thrombocytosis occurs immediately after splenectomy with the platelet level returning to normal within two weeks.^{2,6} Other laboratory abnormalities include an absolute lymphocytosis and monocytosis, increased reticulocyte count and appearance

of giant platelets; all of these phenomena are self-limiting.¹⁵

S. pneumoniae is the most common cause of bacteremia, sepsis, meningitis, pneumonia, sinusitis, and acute otitis media in children, accounting for more than 50% of documented infections in asplenic patients.¹⁷ Children with functional or anatomic asplenia have pneumococcal infection rates 20 to 100-fold higher than healthy subjects in the first 5 years of life.¹⁷ *H. influenzae* type b is the second most common organism related to sepsis and accounts for 32% of the mortality.¹⁸ *N. meningitidis* is the next most commonly implicated organism, although there is no conclusive evidence that meningococemia is more frequent or more severe in hyposplenic patients when compared to healthy individuals.⁶

Post-splenectomy sepsis is fatal in 50% of the cases in children and in about one third of adults.¹² The risk of infection is higher for patients who develop functional asplenia or undergo a splenectomy in infancy or early childhood than those who lose splenic function at an older age although the risk is present throughout life.^{1,2,4,5,8,12,15,19-21} The shorter the interval between the surgery and the septic episode, the greater the likelihood of death, with 80% of fatal cases occurring within two years of the procedure.^{12,22} An individual's overall immune status is also an important variable. Increased infection risk is seen in splenectomy or hyposplenism due to thalassemia, immunodeficiency, malignancy or sickle cell anemia, which is the most common cause of functional asplenia in children.^{1,2,4,6,12,15,21}

In a study by Ein et al,²⁰ splenectomized children due to thalassemia and portal hypertension revealed a mortality rate of 3.3% with an incidence of 6% of serious infections, with the thalassemic patients presenting a much higher incidence of infection (40%), possibly related to repeated hospitalizations. A meta-analysis study of postsplenectomy sepsis cases

Table 1. Splenic Dysfunction and Possible Splenectomy Indications^{1-3,5,10,13,15}

Sickle cell disease	Hairy cell leukemia
Cyanotic heart disease	Cirrhosis, splenic vein thrombosis
Lupus erythematosus	Gaucher's disease
Malabsorption syndromes	Felty's syndrome
Fanconi's syndrome	Hemodialysis splenomegaly
Severe abdominal trauma	Thalassemia major (Cooley's anemia)
Hemolytic anemias	Hypoplastic anemia
Thrombocytopenic purpura	Portal hypertension
Hodgkin's disease	Non-Hodgkin's lymphoma
Chronic autoimmune disorders	Splenic tumors, cysts, hemangiomas
Biliary atresia	Metabolic storage diseases
Spherocytosis, elliptocytosis	Amyloidosis, sarcoidosis
Chronic granulocytic leukemia	Chronic lymphocytic anemia
Secondary hypersplenism	Pyruvate kinase deficiency
Myelofibrosis	Iatrogenic intraoperative injury
Reduction of organ transplant rejection	

from 1952 to 1987 revealed an incidence of 4.4% in children under 16 years of age with a mortality rate of 2.2%; in adults, those figures were 0.9% and 0.8%, respectively.¹⁸ Waghorn, after reviewing 77 cases of children and adults who developed overwhelming post-splenectomy infection (OPSI), showed that the risk of fulminant sepsis persists throughout life, with a mortality rate of 50%, increasing to 70% in hematological malignancy cases.²¹ Two-thirds of cases occurred in patients under 50 years of age, many of whom were in good health.

The onset of OPSI is often subtle yet sudden and fulminant.^{12,23} The initial symptoms are non-specific ("flu-like"), rapidly evolving into septic shock and disseminated intravascular coagulopathy with death occurring within hours.^{6,11,12,15} Other complications include extremity gangrene, convulsions and coma.⁶ Early recognition with aggressive management with empirical antibiotic therapy is a must.⁶ Surviving patients usually undergo a long and complicated hospital course.^{5,6} Splenectomized patients are also at increased risk to contract protozoal infections such as malaria and babesiosis.⁵

Prevention of infection

There is still improvement needed to achieve best practice in the management of asplenic patients.²¹ Besides developing alternatives for splenectomy in order to reduce the risks of post-operative sepsis, prevention strategies are divided into three major aspects: immunization, chemoprophylaxis and education.

