(term encompasses beta-thalassemia major [which is also known as B thalassemia major, Cooley’s anemia, Mediterranean anemia, familial erythroblastic anemia, and beta type microcytemia]; beta-thalassemia intermedia; beta-thalassemia minor [which is also known as B thalassemia minor and 8 thalassemia trait]; sickle beta-thalassemia [which is a form of sickle cell disease]; E beta-thalassemia; alpha-thalassemia major [which is also known as a thalassemia major, hemoglobin Bart hydrops fetalis, and Hb Bart syndrome]; hemoglobin H disease; alpha-thalassemia minor [which is also known as a thalassemia minor and a thalassemia trait]; and alpha-thalassemia Constant Spring.)

Note: This fact sheet focuses on beta-thalassemia major unless otherwise indicated.

**Is the initiation of non-invasive dental hygiene procedures* contra-indicated?**  No

- **Is medical consult advised?** Yes, liaison with the patient/client’s hematologist (blood specialist) or experienced internist, pediatrician, or family physician is advisable regarding the severity and management of the patient/client’s thalassemia before undertaking dental hygiene treatment for the first time. Medical consult is also warranted for suspicious, but as yet undiagnosed, anemia or hemoglobinopathy (e.g., suggestive orofacial features); and if known disease is poorly controlled.

**Is the initiation of invasive dental hygiene procedures contra-indicated?**  Yes. This is a blood disorder that may affect appropriateness or safety, and scaling and root planing, including curetting surrounding tissue, are contraindicated until the patient/client is medically cleared. Other potential contraindications include: spleen damage or splenectomy (resulting in compromised immunity and thus increased risk for serious infections); certain medication side-effects (e.g., reduced white blood cell count [compromised immunity] resulting from iron chelation therapy or from hydroxyurea treatment of sickle beta-thalassemia, or reduced platelet count [abnormal bleeding risk] resulting from hydroxyurea); and bone marrow transplantation (because it variously involves chemotherapy or radiotherapy to destroy the host’s bone marrow followed by a life-long regimen of immunosuppressive therapy to prevent rejection).

- **Is medical consult advised?** See above. The appropriate setting for provision of invasive dental hygiene care should be determined; i.e., whether in the setting of primary or secondary (hospital-based) care. For certain types of thalassemia, close liaison with the patient/client’s hematology team is indicated to determine potential complications when delivering invasive dental hygiene treatment as well as measures to put in place to reduce risk. The severity of the thalassemia, the degree of anemia (as indicated by recent blood test results), and the extent of co-morbidities/multi-system involvement should be established so that risk can be reduced.

- **Is medical clearance required?** Yes, for thalassemia major/intermedia, E beta-thalassemia, sickle beta-thalassemia, and hemoglobin H disease diagnoses (and to confirm type of thalassemia diagnosis — e.g., “relatively benign” thalassemia minor versus “problematic” thalassemia major). Medical clearance may also be required if patient/client is being treated with medications associated with immunosuppression +/- increased risk of infection (e.g., corticosteroids such as prednisone).

- **Is antibiotic prophylaxis required?** Yes, if there is compromised immunity, which places patient/client at risk for distant-site infection from transient bacteremia resulting from invasive procedures. Predisposing factors for infections in thalassemic patients/clients include severe anemia, iron overload, splenectomy, and various immune system abnormalities. Furthermore, daily penicillin is often prescribed until age 5 or 6 years to prevent serious infection in children with sickle beta-thalassemia; some adults also take ongoing antibiotic prophylaxis, particularly if they have had their spleen removed.

- **Is postponing treatment advised?** Yes, until the patient/client has been medically cleared, including addressing of severe anemia, ascertaining if antibiotic prophylaxis is warranted, and reducing propensity for a sickling crisis in sickle beta-thalassemia (e.g., infection treated and adequate hydration ensured). To minimize complications, hemoglobin levels should be above 110 g/L, and the patient/client should be free from symptoms of anemia. Patients/clients who are short of breath and in whom Hb levels are less than 110 g/L, abnormal heart rate is present (e.g., tachycardia), or oxygenation is less than 91% by pulse oximetry are medically unstable; routine dental hygiene treatment should be deferred until health status improves. The timing of treatment should ideally occur within a week after a blood transfusion when the hemoglobin level is highest. If a sickle cell crisis is suspected in sickle beta-thalassemia, emergency protocol should be initiated and prompt transfer to an emergency department is indicated. Patients/clients with heterozygous thalassemia trait (i.e., thalassemia minor), as distinct from homozygous thalassemia major, are generally not at risk for adverse events during dental hygiene treatment.
Disease/Medical Condition

