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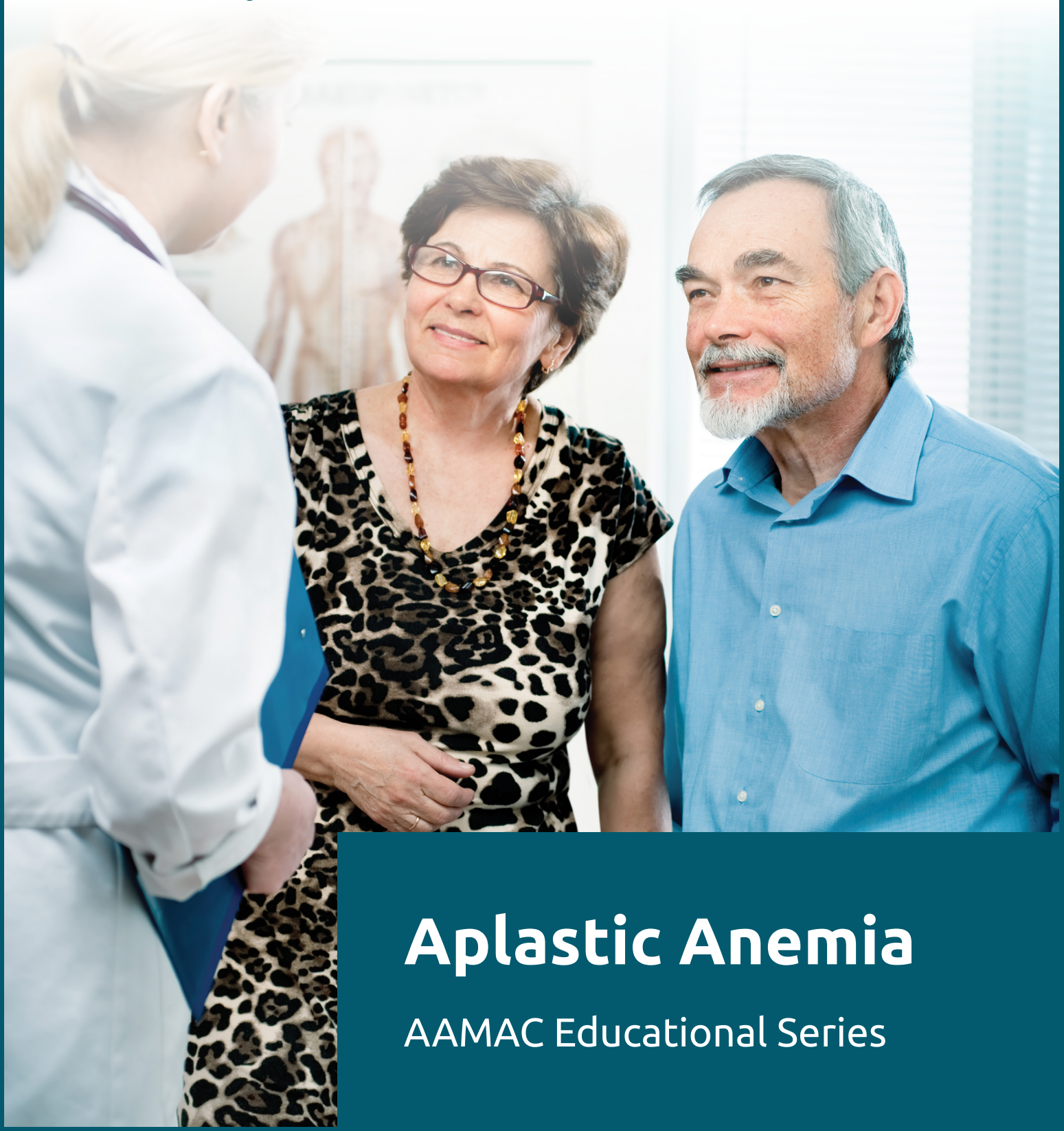
Aplastic Anemia & Myelodysplasia Association of Canada

Association canadienne de l'anémie aplasique et de la myélodysplasie



Aplastic Anemia

AAMAC Educational Series

The Aplastic Anemia & Myelodysplasia Association of Canada (AAMAC) is a federally incorporated and registered national not-for-profit charity guided by dedicated volunteer members of the Board of Directors and a distinguished team of medical advisors from across Canada. Our volunteer-run organization supports patients and caregivers across the country who are living with aplastic anemia (AA), myelodysplastic syndrome (also called MDS or myelodysplasia) and paroxysmal nocturnal hemoglobinuria (PNH). For more than 30 years, AAMAC has focused on education, advocacy, and research, and provides support for patients, and care partners across Canada who are dealing with AA, MDS and PNH.

This educational booklet is a comprehensive resource for Canadians who are living with AA and their loved ones, to support the journey in navigating this disease from diagnosis to treatment and beyond.

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1 | ABOUT THE DISEASE

About Aplastic Anemia

Aplastic anemia (AA) is a rare autoimmune blood disorder resulting from the immune system's attack on blood-forming stem cells within the bone marrow. These stem cells typically mature into three distinct types of blood cells: **red blood cells (RBCs), white blood cells (WBCs),** and **platelets**. In AA, the bone marrow becomes replaced by abnormal fat tissue and is unable to make an adequate amount of blood cells. This has the potential to result in pancytopenia, a serious condition that occurs when a person has low numbers in all three blood measurements[1].

Aplastic anemia can manifest as non-severe, severe, or very severe, depending on the degree of low blood counts. Those with severe or very severe AA face potentially life-threatening infections or bleeding. Thankfully, with timely and appropriate intervention, most people with AA can undergo successful treatment either through medical therapies or bone marrow transplantation. While a bone marrow transplant is the sole definitive cure, many patients can attain remission through non-transplant approaches and maintain a good quality of life.

Incidence of Aplastic Anemia

The estimated annual incidence of AA is two cases per million in Europe and North America, with a notably higher prevalence among people of East Asian heritage.[2] It is typically diagnosed more frequently in people between the ages of 10 and 20, as well as in those over the age of 40, with a slightly higher occurrence in males compared to females.

Causes and Types of Aplastic Anemia

Aplastic anemia can occur at any age, although it typically emerges in adulthood. Although many causes have been identified that can trigger AA, in numerous instances, the underlying cause remains unknown, especially in children. This is called *acquired aplastic anemia*. In a few occurrences, it manifests as an inherited condition, typically in younger individuals or children. This is called *hereditary aplastic anemia.*

1. Acquired AA is an autoimmune blood disorder. Typically, the immune system targets only foreign substances. However, when the immune system turns against the body's own blood cells, low blood counts occur. In particular, the type of immune cells that cause AA are called T-cells.

Approximately 75 out of 100 cases of acquired AA are considered idiopathic, signifying they lack a known cause. In the remaining instances, the cause can frequently be attributed to:

- **Use of specific medications –** These include particular drugs for managing arthritis or hyperactive thyroid, certain psychiatric medications, and a limited selection of antibiotics. The likelihood of AA developing due to these drugs is exceedingly low
- **Exposure to chemicals –** An extensive range of chemicals has been implicated as potential causes of AA. Often the connection between these chemicals and the occurrence of AA is weak. However, certain toxins are more likely to cause AA including certain pesticides, arsenic, and benzene
- **Chemotherapy used in cancer treatment**
- **Radiation exposure –** AA has been linked to exposure to ionizing radiation from radioactive substances
- **Viral infections –** Some people diagnosed with AA have experienced a viral infection in the weeks leading up to their diagnosis. Infections include hepatitis, Epstein-Barr virus, cytomegalovirus, parvovirus B19, and HIV
- **Association with other autoimmune conditions** like rheumatoid arthritis and lupus
- **Pregnancy -** This form of AA may improve spontaneously after childbirth

2. Hereditary Aplastic Anemia is transferred from one generation to the next through genetic inheritance. Typically, it manifests during childhood and is significantly less common than *acquired AA.* People with *hereditary AA* often exhibit

additional genetic or developmental abnormalities that contribute to the development of the condition.

Certain genetic conditions can harm stem cells and result in AA, including:

- Schwachman-Diamond syndrome
- Fanconi anemia
- Dyskeratosis congenita
- Diamond-Blackfan anemia

Defining Severity

Normal bone marrow has an expected level of blood-making cells. In AA, the number of cells is reduced to less than 25% of what is expected, a term called **hypocellular**. As a result, there is an inability to make blood cells and thus a low blood count. Pancytopenia refers to a condition of low blood counts in all the major blood cell lines (white blood cells, red blood cells and platelets). In determining the white blood cell count, neutrophils, a type of white blood cell, are used. Likewise, in determining the red blood cell count, reticulocyte count or young red blood cells is used. Depending on the counts, AA can be categorized as non-severe, severe, or very severe.