If splenectomy is being contemplated, particularly in young children, specific immunization against a small number of organisms with well-characterized immunogenic polysaccharide capsules is a logical approach to prevent OPSI.^{4,11,12,24} Infants do not acquire specific antibodies against encapsulated organisms until relatively late in the development of the normal range of antibody responses.²² A new pneumococcal 7-valent conjugate vaccine (Prevnar, Lederle Laboratories/Wyeth-Ayerst Pharmaceuticals) has been approved for use in children younger than 2 years, showing good antibody response.^{6,17} Pneumococcal vaccination should be done at least two weeks before the surgery because its immunogenicity may be reduced when given after the procedure or while the patient is undergoing chemotherapy.^{6,13-15}

Non-immunized patients who had a splenectomy or who have functional hyposplenism should be vaccinated as soon as their condition is identified, preferably soon after surgical recovery or at time of hospital discharge.^{6,13-15} In children undergoing chemotherapy and/or radiotherapy, it is best to delay immunization for at least 6 months after the treatment is completed, during which time prophylactic antibiotic should be given.^{6,13} Recommendations on the timing of booster vary, with some authors suggesting that children older than 10 years be revaccinated every 5 years or sooner if antibody titers have declined early. For those younger than 10, reimmunization should occur after 3 years.^{6,13,14}

However, pneumococcal vaccination should not lead to a false sense of security because there is a lack of protection of current vaccines against about 15% of pneumococcus types as well as the possibility of subnormal immune responses and of OPSI triggered by non-vaccine organisms.^{6,8,11-13,22} Meningococcal vaccination is not routinely recommended for asplenic patients except when traveling to areas where there is increased risk of group A infection. Otherwise it should be restricted to patients who have close contacts with group A or C disease.¹³ Reimmunization should be considered after 2 years for children who remain at risk. In the US, meningococcal vaccination is not routinely recommended for asplenic patients because the current vaccine lacks the most common North American strain (serotype B).⁶ The efficacy of vaccination and reimmunization against both *H. influenzae* type b and *N. meningitidis* are not as clear as the pneumococcal vaccine.^{6,13,15,22} Influenza vaccine may be of value to asplenic patients by reducing the risk of secondary bacterial infection.¹⁵

The use of antibiotic prophylaxis in asplenic patients is very controversial and many different regimens are reported in the literature. A survey on physicians' knowledge and actions in asplenic patients revealed a lack of understanding of the recommendations for antibiotic prophylaxis.²⁵ There are no controlled studies validating the efficacy of penicillin prophylaxis in the prevention of sepsis in these patients and reports of antibiotics failing to prevent infection are known.^{11,12,19,21} Furthermore, poor patient compliance, fear of creating drug resistance and diminution of naturally acquired immunity from the antibiotic effects on the normal flora are issues to be considered.^{8,11,12,14,19,21,22,24} Timely treatment may be at least as useful as prophylactic antibiotics.¹⁹

Some clinicians recommend prophylactic penicillin in addition to vaccination especially for hyposplenic or asplenic children under 5 years of age and for immunocompromised patients such as in cases of renal transplantation, leukemia or lymphosarcoma.^{12,19} In all other cases, it should remain elective, especially in adults who should be given a supply of standby antibiotics to be taken at the first sign of infection or when traveling, although there is no proof that such early self-treatment lowers the incidence of sepsis.^{4,6,11-15,22}