THALASSEMIA

(term encompasses beta-thalassemia major [which is also known as β thalassemia major, Cooley’s anemia, Mediterranean anemia, familial erythroblastic anemia, and beta type microcytemia]; beta-thalassemia intermedia; beta-thalassemia minor [which is also known as β thalassemia minor and β thalassemia trait]; sickle beta-thalassemia [which is a form of sickle cell disease]; E beta-thalassemia; alpha-thalassemia major [which is also known as α thalassemia major, hemoglobin Bart hydrops fetalis, and HB Bart syndrome]; hemoglobin H disease; alpha-thalassemia minor [which is also known as α thalassemia minor and α thalassemia trait]; and alpha-thalassemia Constant Spring.)

Oral management implications

- The dental hygienist should be aware of the orofacial (and systemic) features of thalassemia so that an early diagnosis can be made and appropriate care can be provided. This is particularly important in Ontario due to immigration patterns, and because most variants of thalassemia are not detected as part of routine newborn blood screening.
- Dental hygiene care should be delivered as part of a coordinated team approach, ensuring close liaison between the dental hygienist, dentist, and hematologist/physician.
- Good oral hygiene and preventive care are very important to reduce the risk of serious infection and the need for extractions (especially in patients/clients taking bisphosphonates, which predispose to osteonecrosis of the jaw). Patients/clients presenting with acute dental infections/abscesses should be referred for urgent dental care and antibiotic therapy, especially if they have had a splenectomy.
- Most patients/clients with thalassemia can safely receive routine dental hygiene care in a primary care setting. However, long procedures should be avoided in patients/clients with more severe forms of the disease; appointments should be kept short to reduce stress. Dental hygiene care should be adapted according to the patient/client’s tolerance of the planned procedures on the day of treatment.
- For patients/clients with thalassemia who receive regular blood transfusions, invasive dental hygiene care should be delivered in the week following a planned exchange, because the patient/client’s blood count will be optimal. However, invasive dental hygiene procedures should be avoided on the same day as the transfusion, because patients/clients are often fatigued following the exchange.
- Dental hygienists should be aware of the presence/extent of transfusion-related iron overload complications, including the degree of cardiac involvement, and implement precautions as appropriate.
- Depression can occur due to lifelong adherence to a complicated medical regimen; this can impact patient/client motivation and willingness to accept oral health interventions.
- Patients/clients with thalassemia may have bone marrow expansion leading to maxillofacial deformity, particularly if they begin blood transfusions late or have been under-transfused. The dental hygienist should promote early orthodontic intervention; correction of drifted maxillary anterior teeth and increased overjet should be undertaken to improve aesthetics, reduce susceptibility to trauma, avoid gingival inflammation, and improve functional ability.
- Patients/clients with thalassemia may be candidates for bisphosphonate therapy to strengthen bone. They should have a comprehensive oral health assessment to ensure that they are as dentally fit as possible prior to the commencement of bisphosphonates. Reduction of mucosal trauma and avoidance of subsequent dental extractions are important ongoing goals. Preventive advice should be given, emphasizing the importance of reporting symptoms such as loose teeth, pain, or swelling, as soon as possible. If a patient/client has spontaneous or chronic bone exposure, referral to an oral surgeon/maxillofacial surgery specialist should be considered.