1. Non-severe/Moderate Aplastic Anemia (MAA) – If you are living with non-severe or moderate AA:

- Your blood cell counts may be lower, but not as low as in severe AA (see below)
- You might experience minimal or no symptoms (see section on Signs & Symptoms)
- Treatment may not be necessary, and your physician may opt for regular monitoring of your blood counts
- Your condition may remain stable over an extended period of time

2. Severe Aplastic Anemia (SAA) – If you are dealing with severe AA, at least two of the following apply:

- Your neutrophil count falls below 500 cells per microliter
- Your reticulocyte count (young red blood cells) is under 60,000 per microliter
- Your platelet count drops below 20,000 per microliter

3. Very Severe Aplastic Anemia (VSAA) – If you are dealing with very severe AA:

- Your neutrophil count is below 200 per microliter
- Your reticulocyte count is under 60,000 per microliter
- Your platelet count drops below 20,000 per microliter

Understanding Aplastic Anemia and Related Conditions

Myelodysplastic Syndromes

- Approximately 15% of people with AA develop **myelodysplastic syndromes** (MDS), a form of blood cancer, over a 10-year period
- Like AA, MDS can lead to low blood cell counts
- In MDS, abnormal bone marrow stem cells produce irregular blood cells, while in AA, bone marrow stem cells generate normal blood cells, although in insufficient quantities
- The risk of developing MDS increases with age

Paroxysmal Nocturnal Hemoglobinuria

- **Paroxysmal nocturnal hemoglobinuria** (PNH) is a rare disease where red blood cells are abnormally broken down prematurely
- Like AA, PNH results from an autoimmune problem in the bone marrow and includes the detection of PNH red blood cells (or PNH **clones**) in blood tests
- PNH red blood cells appear when bone marrow stem cells undergo a genetic mutation in what is called the PIG-A gene. This makes the red blood cells susceptible to immune system attacks and destruction in the bloodstream, a process known as **hemolysis**. In addition, there is a risk of blood clots and other organ involvement
- More than 20% of people diagnosed with AA show evidence of PNH red blood cells around the time of diagnosis, often at low levels
- Due to the low levels, AA patients who have PNH red blood cells typically don't display any symptoms of PNH

A notable historical example is Dr. Marie Curie, renowned for her groundbreaking research in the realm of radioactivity. Tragically, she succumbed to aplastic anemia after prolonged, unprotected contact with radioactive materials, as the harmful consequences of ionizing radiation were not fully understood at that time.

2 | SIGNS & SYMPTOMS

Anemia, bleeding, and infection are the initial manifestations of AA. As the disease progresses, the clinical symptoms gradually worsen and may be accompanied by severe anemia, multi-organ bleeding and sepsis, all of which pose a significant threat to patient health.

Note: *According to the World Health Organization, 'sepsis is a serious condition that happens when the body's immune system has an extreme response to an infection. The body's reaction causes damage to its tissues and organs.*[3]

The symptoms of AA can fluctuate in intensity, depending on the disease's severity and the extent of blood count depletion. Some common symptoms include:

- Fatigue and breathlessness, even with mild physical activity
- Dizziness
- Pale skin
- More easily bruise and bleed
- Prolonged bleeding episodes due to a low count of platelets
- Frequent infections accompanied by fever or chills, in addition to slow healing, because of a lack of normal WBCs, especially neutrophils

At times, people may exhibit no symptoms, and the diagnosis of AA occurs as part of a routine blood test. Some of the mentioned symptoms can also be associated with other conditions, such as viral infections. Therefore, it's essential to consult your physician for a thorough examination and appropriate treatment.

Below are more specific symptoms of AA that are usually associated with deficiencies in each component of the blood.

A **low hemoglobin** is referred to as **anemia**. People who have anemia may encounter symptoms such as:

- Varying degrees of tiredness
- Difficulty concentrating or staying alert
- Loss of weight and/or appetite
- Developing pale skin
- Difficulty breathing
- Rapid heartbeat or heart palpitations
- Dizziness and/or fainting
- Trouble climbing stairs or exercising

A **low count of platelets** is referred to as **thrombocytopenia**. People with a low platelet count are at an increased risk of experiencing excessive bruising even from minor injuries, as well as sudden bleeding from mucous membranes, particularly in the gums and nasal passages. They may experience:

- Bruising
- Heavier menstrual periods than normal
- Nose bleeds
- Flat and small red spots under their skin (called petechiae) due to bleeding
- Bleeding gums after brushing their teeth and following dental work
- Hemorrhoids

IMPORTANT: Uncontrolled bleeding constitutes a medical emergency for people with AA. If a patient experiences bleeding that cannot be halted through standard measures, such as applying pressure, seek immediate medical assistance.

A low overall count of white blood cells (WBCs) is referred to as **leukopenia**. There are several types of white blood cells. The predominant WBC type is neutrophils which are responsible for fighting infections, particularly bacterial infections. People with *leukopenia* face a heightened vulnerability to fungal and bacterial infections. People with a low WBC count may experience:

- Get infections and fevers repeatedly and run a higher risk of becoming more ill with infections
- Experience bladder infections which lead to pain urinating or urinating more often
- Develop lung infections leading to breathing difficulties and coughing
- Severe coughing
- Shortness of breath
- Experience mouth sores
- Get a stuffy nose and sinus infections
- Experience skin infections, redness or swelling
- Experience sore throats
- Get patches in the mouth that are red or white
- Get diarrhea
- Experience Vaginal itching or unusual vaginal discharge

IMPORTANT: A fever in a patient with AA can be a cause for concern. If a fever develops, seek prompt medical attention. A fever is considered a one-time temperature of >38.3 degree Celsius or >38.0 degree Celsius sustained over one hour.

3 | IMPACT OF APLASTIC ANEMIA ON QUALITY OF LIFE

With timely and appropriate medical attention, most people diagnosed with AA can undergo successful treatment, and in certain cases, achieve a complete cure. The majority of patients can return to their regular activities following treatment; however, it might take some time and trying different treatment options to achieve favourable outcomes.

Receiving regular medical care and monitoring for potential complications is crucial to maintaining good health.

A diagnosis of AA can be very difficult for the patient and their loved ones, bringing with it a psychological and emotional burden[4] and a negative impact on quality of life. This is due to severe clinical manifestations of the condition that may create hematological emergencies and result in a significant financial burden on the healthcare system, patients, and their caregivers[5].

In addition, the need for blood transfusions in patients can result in an additional drain on people's time and resources, which can affect their overall quality of life. In a study conducted in 2018 on the value of transfusion independence in severe AA from patients' perspectives[6], respondents indicated that *"transfusion independence would result in less burden on time and costs, greater control on life and better quality of life, less fatigue and less scheduling around medical appointments."*

Patients have often spoken out about their struggles in various forums and spaces either independently or through platforms offered by patient groups worldwide. These struggles can be amplified by the lack of general knowledge about the disease. A 19-year-old who provided her story to the Anthony Nolan Cancer Charity in the UK shared her struggles with mental health in dealing with AA. She wrote, *"Living with this condition is by no means easy. If it isn't the debilitating symptoms, it's the lack of understanding from the world around us. My life often feels like it isn't even really mine because the control this illness has over me is absolutely huge."* In Canada, patients often appeal to people to donate blood and stem cells since blood transfusions and stem cell transplants can be critical and there is often a shortfall in availability.

Considering the impact of the disease on mental health, it is important to connect with and use support systems including community groups, friends and family, patient, or caregiver support groups, and professional counsellors. These types of supports can assist patients to adapt to the disease and cope with the impact on their emotional well-being.

*For **information about support groups and peer-to-peer support programs in Canada for people living with AA,** please contact the Aplastic Anemia & Myelodysplasia Association of Canada (AAMAC) at info@aamac.ca or 1-888-840-0039.*

4 | DIAGNOSING APLASTIC ANEMIA

Aplastic Anemia is a rare condition that many physicians are unlikely to be familiar with or have experience in managing. Consequently, people with this condition may have symptoms for an extended period before receiving an accurate diagnosis and appropriate treatment plan. It is therefore very important to be referred to a hematologist and/or oncologist who specializes in the treatment of bone marrow failure disorders, such as AA, as soon as possible.