Another point to consider is the post-surgery time interval. Since the risk of infection is greatest within two years after surgery, prophylaxis may be important in this period.¹² Most practitioners prescribe oral Penicillin V 250 mg twice daily.^{4,5,12} The British authorities recommend that regimen for children between 5 and 14 years of age and half that dose for those younger than 5.¹³ Other authors recommend that, for children younger than 5 years, 250 mg of amoxicillin daily is the best choice because it presents better gut absorption and better coverage against haemophilus infection.⁴ Because of an increase in worldwide incidence of highly resistant pneumococcal isolates, more physicians are choosing to prescribe broad spectrum antibiotics such as amoxicillin/clavulanic acid, cefuroxime or trimethoprim/sulfamethoxazole.^{6,22}

Another matter of debate is the duration of the antibiotic prophylaxis.^{3,5,11} Some recommend it until 18 years of age for children and for at least 5 years post-splenectomy in adults.⁴ Other authorities advocate continued use of antibiotics for 2 to 5 years or until the age of 21.¹⁵ Therefore, decision-making should be individualized based on the perceived risk for the specific patient.¹¹

Education of health care professionals, patients and their caretakers regarding the infection risk is a must, perhaps more important than any specific surgical or pharmacological intervention.^{11,19,23} Brigden and co-workers²⁵ found that physicians need further education regarding infectious risks associated with asplenia, the need for an appropriate timing of revaccination, and the long-term use of antibiotics in children. White et al²³ showed that splenectomy patients have a low level of knowledge about their susceptibility to infections and precaution measures. In their study, only 11% of the patients were aware of any health precautions without any prompting. Even with prompting, 60% of the subjects were not aware of a greater risk for infection.

Rasmussen et al,²⁶ after examining 175 splenectomized patients' knowledge of prophylactic measures against severe infections, found that only 16% had been provided with penicillin and were aware of how to use it. Half of the patients reported that they would not spontaneously tell an uninformed emergency room physician about their splenectomy. Patients should be requested to wear a Medic-Alert or any other similar identification tags and should be taught to alert all health care professionals, including dentists, about their spleen status.^{4,6,11,15,21,22}

Pediatric dental considerations

Obtaining a detailed health history is of great importance before starting dental care for all children and adolescents, but particular attention should be paid to those patients who present a medical condition. A child with splenic dysfunction or for whom splenectomy is being contemplated is no different. The pediatric dentist must understand the patient's baseline condition and its medical treatment to make necessary modifications for the delivery of dental care. The patient's current medications, allergies, history of surgical procedures, emergency room visits, hospitalizations, infection episodes, current hematological and immune status should be investigated. A detailed oral and dental exam, with prompt attention to potential sources of infection before and after the surgery, is a must.

Education of the patient and the caretaker should include discussion of healthy dietary and oral hygiene habits, and the importance of regular visits to the dentist. Furthermore, they must be reminded that an odontogenic infection needs to be ruled out in cases of fever of unknown origin, which has a potential to be life threatening, regardless of the indication and timing of the splenectomy. Any febrile presentation in splenectomized patients should rise a high index of suspicion.⁶

The execution of the dental treatment plan must consider important aspects of the patient's condition. If the patient is taking corticosteroids, a medical consultation is necessary to evaluate the need for replacement therapy.³ Thrombocytopenia, ie, platelet levels below 150,000/mm³,³ may be present because of leukemia, certain anemias, lymphomas or idiopathic thrombocytic purpura, putting the patient at risk for prolonged bleeding. Clotting and platelet disorders can also be intrinsic to the underlying condition and certain drugs are known to prolong bleeding.²⁷ Patients who have idiopathic or immune thrombocytopenia are also at risk for hepatitis and their liver function should be evaluated to rule out bleeding tendencies and altered drug metabolism.³ A moderate risk of bleeding exists when platelet levels reach 50,000/mm³.²⁷

Elective dental procedures, particularly extractions, should be deferred if possible until the platelet count normalizes or reaches a level in which bleeding can be more easily controlled with local measures, for example, 100,000/mm³. In emergency cases for thrombocytopenic patients, the physician must be consulted to discuss local and systemic means to help minimize the problem.

