BERNARD-SOULIER SYNDROME

AN INHERITED BLEEDING DISORDER

AN INFORMATION BOOKLET

Canadian Hemophilia Society
Help Stop the Bleeding

Canadian Association of Nurses in Hemophilia Care
Association canadienne des infirmières et infirmiers en hémophilie

Acknowledgments

This information booklet on Bernard-Soulier Syndrome was prepared by:

Nathalie Aubin
Nurse Coordinator, Hemophilia Centre
MUHC Montreal Children's Hospital
2300 Tupper Street, A216
Montréal, Québec H3H 1P3

Claudine Amesse
Nurse Coordinator, Hemophilia Centre
Sainte-Justine Hospital
3175 Côte Sainte-Catherine Road
Montréal, Québec H3T 1C5

Louisette Baillargeon
Nurse Coordinator, Hemophilia Clinic
CHUS - Fleurimont Hospital
3001 12th Avenue North
Sherbrooke, Québec J1H 5N4

Francine Derome
Nurse Coordinator, Hemophilia Centre
Sainte-Justine Hospital
3175 Côte Sainte-Catherine Road
Montréal, Québec H3T 1C5

Claude Meilleur
Nurse Coordinator, Quebec Centre for Coagulation Inhibitors
Sainte-Justine Hospital
3175 Côte Sainte-Catherine Road
Montréal, Québec H3T 1C5

Catherine Sabourin
Nurse Coordinator, Hemophilia Centre
MUHC Montreal Children's Hospital
2300 Tupper Street, A216
Montréal, Québec H3H 1P3

We are very grateful to the following persons who kindly undertook to review the medical information contained in this booklet. Their suggestions are very much appreciated.

Dr. Molly Warner
Hematologist
MUHC Montreal Children's Hospital and Royal Victoria Hospital
2300 Tupper Street, A216
Montréal, Québec H3H 1P3

Hélène Néron
Nurse Coordinator, Hemophilia Centre
Hôpital de l'Enfant-Jésus
1401, 18e Avenue
Local J - S 066 Porte D
Quebec City, Québec G1J 1Z4

Editor: Debbie Hum

ISBN 978-1-897489-04-8

The Canadian Hemophilia Society (CHS) strives to improve the health and quality of life for all people with inherited bleeding disorders, and to find a cure.

This booklet provides general information on Bernard-Soulier Syndrome only. The Canadian Hemophilia Society does NOT practice medicine and does not suggest specific treatments. In all cases, we suggest that you speak with a doctor before you begin any treatment.

TABLE OF CONTENTS

Introduction

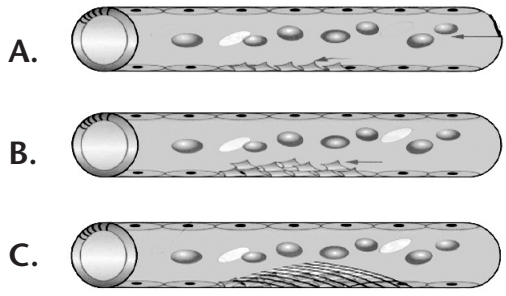
Bernard-Soulier Syndrome (BSS) is a rare hereditary disorder. Learning to cope with this disease is not easy. Discovering that your child has it can be overwhelming. A BSS diagnosis often leads to feelings of insecurity and frustration. What's more, given the rarity of the disease, there is very little written information available to people who are affected.

The complications associated with BSS can range from mild to serious. We hope that this information booklet will be useful to anyone faced with this disorder, regardless of the severity of their particular condition.

Bernard-Soulier Syndrome (BSS)

BSS is a blood clotting disorder that hinders the ability of blood platelets to stick together and spread around a broken vessel.

Blood clotting is a complex process that stops blood from leaking through holes in damaged blood vessel walls. When a blood vessel is injured, it automatically constricts to reduce the blood flow to the damaged area. Normally, small cells circulating in the blood called platelets stick to the damaged vessel wall (a process called platelet adhesion) and clump together to form a plug at the site of injury (called platelet aggregation). The platelet plug is subsequently strengthened with a protein called fibrin.