Diagnosis and Tests

Medical History

To understand what is causing your symptoms and reduced blood cell counts as determined by blood tests, your physician will conduct a comprehensive medical history assessment. As part of that assessment, you may be asked some of these questions:

- What symptoms have you been experiencing?
- Have you used any medications or herbal supplements recently?
- Have you had any exposure to potentially harmful chemicals?
- Did you undergo chemotherapy or radiation therapy in the past?
- Have you noticed dark or tea-coloured urine in the mornings?
- Have you been diagnosed with any recent liver inflammation?
- Have you ever had anemia or been diagnosed with a condition that could lead to anemia?
- Have you encountered symptoms like shortness of breath, dizziness, headaches, or any other indications of anemia?
- Have you previously suffered from infections or displayed signs of infection, including fever?
- Do you tend to bruise easily or experience frequent bleeding?
- Do you have any other medical conditions such as rheumatoid arthritis, system lupus erythematous, hepatitis or HIV?
- Are you pregnant?

Offering a comprehensive health history enables your physician to provide an accurate diagnosis.

Complete Blood Count (CBC) - The CBC is a comprehensive test that examines various components of the blood, including RBCs, WBCs, and platelets and supports monitoring of the disease. If the CBC reveals a reduced count of red blood cells (RBCs), white blood cells (WBCs), or platelets, the physician might conduct a blood smear test, involving a microscopic examination of the cells. Listed below is what the physician reviews:

- **WBCs, RBCs, and platelets.** Reduced counts may indicate aplastic anemia
- **Reticulocyte count,** which assesses the quantity of young RBCs in your blood. People with aplastic anemia typically have diminished reticulocyte levels

Additional blood tests. Additional blood tests are often conducted in addition to the CBC. Their purpose is to identify issues with the bone marrow that can be the cause of low levels of various blood components and to assess the degree of blood cell breakdown

- **EPO level,** also known as **erythropoietin.** EPO is produced in the kidneys in response to low RBCs and anemia. EPO then stimulates RBC production in the bone marrow. A low EPO level may suggest a condition other than AA. Your physician may prescribe synthetic EPO if your levels are low to help stimulate the making of more red blood cells in the body
- **Iron level** examination also referred to as a ferritin test, evaluates the iron concentration in the bloodstream. Iron deficiency anemia can be easily managed with iron supplements. Conversely, excessive iron in the system, known as iron overload, may result from frequent red blood cell transfusions or genetic conditions. Several treatments are available to address iron overload in the body

- **Vitamin B12 and folate level** testing may be performed to exclude other factors contributing to low RBCs. Inadequate levels of vitamin B12 and folate (folic acid) can cause RBCs to assume abnormal shapes, sizes, or appearances, leading to anemia
- **Viral studies** including hepatitis B, hepatitis C and HIV screen among other viruses
- **Kidney and liver tests** to detect the presence of liver or kidney disease
- **Pregnancy test**

Bone Marrow Testing - A bone marrow examination is crucial for diagnosing AA. Initially, a physician extracts a sample of bone marrow aspirate using a hollow needle, usually from either the pelvic or breastbone. In addition, a solid segment of bone marrow is obtained as part of a bone marrow biopsy. This procedure may cause temporary pain when the needle is inserted, but the discomfort is brief and should not persist.

The physician will examine the liquid bone marrow using a microscope and forward the specimen of bone marrow to a laboratory for further analysis. This bone marrow test serves several purposes: it confirms a diagnosis of AA (while ruling out other bone marrow failure diseases), assesses the efficiency of the bone marrow in producing blood cells, determines the cellularity (number of cells within a tissue sample) of the bone marrow, identifies the types and quantities of cells it is generating, checks for levels of iron in the bone marrow, and examines it for any chromosomal (DNA) abnormalities.

Physical exam - Your physician will perform a physical examination to detect any signs of AA. Their objective is to assess the severity of the condition and identify its underlying causes.

During the examination, your physician may look for indicators such as pale or jaundiced skin, as well as any signs of bleeding or infection. They may also perform a thorough assessment, which includes listening to your heart and lungs for any irregularities. Additionally, your physician may examine your abdomen to evaluate the size of your liver, and spleen and check for any swelling (edema) in your legs.

Additional Tests

Symptoms resembling those of AA can be attributed to various other conditions. Therefore, additional tests may be necessary to eliminate these possibilities. These may include:

- **An X-ray, computed tomography (CT) scan,** or **ultrasound imaging** test. These diagnostic tools are used to examine various organs including the liver, kidneys, and bones in the arms and hands. Abnormalities in the bones can be observed in young people with hereditary AA such as Fanconi anemia, a condition that can ultimately lead to AA. Imaging studies can also reveal enlarged lymph nodes which could indicate the presence of blood or other cancers.
- **Chest X-rays** that generate images of the internal structures in your chest, including the heart, and lungs. This diagnostic procedure may be employed to eliminate the possibility of infections

Your physician may also suggest blood tests to detect PNH and assess your immune system for antibodies, which are proteins that can target your bone marrow cells and potentially lead to AA.

5 | COMORBIDITIES

It is important to note that as with any disease, other **comorbid** conditions can exist in people living with AA. It is important to speak to your physician about how to diagnose and manage them.

6 | LIVING WITH APLASTIC ANEMIA

Navigating Care

Preparing for Appointments: It is simple to overlook important questions during an in-person or virtual visit with your AA specialist. Prior to an upcoming appointment, it is important to jot down questions and discuss these thoroughly with the hematologist/oncologist or their support team. It is also helpful to carry a notepad for writing down the responses or, if allowed, record the session to review later. If possible, bring a trusted companion to the appointment to help ensure that all questions are answered.

Managing Medical Information: It is a good practice to keep your health information, including lab results and medical records, in a single location. Consider organizing and storing these documents in a notebook, on your computer, or in an online tool using a smartphone or tablet app to easily access and refer to them whenever needed.

The Treatment Strategy: It is important to collaborate with your physician in developing a treatment plan. This plan should consider the diagnosis, the current treatment options available, and the ultimate goal of treatment. Each person's treatment plan will be unique and tailored to factors such as age, blood count measurements, overall well-being, and other considerations. It is important to thoroughly review the treatment plan provided and ensure that you are comfortable with the approach. A well-crafted treatment plan should empower you, fostering a sense of control and optimism for the future.

Using Support Systems: Coping with AA and undergoing treatment can be challenging. There may be moments of fatigue, illness, or anxiety in this situation. This is why it is important to seek assistance. Consider involving family members or friends in tasks such as shopping or providing transportation to and from medical appointments. You might be pleasantly surprised by the willingness of those around you to lend a hand when asked.

Additionally, think about scheduling an appointment with a counsellor or mental health professional. If possible, seek out someone who has a background in assisting people facing health issues like AA. Ask your physician about the availability of support networks for people coping with AA. Becoming a part of a support group can offer a valuable opportunity to exchange experiences and gather advice on managing life with aplastic anemia or similar conditions. Interacting with people who genuinely comprehend your situation can have a significant impact on your overall quality of life.

*For more **information on aplastic anemia support groups in Canada,** please contact the Aplastic Anemia & Myelodysplasia Association of Canada (AAMAC) at info@aamac.ca or 1-888-840-0039.*

Coping with Stress: Coping with an illness can lead to feelings of being overwhelmed, stressed or down. People often find themselves discontinuing activities they once enjoyed and withdrawing from social interactions. While medications and various treatments can alleviate symptoms and improve blood counts, they may not effectively address emotional well-being. This is why exploring mind-body therapies, which centre on reducing stress and enhancing emotional well-being, is strongly recommended. These therapeutic approaches can also provide relief from pain and enhance vitality. Consider whether treatments or practices such as meditation, deep breathing exercises, aromatherapy, yoga, tai chi, acupuncture, or massage therapy may be worth a try.

Doing other simple things that you love, which make you smile, could also be very meaningful. This could include taking up hobbies, enjoying nature, or other activities that may offer a welcome distraction.

IMPORTANT: *Before exploring mind-body therapies, consult with the physician who oversees your treatment to discuss any potential risks of bleeding or infection. Your healthcare facility may have dedicated professionals who can assist you in devising a plan tailored to your unique needs.*

Dealing with Fatigue: Coping with AA can pose challenges in managing energy levels, with persistent fatigue often taking a toll. Fatigue is characterized by profound exhaustion and the depletion of our body's systems, leading to drowsiness, weariness, and physical, cognitive, and emotional weakness. Its effects are felt in many aspects of daily life, impacting mood, confidence, and emotional stability, and cannot be improved solely with rest. To effectively address this, identify activities that drain your energy and those that rejuvenate you, such as spending time with a close friend or taking a revitalizing nature walk. Energy conservation revolves around striking the right balance in this regard.