Children undergoing chemotherapy and/or radiotherapy, who have had a splenectomy as part of the therapy or as a staging procedure, must have a complete blood count done before dental treatment. The platelet level should be noted as well as the absolute neutrophil count (ANC), which is a measure of the patient's capacity for defense against bacteremias and infections. The ANC is calculated by adding the percentage of mature neutrophils (segs) and immature cells (bands) and multiplying that percentage by the white blood cell count.²⁷ When the ANC is less than 1,000/mm³, elective dental work should be postponed because the risk for sepsis increases greatly.²⁸ If a child is neutropenic and the dental treatment cannot be deferred, a medical consultation is warranted before treatment starts. Although these patients often take prophylactic antibiotics, the physician may elect to give a supplemental regimen or may increase the current dose to help boost the patient's defense system.

The majority of these patients have a central line which is an indwelling catheter inserted into the right atrium through the subclavian, cephalic or jugular vein exiting the skin via a subcutaneous tunnel usually located on the superior aspect of the chest. The purpose of the central line is to minimize needle sticks and accidental leakage of chemotherapeutic agents around the veins, and to allow multiple daily blood draws, administration of drugs, transfusion of blood elements, parenteral nutrition, etc.²⁹ When the line is present, antibiotics against endocarditis must be prescribed.³⁰

Sickle cell disease children are at risk for serious bacterial infections because they commonly present functional asplenia or splenectomy. These patients present a 400-fold increased risk of pneumococcal septicemia/meningitis.³¹

Prophylactic use of penicillin (125 mg bid up to age 3 years, then 250 mg bid) is very effective in reducing the number of life-threatening pneumococcal sepsis in sickle cell children younger than 5 years.³¹ However, prophylaxis in older children has not been shown to be beneficial and may be unnecessary after pneumococcal vaccination.³¹

The latest edition of the National Institutes of Health (NIH) Management and Therapy of Sickle Cell Disease (1995)³¹ state that dental cleaning and restorations do not require special modifications but extractions and root canal treatments should be "preceded and followed by standard

rheumatic fever antibiotic prophylaxis". On the other hand, the adult health care section of the same document states that prophylactic antibiotics should be used for extractions and endodontic therapy "if there is a question of rheumatic heart disease or mitral valve prolapse or if an orthopedic prosthesis has been implanted." It is important to note, however, that the aforementioned NIH document was written before the current AHA guidelines for endocarditis protection.³⁰

Because there are no controlled studies to date to show the efficacy of antibioticotherapy in the prevention of post-splenectomy infection, recommendations in the dental setting can also be controversial. There are no proven benefits or recommendations for the use of antibiotic prophylaxis in splenectomized patients receiving invasive dental procedures.³² Indiscriminatory use of antibiotics may induce resistance of serious pathogens and increase the risk of allergy and toxicity which, when combined with financial costs, may not present an acceptable risk-benefit ratio.³³ Early studies recommended that in dental situations in which bacteremia is highly predictable, it would seem appropriate that antibiotic prophylaxis be used until research proves otherwise.³⁴ However, other authors believe that, because most of the organisms that cause infections in asplenic patients are not endogenous to the oral cavity, these patients are not at risk of developing sepsis as a result of dental procedures.^{3,33}

Furthermore, viridans streptococci are rarely if ever implicated, the causative organisms are not likely to be susceptible to commonly used prophylactic antibiotics and no sound risk-benefit ratio has been established.³³ Based on these facts, antibiotic prophylaxis prior to dental procedures is not indicated for healthy asplenic patients nor for those who had splenectomy due to trauma.^{3,32,33} Nevertheless, a medical consultation should be sought when treating patients who are immunosuppressed, in poor health or who had a splenectomy within the past two years, particularly in young children.^{1,2,4,8,12,19,20,32}

In our hospital practice, pulpally involved primary teeth and permanent teeth with poor prognosis are indicated for extraction for those patients who are immunocompromised, in poor health, or less than 2 years post-splenectomy.