This figure illustrates platelet adhesion to a damaged blood vessel wall (**A**). Subsequently, these platelets aggregate and form a plug (**B**). The platelet plug (or clot) is stabilized by a meshwork of fibrin (**C**).
(Adapted from Israels S, Man-Chiu P, Margaret L.R. Disorders of Platelet Function: An Information Booklet for Patients, Families and Health Care Providers. On behalf of the Canadian Children's Platelet Study Group, 2002)

Patients with BSS have an insufficient number of platelets. In addition, their platelets are larger than normal and do not function properly. The disorder is caused by a deficiency in glycoprotein Ib/IX/V, which is a protein found on the surface of platelets. This protein is essential to the aggregation of platelets around injured blood vessels. Any deficiency in this protein will result in prolonged bleeding episodes because platelets fail to form a clot.

Discovery of the disease

Bernard-Soulier Syndrome was discovered in 1948 by two French hematologists named Jean Bernard and Jean-Pierre Soulier. In an article, they described the case of a young boy who had been suffering abnormal bleeding episodes from birth and whose older sister had hemorrhaged to death. The researchers established that the boy had considerably larger than normal platelets that lacked the ability to stick adequately to blood vessel walls, resulting in prolonged bleeding.

How the Disease is Inherited

BSS is generally an inherited bleeding disorder. While there are documented cases of acquired BSS in medical literature, most of them were associated with other conditions. Since acquired BSS is extremely rare, this booklet only deals with inherited BSS that is passed on from parent to child at conception. This particular platelet disorder is caused by an abnormal gene.

Each cell of the body contains structures called chromosomes. A chromosome is a long chain of chemicals known as DNA. This DNA is arranged into approximately 30,000 units or genes. These genes determine characteristics such as eye colour. In the case of BSS, one of the genes located on a particular chromosome has a defect.

The defective gene in BSS is on a chromosome that does not determine the sex of a child. This means that BSS can affect both males and females, unlike other bleeding disorders such as factor VIII deficiency (also called hemophilia A) where severe cases are only observed in males since the defective gene is gender-related.

A “carrier” is a person who has the defective gene without being affected by the disease. In order for a person to inherit BSS, both parents must be carriers or affected. In such cases, a baby inherits two defective genes, one from the mother and the other from the father. A person who inherits the defective gene from only one of their parents will be a carrier who is unlikely to exhibit any symptoms of the disease.

The five illustrations below show how BSS can be passed on.

Figure 1 shows what can occur when a carrier of BSS has children with a non-carrier. There is a 1-in-2 chance that a child will be a carrier. There is also a 1-in-2 chance that a child will be normal.

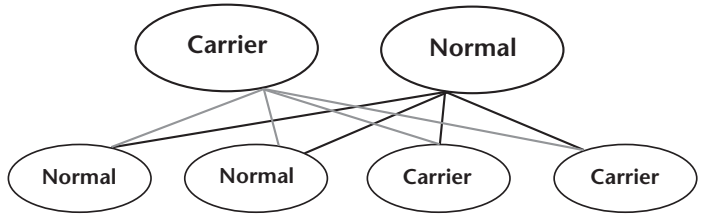


Figure 1

Figure 2 shows what can happen when a carrier of BSS has children with another carrier. There is a 1-in-4 chance that a child will be affected with BSS, a 1-in-2 chance that a child will be a carrier and a 1-in-4 chance that a child will be normal.

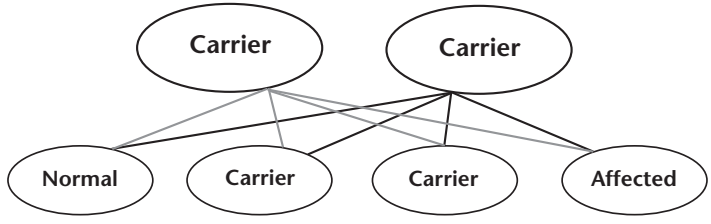


Figure 2

Figure 3 shows what can occur when someone with BSS has children with a non-carrier. All of their children will be carriers, but none of them will have the disease

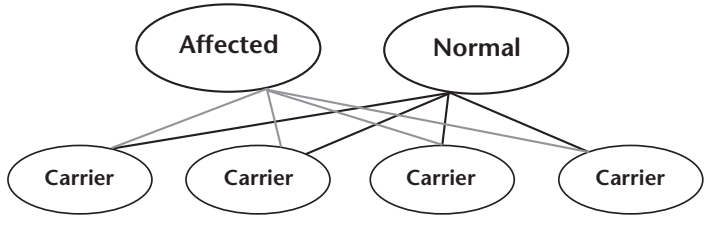


Figure 3

Figure 4 shows what can happen when someone with BSS has children with a carrier. There is a 1-in-2 chance that a child will be a carrier. There is also a 1-in-2 chance that a child will have BSS.