1. **Prioritize and schedule your time -** Evaluate your tasks and identify your top priorities. Avoid overloading your schedule, especially if it affects your concentration or memory. Use lists for shopping and maintain diaries or notepads for appointments
2. **Regulate your pace and positioning -** Plan regular rest breaks throughout the day. Acknowledge your accomplishments, seek assistance when needed, and don't hesitate to decline additional commitments. Organize your environment to minimize unnecessary bending or reaching
3. **Use relaxation techniques -** Incorporate practices like visualization, breathing exercises, or meditation into your daily routine. These practices can help you feel more in charge of your situation.
4. **Address mental fatigue -** Understand that fatigue doesn't impact solely your physical well-being; it can also trigger feelings of anxiety, stress, and overwhelm. If comfortable, share your feelings with those around you to seek support and understanding

Nutrition and Exercise: It is crucial to maintain proper nutrition and dietary habits, in addition to following your treatment plan. Ideally, your healthcare provider can assist you in devising an optimal nutrition plan. For people living with bone marrow disorders like AA, it is advisable to follow a wholesome and balanced diet that is rich in fruits, vegetables, legumes, and whole grains, focus on eating food items rich in minerals, vitamins, fibre, energy and protein, and watch sodium intake. To ensure your body receives adequate folic acid and iron, your physician may recommend an over-the-counter supplement. Folic acid and iron play a notable role in the production of red blood cells.

IMPORTANT: *Always consult with your healthcare provider to determine the most suitable supplements for your needs and seek their guidance before taking any medications, vitamins, or herbal supplements.*

Physical exercise can also improve your overall well-being while managing AA. While you might have faced certain physical limitations in the past, receiving treatment may enable you to reintegrate simple activities such as walking or light household chores, and even expand your physical capabilities. However, it is important to remember that some of the symptoms you experienced before treatment may persist, so it is advisable to begin any new exercise routine only when you are in optimum health and with the approval of your physician.

Beware of Sepsis: As a person dealing with AA, your heightened susceptibility to infection and neutropenia increases your risk of sepsis. Therefore, recognizing the symptoms of sepsis is crucial for your well-being.

IMPORTANT: *If you experience any of the following symptoms along with a fever (one-time temperature of >38.3 degree Celsius or >38.0 degree Celsius sustained over one hour) or chills, seek immediate medical attention. Please be aware that if you are neutropenic (have too few neutrophils, a type of white blood cell) and you develop a fever, even without any other symptoms, you should still seek immediate help.*

Source: UK Sepsis Trust as published by The Aplastic Anemia Trust

SEPSIS SYMPTOMS

ADULT

An adult may have sepsis if they show any of these signs:

Slurred speech or confusion
Extreme shivering or muscle pain
Passing no urine (in a day)
Severe breathlessness
It feels like you're going to die
Skin mottled or discoloured

CHILDREN

A child may have sepsis if he or she:

- **Is breathing very fast**
- **Has a "fit" or convulsion**
- **Looks mottled, bluish, or pale**
- **Has a rash that does not fade when you press it**
- **Is very lethargic or difficult to wake**
- **Feels abnormally cold to touch**

When it comes to sepsis, remember:

- Don't delay going to the hospital
- Keep a prepared bag in your car or near the front door, just in case. Even the time it takes to pack an overnight bag can impact the success of treatment
- Be aware of your usual state of health. Understand what feels normal for you, and if something doesn't seem right, seek medical attention. It is better to be cautious
- If a healthcare provider, such as a physician in the Emergency Room, examines you and sends you away, but your condition continues to worsen, don't hesitate to return. Advocating for your health is essential, as your life could be at risk
- Ensure that your friends and family are familiar with the symptoms of sepsis and know what steps to take if they suspect you might have it. You may not be thinking clearly if you are suffering from sepsis
- Remember that if you identify any of the sepsis symptoms mentioned earlier or experience an unexplained fever and a general sense of discomfort, seek prompt medical attention

Good Oral Hygiene when Neutropenic: The mouth contains numerous bacteria, even in a healthy person. Therefore, maintaining good oral hygiene if you are neutropenic is a vital precaution to minimize the risk of infections. This is especially critical if you are receiving horse ATG (ATGAM) treatment or undergoing a stem cell transplant. When you are immunosuppressed due to treatments like chemotherapy or other medications, you may experience mouth sores and occasional ulcers in your gastrointestinal tract. These conditions can serve as entry points for bacteria into the bloodstream, potentially leading to systemic infections or even endocarditis (heart infections).

Cleaning your teeth - Regularly brushing your teeth with a soft-bristle toothbrush can help reduce the risk of gum disease and oral infections. Use a soft-bristle toothbrush to avoid inadvertent damage to your gums that may result from vigorous brushing or using a toothbrush with harder bristles. Your healthcare team may also prescribe an antimicrobial mouthwash, typically containing chlorhexidine. When you have an increased vulnerability to infections, it is advisable to brush your teeth four times a day, followed by using an antimicrobial mouthwash.

Managing Increased Urinary Urgency and Frequency - Certain AA patients undergoing treatment may notice heightened urgency and frequency of urination. This can put added strain on your kidneys. Your healthcare team will provide guidance on staying adequately hydrated and encourage you to drink plenty of water, especially when taking cyclosporin (an antibiotic). Boosting your daily fluid intake to 2-3 litres can occasionally result in increased urine production. However, inadequate fluid intake can lead to the accumulation of concentrated urine in your bladder, potentially causing bladder irritation, symptoms of overactivity, or even a urinary tract infection.

Caffeine's influence - Reducing your caffeine consumption could also alleviate urinary urgency and frequency, as highly caffeinated beverages possess diuretic properties that lead to more frequent urination. Consider switching to decaffeinated options or aim to avoid high-caffeine drinks after lunchtime. This adjustment may contribute to reducing these symptoms at night.

Bladder training - You can also consider bladder retraining. People facing urinary urgency often develop a habit of frequent toilet trips. This habit can make urgency issues worse, as the bladder becomes accustomed to holding smaller amounts of urine and is increasingly sensitive or overactive. Bladder retraining can be effective in addressing or even resolving overactive bladder problems.

Managing a Nosebleed: People diagnosed with severe AA who also have significant thrombocytopenia (low count of platelets) face an elevated risk of life-threatening bleeding episodes as well as general bleeding. These can occur spontaneously and can manifest as bleeding from the mouth or nose. If you find yourself with a nosebleed that persists at home, contact your healthcare provider for guidance. They may recommend that you head directly to your local Emergency Room, as you may require a platelet transfusion to stop the bleeding. While these symptoms can be distressing, basic first-aid measures can help mitigate the bleeding until you can access medical care.

To effectively stop a nosebleed, you can follow these steps:

1. Sit down and apply firm pressure to the soft area of your nose, right above the nostrils, for a minimum of 10-15 minutes
2. Gently lean forward and breathe through your mouth, which will encourage the blood to drain into your nose rather than flowing down the back of your throat

Financial Planning: People living with diseases like AA frequently describe a negative impact on their financial circumstances while undergoing treatment. Monthly expenses can escalate and might be due to an increase in travel expenses, childcare, and the need to take time off work for medical appointments. The household income could diminish if you or your caregiver need to stop work or reduce hours, either on a permanent or temporary basis, due to the diagnosis. To help reduce stress and worry, consider following the steps below:

- Start by **evaluating your income and financial assets.** Questions to ask include:
  - What kind of paid or unpaid medical leave is available to you and/or your caregiver?
  - Can either you or your partner consider part-time employment?
  - Do you have any Income Protection or any critical illness insurance, or is it integrated into a life insurance policy?
  - Do you have access to existing funds or a line of credit, if needed?

- Next, **make a list of any expenses that must be addressed in the near term.** If you don't already have one, create a budget that reflects the realities of managing finances while undergoing treatment.

- You may wish to check if **getting life insurance** is possible at this stage, if you didn't have it before your diagnosis

- If you are **incapable of meeting your usual mortgage or loan obligations due to severe health issues,** it's recommended that you promptly inform the appropriate institutions. Banks and similar financial entities usually offer specific accommodations for customers facing financial distress due to health-related challenges

*For **information regarding financial assistance available to Canadians dealing with aplastic anemia,** feel free to reach out to the Aplastic Anemia & Myelodysplasia Association of Canada (AAMAC) at info@aamac.ca or 1-888-840-0039*

Discussion with Employer: It is your choice as to whether or not to inform your employer that you have been diagnosed with AA. Regardless, it is important to be aware of the criteria for short and long-term disability leave and other private health care coverage you may have through your employer.

While the majority of employers support employees dealing with an illness equitably and within the bounds of the law, certain employers may impose unwarranted and occasionally unlawful obstacles on their staff in such situations.

Concerns may arise regarding potential termination, lack of employment, reduced job status, rejection of advancement, denial of benefits, unwelcome reassignment, or unjust treatment by colleagues.