Oral manifestations

- Characteristic facial findings in beta-thalassemia major result from malformation of the facial bones due to marrow expansion and faster rate of growth of the jaw. These manifestations include prominent cheekbones; depression of the nasal bridge; prominent premaxilla and enlargement of the upper jaw (“chipmunk face”); protrusion, flaring, or migration of — and spacing between — the maxillary anterior teeth (particularly rotation or forward drift of the maxillary incisors); and varying degrees of malocclusion (overbite, open bite, overjet).

cont’d on next page...
Disease/Medical Condition

THALASSEmia

(term encompasses beta-thalassemia major [which is also known as β thalassemia major, Cooley’s anemia, Mediterranean anemia, familial erythroblastic anemia, and beta type microcytemia]; beta-thalassemia intermedia; beta-thalassemia minor [which is also known as β thalassemia minor and β thalassemia trait]; sickle beta-thalassemia [which is a form of sickle cell disease]; E beta-thalassemia; alpha-thalassemia major [which is also known as α thalassemia major, hemoglobin Bart hydrops fetalis, and Hb Bart syndrome]; hemoglobin H disease; alpha-thalassemia minor [which is also known as α thalassemia minor and α thalassemia trait]; and alpha-thalassemia Constant Spring.)

Oral manifestations (con’t)

- Development of dentition may be delayed, as may be air cavity development of the maxillary sinuses.
- Teeth may be discoloured, with short crowns and roots as well as taurodents (large pulp cavities with reduced roots) and attenuated lamina dura.
- Dental caries is a common finding, for a variety of reasons, and decay is often advanced by time of presentation to the dental hygienist or dentist.
- There is a tendency toward higher rates of plaque, gingivitis, and periodontitis.
- Mucosal pallor and/or jaundice (particularly yellow discolouration of the gingiva) may arise from the hemolytic anemia associated with thalassemia.
- Macroglossia (enlarged tongue) is found in some thalassemic patients/clients. Sore or burning tongue may result from chronic anemia and/or folate deficiency.
- Painful swelling of the salivary glands occasionally results from iron deposition, and xerostomia (due to iron deposition) may be present. Reduced salivary protection results from reduced IgA production.
- Oral ulceration occurs occasionally, and necrotizing gingivostomatitis (possibly linked to reduced white blood cell count due to iron chelation agents) very rarely.
- Osteonecrosis of the jaw can result from the taking of bisphosphonates (e.g., alendronate) by patients/clients with beta-thalassemia major to combat weakened bones.
- Radiographs show reduced trabeculation of the maxilla and mandible, with prominence of some trabeculae and a blurring and disappearance of others (“salt and pepper” effect). Tooth-bearing bone may have a “chicken wire” radiological appearance. Thinning of the lamina dura and radiolucencies in the alveolar bone may also be seen. Thickened frontal bone, thinned cortex of the mandible, and faint inferior dental canal may also be seen.

Related signs and symptoms

- Thalassemia is a group of inherited red blood cell (RBC) disorders, which involves decreased production of normal adult hemoglobin1 (Hb A).
- Beta thalassemia occurs when one or both of the two genes that make beta-globin don’t work or only partly work. Beta-thalassemia minor, in which there may be mild anemia but generally no need for treatment, is the heterozygous condition (i.e., one normal gene and one beta-thalassemia gene). Beta-thalassemia major, in which there is severe anemia and need for lifelong treatment, is the homozygous condition (i.e., two βthal genes). Beta-thalassemia intermedia2, in which there is moderate to severe anemia that may require blood transfusions, is intermediate in clinical presentation between the minor and major forms of beta-thalassemia; children with this form of thalassemia start to develop symptoms later in life than those with beta-thalassemia major.

1 Normal adult hemoglobin consists of two alpha and two beta chains; i.e., α2β2.
2 Some classification systems of beta-thalassemia divide thalassemia minor into two categories, depending on the patient/client’s presentation:
   - thalassemia minima, in which a person has few or no symptoms; and
   - thalassemia intermedia, in which a person has moderate to severe anemia.
## THALASSEMAIA

(term encompasses **beta-thalassemia major** [which is also known as β thalassemia major, Cooley’s anemia, Mediterranean anemia, familial erythroidic anemia, and beta type microcytemia]; **beta-thalassemia intermedia**; **beta-thalassemia minor** [which is also known as β thalassemia minor and β thalassemia trait]; **sickle beta-thalassemia** [which is a form of [sickle cell disease]]; **E beta-thalassemia; alpha-thalassemia major** [which is also known as α thalassemia major, hemoglobin Bart hydrops fetalis, and Hb Bart syndrome]; **hemoglobin H disease; alpha-thalassemia minor** [which is also known as α thalassemia minor and α thalassemia trait]; and **alpha-thalassemia Constant Spring**.)