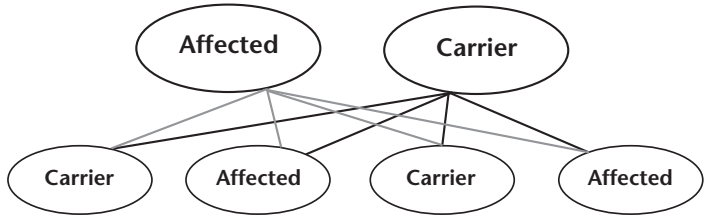


Figure 4

Figure 5 shows what can occur when two people with BSS conceive children together. In this case, every child will have BSS.

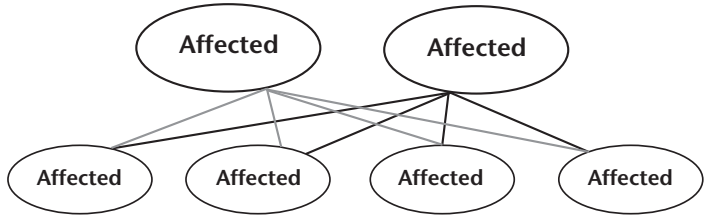


Figure 5

Incidence

BSS is extremely rare. It has been estimated that this disease affects less than one person in a million. To date, there are only 100 documented cases in medical literature.

Diagnosis

BSS is generally diagnosed in newborns or toddlers who experience unusual bleeding. Subsequent laboratory blood tests confirm the diagnosis.

Symptoms

People with BSS show signs of abnormal bleeding episodes during their first year of life.

Generally, BSS manifests itself as:

- Purpura (bruising just under the skin)
- Epistaxis (nosebleed)
- Bleeding from the mouth
- Menorrhagia (heavy menstrual flow)
- Bleeding in the urinary or gastrointestinal track (in rare instances)

Purpura has no apparent cause. Although very frequent, it is painless and does not pose any danger.

Bleeding from the mouth or nose (as when children grow their first teeth or bite their tongue or cheek) is the hardest type to control.

Menorrhagia is a major bleeding problem in young women at puberty.

On rare occasions, hemorrhaging has been observed in the gastrointestinal tract.

The most severe bleeding episodes are generally triggered by trauma or a surgical procedure.

The severity and incidence of bleeding episodes will vary from one patient to the next.

Treatment

Fast and appropriate action is the key to successful treatment. Thankfully, there are effective ways to stop the bleeding.

- People with cuts and scrapes should:
  - apply prolonged pressure on the wound with a compression dressing;
  - rest and raise the affected limb.

- Individuals experiencing a nosebleed (also called epistaxis) should:
  - sit upright;
  - firmly pinch the widest part of their nostrils together for 10 to15 minutes;
  - take an anti-fibrinolytic agent such as tranexamic acid (Cyklokapron® or Amicar®) tablets to help prevent blood clots from dissolving;
  - avoid hot drinks and strenuous exercise for 24 hours after bleeding;
  - sleep in a seated position the night following the bleeding episode;
  - pack nostril(s) with gauze.

- People bleeding from the mouth should:
  - sit upright;
  - bite on a compress for 20 minutes, if possible;
  - limit their food intake to soft, cold items (e.g. Jell-O, ice cream and Popsicle) for 24 to 48 hours;
  - sleep in a seated or slightly reclined position the night following the bleeding episode;
  - take an anti-fibrinolytic agent such as tranexamic acid (Cyklokapron® or Amicar®) tablets.

- There are two treatment options for severe bleeding:
  - a platelet transfusion or replacement therapy, which has proven to be effective to stop hemorrhages in patients with BSS;
  - the administration of recombinant factor VIIa (Niastase®), although scientists do not fully understand how this product works in this specific platelet disorder.

Prevention

Here are some tips to prevent bleeding from happening in the first place:

- Never take aspirin (ASA) or any medication containing aspirin – use alternate medications recommended by your treatment centre. Talk to your physician or nurse before taking any nonsteroidal anti-inflammatory medication such as ibuprofen.

- Let your physician and dentist know that you have BSS so that they can weigh the risks and benefits associated with certain medications and procedures such as biopsies.