IMPORTANT: *Depending on your specific circumstances, it may be advisable to consult with an expert in employment law who is knowledgeable about employment rights for people coping with serious illness.*

Advocating for Yourself: At any point in your journey with AA, you could face a situation where you may need to advocate for yourself or your loved one. These opportunities may require you to communicate with decision-makers at various levels including your physician, the hospital where you or your loved one is treated, or the government to gain access to care and treatment.

A first step to addressing any roadblocks along the way may be discussing your situation with a support group where others may have lived through a similar experience and could potentially help you with useful advice. For assistance in navigating situations requiring advocacy for yourself or your loved one, you may also wish to contact the Aplastic Anemia & Myelodysplasia Association of Canada (AAMAC).

7 | TREATMENT

People with mild or moderate AA may not require treatment if their condition remains stable. However, those with severe AA should seek immediate medical intervention to prevent complications. In cases of very severe AA, emergency hospital care may be required, as it can be life-threatening if left untreated. Additionally, eliminating known causes of AA, like toxin exposure, may lead to a cure for the condition.

Below are some approaches used by physicians to treat people with AA:

Supportive Therapy

Antibiotics: Numerous people living with AA are prone to infections and may struggle to fight them effectively due to insufficient WBCs (neutrophils), or neutropenia. Antibiotics can help, but starting treatment promptly is crucial for patients with low neutrophil counts and fevers.

If you have AA and develop a fever, reach out to your physician right away or seek immediate care at the Emergency Room.

Blood Transfusions: A blood transfusion is a standard medical procedure. The majority of people with bone marrow failure disorders, such as AA, will undergo at least one blood transfusion. During a blood transfusion, components of donated blood are introduced into the circulatory system intravenously to help boost diminished blood counts. Some side effects of a blood transfusion are:

- **Iron Overload -** Receiving frequent blood transfusions may result in an accumulation of excess iron in the body that can be harmful if not appropriately managed. Iron overload can be managed using medications known as iron chelators that remove the excess iron (see below).
- **Transfusion Reactions -** Platelet transfusions have a higher likelihood of triggering an allergic response, which can cause symptoms like chills and elevated body temperature. Blood transfusion may also lead to what is called a **Hemolytic Transfusion Reactions.** This is a complication where the RBCs given to a patient are destroyed by their immune system. Its symptoms may include blood in urine, dizziness, or fainting, a flushed look on the skin, fever, back pain and more.[7]

Transfusion-associated circulatory overload or TACO is also a common reaction to transfusion where patients could develop **pulmonary edema** - referring to an unusual fluid build-up in the lungs – mainly due to a large overload of blood.[8]

Iron Chelation Therapy: People with AA who undergo frequent blood transfusions may experience iron accumulation in their bodies. This is evaluated through periodic blood tests, such as serum iron saturation test, and serum ferritin test, to measure the amount of iron in the blood. If recommended by a physician, several therapies can lower the amount of iron through chelation. Iron chelation therapies (oral, subcutaneous, or intravenous) approved in Canada that have been proven to address iron overload include deferasirox (Exjade®, Jadenu®), and deferoxamine (Desferal®).

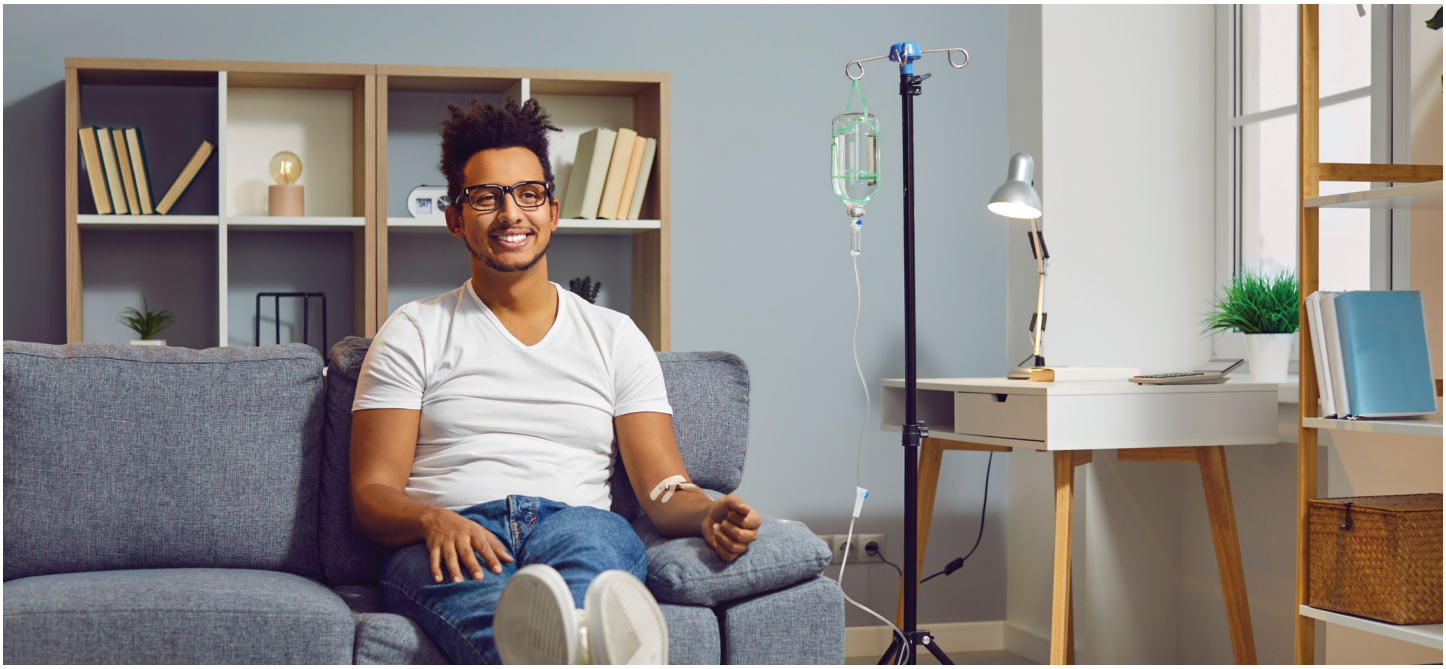
Iron chelation therapy can potentially lead to an increased risk of impaired colour vision and hearing loss among other side effects. Patients taking these treatments should undergo periodic vision assessments conducted by an ophthalmologist and hearing evaluations conducted by an audiologist.

Growth Factors: These are hormones naturally present in our body, which convey signals to our bone marrow to produce specific types of blood cells in greater quantities. In some cases, synthetic growth factors may be administered to people with bone marrow failure conditions to assist in elevating RBCs, WBCs, or platelet counts.

- **Red Blood Cell (RBC) Growth Factors:** Erythropoietin (also called EPO) is a growth factor produced by the kidneys which stimulates the bone marrow to produce an increased quantity of red blood cells. When there is a deficiency of red blood cells, synthetic EPO medications can be used to assist the bone marrow in generating more of them. These medications are referred to as erythropoiesis-stimulating agents (ESA) and are administered via injection in the skin. ESAs approved in Canada include epoetin alfa (Eprex®) and darbepoetin alfa (Aranesp®).
- **White Blood Cell (WBC) Growth Factors:** If you develop an infection due to low levels of WBCs, these medications can assist your bone marrow in producing more white cells.

Research has indicated that incorporating these drugs into the treatment of people with bone marrow failure offers minimal or no significant benefit. Therefore, physicians typically suggest the short-term use of these medications to increase white cell counts before procedures, such as surgery or in the event of a severe infection. These medications are administered via skin injection, and there are two types:

- ***Granulocyte-colony stimulating factor*** (G-CSF) is a hormone that stimulates the production of WBCs. G-CSF medications approved in Canada include filgrastim (Neupogen®) and pegfilgrastim (Neulasta®).
- ***Granulocyte macrophage-colony stimulating factor*** (GM-CSF) represents another type of growth factor. Sargramostim (Leukine®) is an example of a GM-CSF medication that is approved in Canada. These medications can support patients experiencing low neutrophil (white blood cell) levels who tend to develop infections.
- **Platelet growth factors:** Eltrombopag (sold as Revolade® in Canada) is a growth factor that encourages platelet production in the bone marrow. It is taken as a pill by mouth. Eltrombopag in higher doses has been shown to improve response when used together with immunosuppressants. Your physician may prescribe eltrombopag in conjunction with an immunosuppressant to boost the quantity of blood cells in your system.



Treatments for Aplastic Anemia

Immunosuppressive Therapy: This therapy modulates the body's immune system and prevents it from attacking the bone marrow stem cells so that cells can grow and blood counts improve. Treatment often takes many months to complete. Once the body has responded, there is a slow withdrawal of medications to prevent relapse.