### Related signs and symptoms (con’t)

In **sickle beta-thalassemia** (hemoglobin SB thal), there are two different defective hemoglobin genes, which results in a disorder with characteristics of both thalassemia and sickle cell disease (SCD). **E beta-thalassemia** (usually found in people of Southeast Asian ancestry, such as Cambodians, Vietnamese and Thai) tends to manifest as a moderately severe anemia, and is similar in signs/symptoms to beta-thalassemia intermedia.

- **Alpha thalassemia** occurs when one or more of the four genes that make alpha-globin are missing or damaged. The **silent carrier** state, in which RBCs may be somewhat smaller than normal but in which there are no symptoms or need for treatment, occurs if one gene is missing or damaged. **Alpha thalassemia minor**, in which there is mild anemia but usually no need for treatment, occurs if two genes are missing or damaged. **Hemoglobin H disease**, in which there is mild to moderately severe anemia sometimes requiring blood transfusions, occurs if three genes are missing. **Alpha thalassemia major**, which causes hydrops fetalis, occurs when all four genes are missing; it is nearly always fatal before or shortly after birth.

- **Beta-thalassemia** is classically found in persons of Mediterranean (particularly Italian and Greek) ancestry. Other persons at elevated risk includes those of North African, Middle Eastern, Iranian, Indian, Central Asian, southern Chinese, and Southeast Asian descent. Similarly, alpha-thalassemia occurs most frequently in people from Mediterranean countries, North Africa, the Middle East, India, and Central Asia.

- In Canada, there are estimated to be several hundred transfusion-dependent persons with beta-thalassemia. The Greater Toronto Area (GTA) has a particularly high concentration of such persons due to historical immigration and genetic patterns.

- Diagnosis of thalassemia includes the use of red blood cell indices, hemoglobin electrophoresis, and molecular and genetic tests. Hemoglobin (Hb) level and erythrocyte count are typically reduced, and the RBCs are microcytic (small).

- All newborns in Ontario are specifically screened for sickle beta-thalassemia (HbSB) on their newborn blood screening test. While some other hemoglobinopathies, including hemoglobin E trait (the “silent” carrier state related to E beta-thalassemia), may also be detected as part of this newborn screen, most variants of thalassemia are not detected as part of Ontario’s newborn screening program.

- **Beta-thalassemia major** presents early in postnatal life (as early as 4 to 6 months), during the switch from fetal hemoglobin (HbF) to adult hemoglobin. Untreated children develop life-threatening anemia. The affected child has pallor, jaundice, malaise, weakness, and sometimes fever. Hepatomegaly (enlarged liver) and splenomegaly (enlarged spleen) are common. Chronic anemia leads to growth retardation, and puberty is often delayed. Bones may be misshapen and prone to fractures.

- People with beta-thalassemia are at increased risk of developing abnormal blood clots, as well as **osteoporosis**.

- Severe anemia may manifest as dizziness, fatigue, shortness of breath, headache, leg cramps, and difficulty concentrating.

- Treatment of beta-thalassemia major involves repeated blood transfusions (“exchange transfusions”), sometimes splenectomy (surgical removal of the spleen), and, more rarely, bone marrow transplantation. However, chronic blood transfusions can result in iron overload; complications over time include impairment of heart, lung, and liver function, as well as elevated risk of **diabetes mellitus**, hypothyroidism (fatigue, coldness, weight gain, etc.), hypoparathyroidism (cramps and muscle spasms and potentially seizures due to decreased calcium and phosphorus in the blood), and adrenal insufficiency (fatigue, body aches, and weight gain amongst other problems).

3 Hydrops fetalis is a very serious fetal condition defined as abnormal accumulation of fluid in two or more fetal compartments, including ascites, pleural effusion, pericardial effusion, and skin edema.