Table 2. Recommendations for Dental Care of the Patient with Splenic Dysfunction

At the initial or recall visit, before dental treatment
Review of the medical history including
Underlying cause of spleen dysfunction and associated problems
History of surgeries, infections, hospitalizations and emergency visits
Current medications and allergies
Overall health condition, particularly hematological and immune system status
Education of patient and caretakers
Importance of oral health and prevention of dental disease
Consider dental infection in cases of fever of unknown origin
Detailed oral/dental examination
Consult physician regarding antibiotic prophylaxis when splenectomy was done within the past two years, when treating immunocompromised patients and/or those in poor health
During dental treatment and emergency situations
For healthy patients, two year or more post-splenectomy
No pre-operative antibiotic prophylaxis indicated unless patient presents a condition that warrants SBE prophylaxis
Routine dental care
Timely treatment of odontogenic infection with antibiotics (if appropriate) and removal of the offending tooth
For patients who are immunocompromised, in poor health or within two years of the splenectomy
Consult physician regarding need for prophylactic antibiotics
ANC > 1,000/mm ³ and platelets > 100,000/mm ³
If below these levels, postpone elective procedures until counts are close to or at normal levels
In emergency situations or when procedure can't be deferred, consult with physician before proceeding
SBE prophylaxis for patients who present a condition that warrants it
Extraction of primary teeth that are pulpally involved and of permanent teeth with poor prognosis
Endodontic treatment for permanent teeth with good prognosis when ANC and platelets are close to or at normal levels. Palliative care and antibioticotherapy (in consultation with physician) in the meantime
Timely treatment of odontogenic infection with antibiotics (if appropriate) and removal of the offending tooth
After dental treatment
Recall visits as appropriate for each individual patient

Endodontic treatment of permanent teeth with good prognosis is done when the patient is in better health condition. In the meantime, palliative treatment is provided and the patient is prescribed antibiotics in consultation with his/her physician, with close dental monitoring until definitive care can be delivered. Individuals in good health who had a splenectomy for longer than two years receive routine dental care without antibiotic prophylaxis.

In cases of odontogenic infections, timely management of the problem with institution of antibioticotherapy can help prevent harmful consequences. In case the patient is on prophylactic antibiotics, a different drug should be prescribed for control of the infection and endocarditis precaution for those patients who need it. Table 2 summarizes the treatment recommendations for the pediatric patient who has a dysfunctional spleen.

The medical literature shows that the optimal strategy is difficult to be agreed upon. The recommendations herein discussed and in place in our hospital pediatric dental service were arrived at after a literature review and discussion with our Pediatric Hematology colleagues.

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ABSTRACT OF THE SCIENTIFIC LITERATURE



ORAL COLONIZATION OF *STREPTOCOCCUS MUTANS* IN SIX-MONTH-OLD PREDENTATE INFANTS

The majority of studies report that *S. mutans* first appears in the mouth with the eruption of the first tooth (Berkowitz et al, 1975; Caufield et al, 1993). However, recent studies indicate that *S. mutans* may be found in the mouth prior to tooth eruption (Milgrom et al, 2000; Wan et al, 2000; Wan et al, 2001). Since caries risk increases with the earlier acquisition of *S. mutans*, the finding that *S. mutans* can colonize predentate children holds significance with regard to the etiology of early childhood caries.

It was hypothesized that pre-term infants because of their relative immaturity, are more susceptible to early oral colonization of *S. mutans*. One hundred seventy-two predentate, six-month-old infants (60 pre-term, 112 full-term) were included in this study. It was found that 50% of pre-term and 60% of full-term infants harbored *S. mutans*. The colonization was confirmed by repeat sampling. In both groups, increased frequency of sugar intake was ranked the most important factor associated with colonization, followed by breast-feeding and habits which allowed saliva transfer from mother to infant. By contrast, non-colonization of *S. mutans* was associated with multiple courses of antibiotics. There were higher percentages of full-term infants who had feedings and sugar exposures at night. Mothers with infected infants had *S. mutans* levels greater than 5×10^5 CFU/ml saliva, poorer oral hygiene, more periodontal disease, lower socio-economic status and snacked more frequently when compared to mothers with non-infected infants.

Address correspondence to K.seow@mailbox.uq.edu.au

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