Immunosuppressive therapy includes a combination of:

1. Antithymoglobulins (intravenous), and
2. Cyclosporine (oral) and/or
3. Corticosteroids (oral). Corticosteroids, such as **methylprednisolone** ([Pr]Medrol, Solu-Medrol®), are frequently administered alongside other immune suppressive medications. While they can be effective, these drugs potentially further suppress the immune system. Additionally, there is a chance of anemia recurring once the drugs are discontinued.

Antithymoglobulin (ATG) is produced by injecting human white blood cells (T-lymphocyte cells) into a horse or a rabbit, and then extracting the antibodies (proteins) they generate to create a serum. This treatment is sometimes called horse ATG (hATG) or rabbit ATG (rATG). Your physician may prescribe eltrombopag in combination with ATG and cyclosporine to enhance the quantity of blood cells in your system.

ATG functions by eliminating particular cells within the immune system known as T-lymphocytes — the cells responsible for attacking the bone marrow stem cells. This enables your bone

marrow to replenish its reservoir of blood-forming stem cells.

ATG is typically administered via intravenous infusion (IV) through the veins for 4-12 hours each day over a span of four consecutive days (the physician's recommendation may vary). The specific regimen is determined based on your requirements, the type of ATG used, and your physician's or hospital's protocols.

ATG may cause certain side effects, such as chills, fever, hives, and flushing, but these typically subside after treatment. However, there are also less common and potentially long-term side effects associated with ATG that you should be aware of before undergoing treatment:

- In very rare cases, some patients may experience a severe allergic reaction known as **anaphylaxis,** which can lead to a drop in blood pressure and difficulty breathing. Before undergoing ATG treatment, you will receive a skin test to ensure you do not have this type of reaction
- Occasionally, patients may develop **serum sickness,** a condition in which the immune system reacts to the 'foreign' proteins in the ATG medication, resulting in symptoms like joint pain, rash, muscle aches and fever. This typically occurs a few weeks following treatment and lasts for several days. To prevent serum sickness, physicians often prescribe medications like prednisone
- On rare occasions, patients may develop **avascular necrosis** of the hip, characterized by reduced blood flow to the hip joint. This condition may manifest months or even years following treatment and may cause groin pain in addition to difficulty walking. Physicians monitor for this condition, so it is essential to report any issues promptly

Effectiveness of ATG:

- When used as a standalone treatment, ATG enhances blood counts approximately 50% of the time
- When combined with cyclosporine, ATG enhances blood counts in approximately 70% of cases
- When used in combination with cyclosporine and eltrombopag, blood marrow response is higher
- If successful, ATG typically eliminates the need for transfusions within three to six months, although complete recovery may take over a year
- If the initial ATG treatment yields unsatisfactory results, your physician will explore alternative strategies

Stem Cell Transplantation: In this procedure, healthy stem cells from a donor completely substitute all the patient's bone marrow stem cells. This remains the sole treatment capable of providing the potential for cure from AA. Nevertheless, it brings with it substantial risks and challenges including finding a compatible donor which is essential for transplantation.

Stem cell transplantation is contemplated when bone marrow failure reaches a critical stage and does not improve with immunosuppressive treatment or when the goal of treatment is to try to achieve a cure. To obtain a more thorough understanding of stem cell transplantation, speak with your hematologist/oncologist. Due to the risk of bone marrow transplantation, there is an extensive assessment of the patient and the disease severity to determine if someone is eligible for bone marrow transplant. When considering stem cell transplantation, ensure you understand the potential for complications, occurrences of treatment ineffectiveness, and even the risk of death.

What to Expect: Stem cell transplantation is a significant medical intervention. It involves hospitalization and a series of treatments, including chemotherapy, immune suppression therapy, and possibly radiation, aimed at eliminating a major portion of your existing bone marrow to create space and reduce the risk of rejection for the incoming donor cells. Throughout this period, you must remain hospitalized to safeguard against potential infections and the duration of hospitalization can vary, ranging from as brief as a week to potentially more than a month.

Your physician will introduce the healthy stem cells from your donor into your bloodstream through an infusion process resembling a blood transfusion. The compatible donor can be a family member (such as a sibling) or an unrelated donor. In situations where a perfect match is unavailable, a half-match (haploidentical match) may be considered a viable option for several patients, following appropriate pre-transplant preparation.

If successful, these newly introduced, healthy donor stem cells will migrate to your bone marrow and initiate the process of self-replication, a phase known as engraftment, which may extend for up to one month. Your medical team will closely monitor your blood cell counts to ensure the proper functioning of the new cells. If the transplant is successful, the newly established healthy cells will assume control, generating all the required RBCs, WBCs, and platelets.

Risks and Side Effects: Stem cell transplants entail significant risks, and it is important to engage in a comprehensive discussion about them with your physician. The treatment may lead to side effects stemming from chemotherapy and radiation, which can include gastrointestinal issues such as nausea and diarrhea, hair loss, and in rare cases, organ damage. Serious infections may also arise, necessitating blood transfusions due to severely depleted blood cell levels.

In certain instances, the transplanted cells may initiate an immune response against your body, resulting in a condition known as **graft-versus-host disease (GVHD)**, which can pose a life-threatening risk. The symptoms of GVHD can vary

from mild, such as a temporary skin rash, to severe, including persistent diarrhea with damage to the intestinal walls. It is important to note that GVHD can manifest even when you are receiving medications (such as cyclosporine or others) intended to prevent its occurrence. The likelihood of GVHD is higher if you are of advanced age, if your donor is not related to you, or if there is not a perfect match between you and the donor.

Other Treatments: Aplastic anemia resulting from radiation and chemotherapy used in cancer treatments typically shows signs of improvement once these treatments are discontinued. This pattern also holds for the majority of other medications known to trigger AA, like phenylbutazone, sulfonamides chloramphenicol, cimetidine, anticonvulsants, and others[9].

Pregnant people diagnosed with AA receive blood transfusions as part of their treatment plan. In many cases, pregnancy-related AA shows signs of improvement following the conclusion of the pregnancy. However, if this improvement doesn't occur, ongoing treatment remains essential.

***Note:** Prior to beginning a new therapy, it is advised that patients review the product monograph and discuss with their physician the pros and cons of taking the medication. The product monograph will include possible side effects, risk factors and other information to consider when beginning a new medication.*

Clinical Trials

Clinical trial research studies involve human participants to evaluate the safety and/or impact of a specific treatment. Results from clinical trials could be used for the approval of new treatments typically compared against established approaches to treating a disease. Visit the Government of Canada website to learn about clinical trials in greater detail.

Visit the Aplastic Anemia & Myelodysplasia Association of Canada (AAMAC) website clinical trials page for updates on the latest clinical trials for AA and speak with your physician about any clinical trials that you may be eligible for.

Relapse

People dealing with AA may exhibit lasting bone marrow damage after undergoing treatment, even if their blood counts return to normal. Some patients who have effectively been treated for AA can also experience a recurrence or relapse. Typically, this relapse is not linked to re-exposure to the initial trigger of the disease. Instead, relapse can be associated with factors such as pregnancy or when the immune system faces significant challenges.

Side Effects of Treatments to Address Immediately

During treatment for AA, reach out to your physician or hospital promptly if you experience any of the following:

- A temperature exceeding a one-time reading of 38.3 degrees Celsius (even if it returns to normal) and/or an episode of uncontrolled shivering
- Bruising or bleeding, such as blood in your urine, feces, saliva, bleeding gums, or a continuous nosebleed
- Intense nausea or vomiting that hinders your ability to eat, drink, or take your regular medications
- Severe diarrhea, constipation, or abdominal cramps
- Coughing or experiencing breathlessness
- A fresh rash, skin redness, or itching
- A persistent headache
- New discomfort or tenderness in any area of your body
- An accidental cut or other injury
- Pain, swelling, redness, or pus anywhere on your body

8 | VACCINATIONS

People with conditions that compromise or weaken their immune system, such as AA, face an elevated risk of experiencing more severe health complications due to viral infections like influenza (flu), rhinovirus (common cold), or COVID-19. Seasonal flu vaccines are designed to protect against the specific influenza viruses that research suggests will be prevalent during the cold season.

There is ongoing debate regarding whether people with AA should receive the flu vaccine, so it is essential to have a discussion with your physician before deciding whether it is right for you. Personalized risk assessments may be conducted to help you make an informed decision.

Theoretically, there is a risk of AA relapse or a decline in blood counts after receiving any vaccination, especially the flu vaccine. However, it is important to note that the available evidence is limited and primarily relies on anecdotal reports. There is also an awareness that viral infections may play a significant role in the development of AA. Whether to receive the flu vaccination should be discussed with your physician, weighing the benefits and risks. The exception is patients who have undergone a hematopoietic stem cell transplant. For these people, it is advisable to follow a recommended vaccination schedule, which is standard practice for all patients, post-transplant.