4 Anemia is generally defined as Hb level less than 120 g/L in women and less than 130 g/L in men.
THALASSEMIA

(term encompasses beta-thalassemia major [which is also known as B thalassemia major, Cooley’s anemia, Mediterranean anemia, familial erythroidastic anemia, and beta type microcytemia]; beta-thalassemia intermedia; beta-thalassemia minor [which is also known as B thalassemia minor and B thalassemia trait]; sickle beta-thalassemia [which is a form of sickle cell disease]; E beta-thalassemia; alpha-thalassemia major [which is also known as α thalassemia major, hemoglobin Bart hydrops fetalis, and Hb Bart syndrome]; hemoglobin H disease; alpha-thalassemia minor [which is also known as α thalassemia minor and α thalassemia trait]; and alpha-thalassemia Constant Spring.)

Related signs and symptoms (con't)

- Patients/clients undergoing repeated blood transfusions will often take iron-chelating agents (e.g., deferoxamine, deferasirox, and deferiprone) after transfusions to remove excess iron from the body. Deferoxamine can be deposited in the skin, and thus some thalassemic patients/clients have a grayish skin colour.
- Dental hygienists in Ontario are more likely to encounter B-thalassemic major patients/clients with signs/symptoms of iron toxicity (secondary to blood transfusion treatment and inadequate chelation therapy) than with many of the classic manifestations of untreated disease.
- Untreated beta-thalassemia major typically results in early childhood death. In North America, persons with B thalassemia major who are diagnosed early and treated appropriately have a life expectancy extending well into adulthood.
- While the dental hygienist is extremely unlikely to ever encounter a patient/client with alpha-thalassemia major, Hb Bart syndrome in the fetus can cause serious health problems for women during pregnancy, including dangerously high blood pressure with swelling (preeclampsia), premature delivery, and abnormal bleeding.
- The most likely symptomatic alpha-thalassemic patient/client to be encountered by the dental hygienist is one with Hemoglobin H disease. HbH disease causes mild to moderate anemia, hepatosplenomegaly, and jaundice of the eyes and skin. Some affected persons also have bone changes, such as overgrowth of the upper jaw and an unusually prominent forehead. The features of HbH disease usually appear in early childhood, but affected persons usually live into adulthood.

References and sources of more detailed information

- Thalassemia Foundation of Canada
  http://www.thalassemia.ca
  http://www.thalassemia.ca/disease-treatment/disease-2/thalassemia-intermedia/
- United Kingdom Thalassemia Society
  http://ukts.org/
  http://ukts.org/pdfs/aboutthal/dental.pdf (Kumar N. The Importance of Dental Care for Individuals with Thalassemia.)
- Cooley’s Anemia Foundation
  http://www.thalassemia.org
- HealthLink BC http://www.healthlinkbc.ca/healthtopics/content.asp?hwid=hw184660
  http://www.iasj.net/iasj?func=fulltext&aid=31919

cont’d on next page...
THALASSEIA

(term encompasses beta-thalassemia major [which is also known as β thalassemia major, Cooley’s anemia, Mediterranean anemia, familial erythroblastic anemia, and beta type microcytemia]; beta-thalassemia intermedia; beta-thalassemia minor [which is also known as β thalassemia minor and β thalassemia trait]; sickle beta-thalassemia [which is a form of sickle cell disease]; E beta-thalassemia; alpha-thalassemia major [which is also known as α thalassemia major, hemoglobin Bart hydrops fetalis, and Hb Bart syndrome]; hemoglobin H disease; alpha-thalassemia minor [which is also known as α thalassemia minor and α thalassemia trait]; and alpha-thalassemia Constant Spring.)

References and sources of more detailed information (con’t)

- MedicineNet.com
  http://www.medicinenet.com/beta_thalassemia/article.htm
  http://www.medicinenet.com/alpha_thalassemia/article.htm
- Genetics Home Reference, U.S. National Library of Medicine
- National Center for Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention
  http://www.cdc.gov/ncbddd/thalassemia/facts.html
- Johns Hopkins Medicine
  http://www.hopkinsmedicine.org/healthlibrary/conditions/hematology_and_blood_disorders/beta_thalassemia_cooleys_anemia_85,P00081/
- Newborn Screening Ontario http://www.newbornscreening.on.ca/bins/content_page.asp?cid=7-21-350

* Includes oral hygiene instruction, fitting a mouth guard, taking an impression, etc.

** Ontario Regulation 501/07 made under the Dental Hygiene Act, 1991. Invasive dental hygiene procedures are scaling teeth and root planing, including curettting surrounding tissue.

Date: October 2, 2015