- Get vaccinations against influenza, hepatitis A and hepatitis B – on extremely rare occasions, these viruses can be transmitted through blood transfusions.

- Always wear a helmet when doing physical activities such as riding a bicycle or skiing. Avoid full-contact sports (e.g. boxing, football and hockey) due to their higher risk of injuries that can lead to bleeding.

- See your dentist once every six months to prevent dental problems and gingivitis. Your treatment centre can recommend a dentist who is familiar with bleeding disorders.

- Keep the nails of small children short so that they do not accidentally scratch themselves.

- Protect children from insect bites as these can cause bleeding.

- Always check with your hemophilia treatment centre before taking any new medications, herbal products or vitamins that are sold without a drug identification number (DIN).

- Always wear a Medic Alert bracelet or necklace that will notify healthcare professionals of your BSS condition in an emergency situation.

Problems specific to women

Menorrhagia

Menorrhagia is a major bleeding problem for women after the age of puberty. The use of oral contraceptives can regularize menstrual cycles and reduce heavy bleeding. Tranexamic acid (Cyklokapron® or Amicar®) can be given at the same time. These anti-fibrinolytic drugs act by slowing down the body's own destruction of clots that form.

Hemorrhages can be especially severe at the time of a girl's first menstruation.

Bleeding in pregnancy and childbirth

Because BSS is so rare, there is very little documentation about bleeding in pregnancy and at the time of childbirth.

A woman with BSS who is expecting a child should be followed in a treatment centre that has experience with such patients. Expectant mothers should discuss the risks of receiving an epidural (a common form of anesthesia during childbirth) with their physician ahead of time.

Evolution of the disease and prognosis

While the bleeding problem is lifelong, with modern medical care, Bernard-Soulier Syndrome is associated with a relatively low death rate from hemorrhage.

For a woman, the problems associated with BSS diminish with time, through different stages of life – notably, childhood, puberty and the childbearing years.

The comprehensive care team

As the name suggests, a hemophilia comprehensive care team is a team of specialists that provides most of the medical services required by a child or adult with an inherited bleeding disorder. The team is made up of several professionals, including:

- a medical director (usually a hematologist);
- a nurse coordinator;
- a physiotherapist;
- a social worker.

The team works closely with other specialists, such as a surgeon, orthopedist, rheumatologist, dentist, geneticist and psychologist. The purpose of this multidisciplinary team is to ensure the well-being of the patient, and in the case of a child, his parents as well.

For more information

You can obtain a list of Hemophilia Treatment Centres by contacting the National Office of the Canadian Hemophilia Society at the following address:

Canadian Hemophilia Society
625 President Kennedy Avenue
Suite 505
Montréal, Québec
H3A 1K2
Telephone: 514 848-0503
Toll free: 1 800 668-2686
Email: chs@hemophilia.ca
Website: www.hemophilia.ca

Bibliography

Amesse C, Lacroix S, Lupien G., Canadian Hemophilia Society. Factor VII Deficiency: An inherited bleeding disorder, 2001.

Geil, John D. Bernard-Soulier Syndrome. Emedicine online, 2005.

Israels S, Man-Chiu P, Margaret L.R. Disorders of Platelet Function, 2002.

Lanza, François. Review of Bernard-Soulier syndrome (Hemorrhagiparous thrombocytic dystrophy) Orphanet journal of rare diseases, 2006: 1-46.

Lupien G, Amesse C, Bissonnette D, Lacroix S., Canadian Hemophilia Society. Glanzmann Thrombasthenia: An inherited bleeding disorder, 2001.

Peters M, Heijboer H. Treatment of a patient with Bernard-Soulier syndrome and recurrent nosebleeds with recombinant Factor VIIa. Thrombosis and Haemostasis 1998; 352

Poon M-C, d'Oiron R, and the International Registry on Recombinant Factor VIIa and congenital platelet disorders group. Recombinant activated factor VII (NovoSeven) treatment of platelet-related bleeding disorders. Blood coagulation and Fibrinolysis 2000, 11 (suppl 1):S55-S68

Shapiro, Amy D. World Federation of Hemophilia. Platelet function disorders, 1999.

BERNARD-SOULIER SYNDROME

AN INHERITED BLEEDING DISORDER

AN INFORMATION BOOKLET

Canadian Hemophilia Society
Help Stop the Bleeding

Canadian Association of Nurses in Hemophilia Care
Association canadienne des infirmières et infirmiers en hémophilie