9 | DISEASE MANAGEMENT

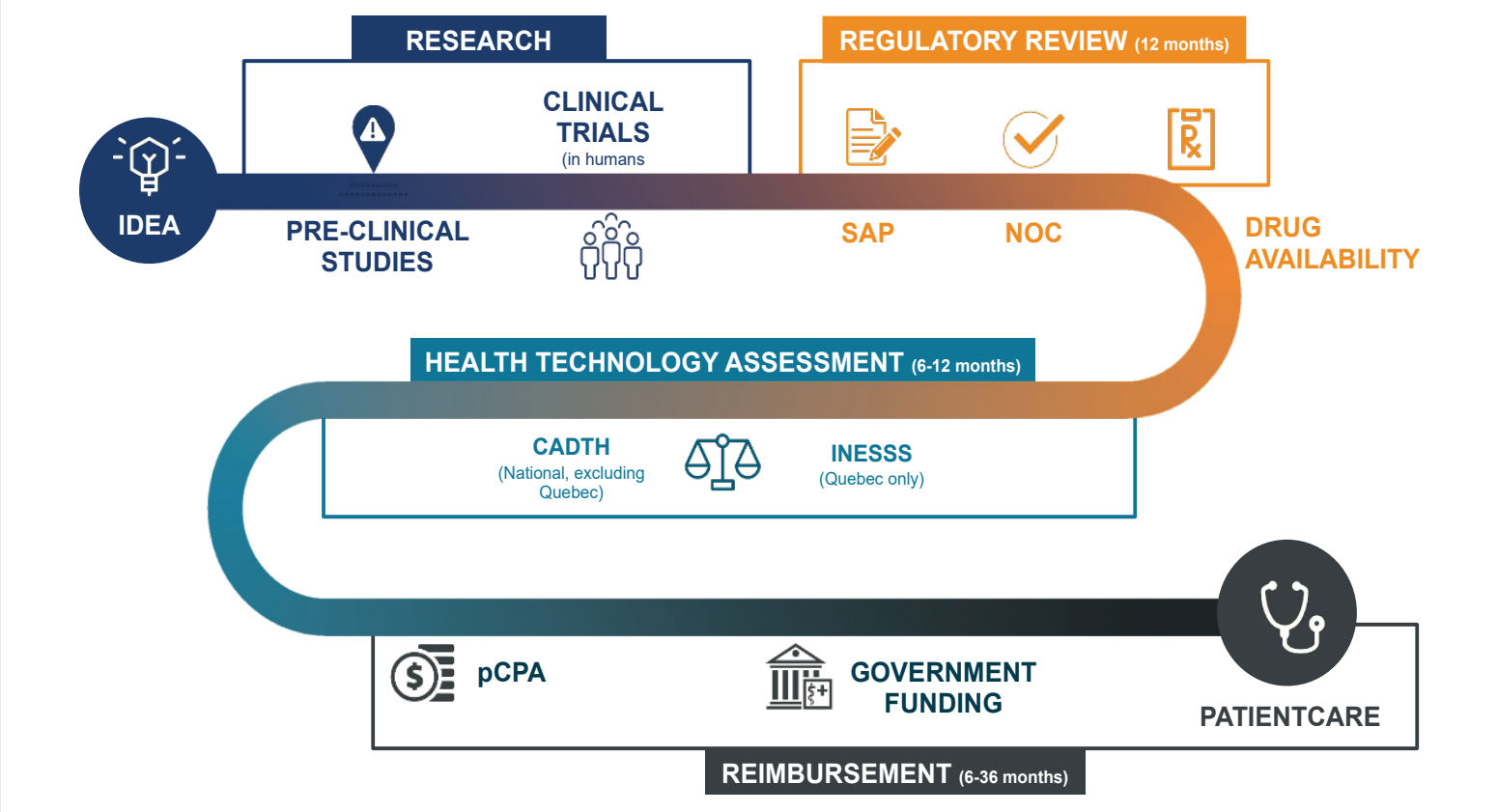
In order to take ownership of managing your AA by tracking your symptoms and progress with treatments, try using the following resources from the **Aplastic Anemia and Myelodysplastic Association of Canada (AAMAC)** and the **Aplastic Anemia and MDS International Foundation (AAMDSIF):**

1. Patient Tracker
2. Appointment Tracker
3. Blood Transfusion Record
4. Symptom Tracker
5. Platelet Transfusion Record
6. My Health Care Team
7. Emergency Room Card

Living with a disease like AA brings various challenges, and you will have good days and not-so-good days. As you go through your journey with AA, you will find that knowledge combined with the right support from health care experts, family and friends will make all the difference to your wellbeing and quality of life.

10 | ACCESS TO TREATMENTS IN CANADA

Processes Involved in the Approval and Public Funding of Treatments in Canada



Source: EVERSANA

Regulatory Review

For a medication to be available to Canadians, Health Canada (a department of the Government of Canada) must first approve it for safety, efficacy, and quality. As part of the regulatory review process, Health Canada examines various scientific data, including clinical trial studies, to assess the potential benefits and risks of the medication. Once approved, the treatment will be issued with a **Drug Identification Number (DIN)** and a **Notice of Compliance (NOC)**. The NOC then allows a pharmaceutical company to market and sell that drug in Canada, as well as qualified healthcare professionals to prescribe the treatment.

For more information, visit the Health Canada Drug and Health Products page.

Special Access Program

In cases of severe or life-threatening illnesses, when conventional treatments have proven ineffective, are unsuitable, unavailable, or offer limited choices, a physician may make an application on behalf of a patient **for a**

medication that has not yet been approved by Health Canada. Application is made to the Special Access Program (SAP) within Health Canada's Therapeutic Products Program. If approved, the SAP then authorizes the release of the drug to the physician, who in turn administers it to the patient. While a successful SAP application allows a non-approved medication to be brought into the country, it does not address who is required to pay for treatment.

For more information, visit the Health Canada Special Access Programs: Overview page.

Health Technology Assessment (HTA)

Health Technology Assessment (HTA) is the process whereby a health technology or treatment is assessed to determine the value of that technology and how it should be used in a health system. In Canada, we have two HTA bodies – the Canadian Agency for Drugs and Technologies in Health (CADTH) and the Institut national d'excellence en santé et en services sociaux (INESSS).

CADTH

CADTH is the national agency (excluding Quebec) that makes recommendations to the public drug plans in Canada as to whether or not a particular medication should be publicly funded. They do so through what is called a Reimbursement Review, which is a comprehensive assessment of the clinical effectiveness and cost-effectiveness, as well as patient and clinician perspectives, of a treatment. While these reviews are non-binding on the public drug plans, they do help to guide the ultimate reimbursement decisions of the federal, provincial, and territorial governments.

For more information, visit the CADTH website.

INESSS

INESSS is the provincial agency in Quebec that makes recommendations to the Minister of Health and Social Services as to whether or not a particular medication should be publicly funded. Assessments by INESSS focus on therapeutic value, cost-effectiveness (compared with other drug options), unmet need and the impacts of a listing on the public health budget. While also non-binding, INESSS recommendations play a critical role in guiding the final drug funding decisions of the Government of Quebec.

For more information, visit the INESSS website.

Drug Reimbursement

The final step to accessing treatments in Canada through public funding consists of two parts: the pan-Canadian Pharmaceutical Alliance (pCPA) and Product Listing Agreements (PLAs).

The pCPA conducts joint federal, provincial, and territorial negotiations in which member jurisdictions engage drug manufacturers to determine if a particular drug will be publicly funded, at what cost, and with which reimbursement criteria. If a negotiation is successful, a Letter of Intent (LOI) is issued. A drug company then takes that LOI to each of the public drug plans in Canada and uses it as the basis for finalizing a PLA – a legally binding agreement that will trigger publicly funded access to that treatment in the jurisdiction.

For more information, visit the pCPA website.

PATIENT AND CLINICIAN INPUT: A vital part of the CADTH and INESSS review processes is patient, caregiver, and clinician input. Both CADTH and INESSS post calls for input from patient organizations and clinician groups (for INESSS, individual members of the public can also submit input) when conducting reimbursement reviews. Patient and clinician groups are encouraged to share their experiences and perspectives on the disease, existing treatments, including the drug under review, as well as insights into unmet needs addressed by the drug under review. The combined input from patients, caregivers and clinicians serves to inform the review processes at the two agencies.

The Aplastic Anemia & Myelodysplasia Association of Canada (AAMAC) provides input into HTA reviews for treatments in aplastic anemia, myelodysplastic syndromes, and paroxysmal nocturnal hemoglobinuria.

For more information, visit the CADTH Patient Group Input and Feedback page.

For more information, visit the CADTH Clinician Group Input and Feedback page.

For more information, visit the INESSS Public Input page.

Formal and Informal Advocacy to Support Access to Treatment

Numerous patient organizations, like Aplastic Anemia & Myelodysplasia Association of Canada (AAMAC), across the country advocate on behalf of their communities around issues such as access to treatment. Many provide opportunities for people to share their experiences and opinions as treatments make their way through the approval and reimbursement processes across Canada. Such engagement can be divided between formal and informal advocacy opportunities.

As part of the structured drug approval and public reimbursement processes, the only formal opportunities for input from patients, caregivers, and physicians are within CADTH and INESSS. Beyond formal advocacy, individuals and the groups or organizations who represent them can make their voices heard around an issue related to access to treatment in a variety of ways. Some examples of informal advocacy include meetings with elected officials and bureaucrats, letter-writing campaigns, petitions, and social media campaigns.

*For more **information on aplastic anemia support groups in Canada,** please contact the Aplastic Anemia & Myelodysplasia Association of Canada (AAMAC) at info@aamac.ca or 1-888-840-0039.*

11 | ACKNOWLEDGEMENTS

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We would also like to express our gratitude to AAMAC's patient representative and EVERSANA for their support in preparing this educational resource.

12 | APPENDIX

Being diagnosed with a complex disease like AA can be overwhelming and the learning curve can be steep. Below are some points to help you prepare for medical appointments and to ask your physician if they are not addressed during your appointment.

Points to address with your physician at every stage in your journey with AA.

Note: *These lists are compiled from resources by AAMAC and AAMDSIF*

Points to address with your physician as a newly diagnosed patient

1 Can you explain what Aplastic Anemia (AA) is? Is it like cancer?

2 How sure are you about the diagnosis of AA?

3 How long does it take to receive a definitive diagnosis of this condition?

4 What factors are responsible for the development of this condition,

5 Is this life-threatening? What is the anticipated life expectancy, and what can I expect regarding my prognosis?

6 Is there a cure or treatment for aplastic anemia? Is there a possibility of remission?

7 Is AA genetically inherited? Are there any long-term implications of AA that I should be aware of?

8 I've come across information stating that AA is classified as an autoimmune disease. Is there any association with conditions like lupus, rheumatoid arthritis, or Crohn's Disease, which are prevalent in my family?

9 I am aware that having AA or severe AA implies my immune system is compromised, but what precisely does that mean?

10 Which healthcare professionals should be included in my medical team? Are there any specialists or should I consult with my primary care physician?

11 Will additional tests be necessary? How frequently should I anticipate undergoing a bone marrow biopsy?

12 What is the severity of my specific type of AA?

13 What steps should I take to seek a second medical opinion?

14 Are there conditions or illnesses that AA could be mistaken for?

15 How will AA affect my overall quality of life?

16 What is the significance of having diminished blood counts, and when does it escalate to severe AA? What do my blood counts mean for me? (Hg, WBC, neutrophils, platelets)

17 Are there factors that could affect my outlook or treatment options?

18 Am I able to travel by plane, both within Canada and internationally?

19 Is it advisable for me to use a face mask?

20 What should I do if I contract the flu or another illness during my treatment?

21 Are vaccines such as COVID-19, flu, and pneumonia safe for me?

22 Is there written literature or informational resources available about AA?

23 Are there any new treatments or medications on the horizon?

Points to address with your physician when deciding on a treatment

1 Tell me more about the usual treatment for AA (ATG, Cyclosporin, Prednisone, Valtrex®). Which treatment do you recommend, and why?

2 What are the treatments' side effects, and when do they typically manifest?

3 How are these side effects managed?

4 Do I need any other tests before we can decide on treatment? Is there any genetic testing I should do before treatments? Can you explain the types of tests to me?

5 How soon should I start treatment?

6 How much experience do you have treating AA?

7 What should I do to be ready for treatment?

8 How long will treatment last? What will it be like? Does it hurt? Will I be nauseous? Where will it be done? Will I need to be hospitalized?

9 When can I anticipate a treatment response? Will there be noticeable improvements, or will we rely on lab tests to gauge the treatment's effectiveness?

10 What are the risks or side effects of the treatments that you recommend? How long are they likely to last?

11 Am I a candidate for transplant (if relevant)? What are the side effects and dangers?

12 Could you explain the concept of being transfusion-dependent during treatment?

13 How frequently will blood transfusions be required, and is it recommended to monitor my CBC results?

14 Is it mandatory for my caregiver to accompany me during the blood transfusion?

15 Will I be fit to drive home independently after a blood transfusion?

16 When is it likely that I won't need transfusions anymore?

17 Could you explain the distinctions between Horse and Rabbit ATG? Is one more effective than the other?

18 Are additional tests necessary before starting ATG treatment?

19 What is the duration and location of ATG treatment sessions? Will I need hospitalization?

20 What are the advantages and drawbacks of ATG treatment?

21 Will I lose my hair with ATG treatment?

22 How does ATG treatment affect fertility? If I am younger, should I consider freezing my eggs or sperm before any treatment? Are there any safety concerns I should be aware of if I am contemplating pregnancy?

23 How is the treatment administered? Is a PICC or port required? Is surgical insertion necessary for a PICC line or port?

24 What alternatives are available if the ATG treatment proves ineffective?

25 What are the consequences of opting not to undergo ATG treatment for my condition?

26 Could you explain the distinctions between cyclosporine and eltrombopag? Is it necessary to use both?

27 Is the ATG treatment regimen involving cyclosporine and eltrombopag that you're recommending covered by my health insurance?

28 Do you provide written materials explaining the ATG treatments you've proposed?

29 Which foods should I avoid or restrict? What is your guidance on alcohol consumption?

30 Are there any clinical trials I ought to be aware of before deciding on a standard treatment?

31 What travelling is involved? I am, (or I am not) able to travel far for a clinical trial.

32 Will I be treated any differently if I enrol in a trial?

Points to address with your physician during treatment

1 I am currently grappling with severe nausea, fatigue, and mouth sores. What strategies can you suggest to help me better manage these symptoms?

2 How will we know if the treatment is working?

3 How extensive will my post-ATG medication regimen be, including drugs like cyclosporine and eltrombopag?

4 What is the recommended duration for adhering to a neutropenic diet?

5 Are there specific supplements I should consider taking to support my immune system?

6 What indicators should I watch for to detect a potential relapse of my condition

7 What approaches are available for treating relapsed disease?

8 How frequently will I require follow-up examinations and medical tests?

9 What are the limits on what I can do? How much and how often can I exercise? When can I expect to return to my regular activities, including exercise and work?

10 Will I remain immunocompromised indefinitely unless I undergo a transplant?

11 Is ongoing monitoring necessary throughout my life to detect the emergence of other bone marrow failure conditions like MDS and/or PNH?

12 If I continue to rely on transfusions, should I contemplate a second ATG therapy?

13 What is the rationale behind your recommendation of a bone marrow transplant over medication?

14 What steps are involved in locating a suitable donor for the transplant?

15 Should I encourage my friends and family to undergo testing for potential donations? Where can they get tested?

16 Could you explain the procedure for receiving a transplant?

17 Will I need to undergo chemotherapy as part of the transplant preparation, and what potential side effects should I be prepared for?

18 What will be the duration of my hospital stay?

19 Will I require a caregiver throughout the transplant process and during the recovery period?

20 Should I think about fertility preservation before the transplant?

21 What are the potential risks and benefits associated with the transplant in my specific case?

22 Can you explain graft-versus-host disease (GVHD)?

23 What is the likelihood of me developing GVHD?

24 How is GVHD typically treated, and is it possible to cure GVHD?

25 What symptoms or side effects should I tell you about right away?

26 If the treatment is unsuccessful, what alternatives or options are available to me?

Other support

1 What supports do you suggest I get?

2 Are there others with this disease that I can talk with?

3 Do you have any written information?

4 Can you suggest a mental health professional I can see to help me and my family adjust to this diagnosis? Where can I find more information and support?

Top tips

1 Take a pen and paper and write your questions down.

2 A detailed summary is usually documented by the physician at every medical visit. While recording the consultation should not be necessary, if the physician is unable to provide this, with their permission, you can sometimes electronically record the consultation if you feel you cannot take all the information down.

3 We recommend you attend most consultations with a family member or friend, as it can be difficult to remember all that is said in a conversation.

4 Find a peer who has been diagnosed with AA and understands what you're going through – ask your physician or search online for groups; you're not alone.

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