

MONITORING YOUR NON-TRANSFUSION-DEPENDENT THALASSEMIA (NTDT)

Whether you have alpha- or beta-thalassemia, knowing which tests are needed can help you and your doctor prevent and manage complications. It's important to work with your care team to build a personalized monitoring plan based on your thalassemia type and transfusion experience. Together, you can track your plan over time.

The guide below shows recommended testing and frequency for people living with non-transfusion-dependent alpha- or beta-thalassemia who are aged 18 and over. The schedule was created based on input from the Thalassaemia International Federation (TIF) guidelines and leading thalassemia experts. If you only see your hematologist once a year, another member of your care team may order some of these tests.

You can use the "Date" columns to keep track of your tests. This information can be used in conversations with your doctor about monitoring. It's also important to share how your thalassemia impacts your quality of life.

These Monitoring Guidelines were written by a Steering Committee of leading thalassemia experts organized by Agios; these experts were compensated by Agios for their time.

This is not medical advice. Please consult with your doctor.

RECOMMENDED TESTS AND EXAMS FOR EVERY VISIT

Medical history, including quality of life, which should be reviewed and compared to the last visit

Physical exam

Laboratory tests

Complete blood count* (If you are on an iron chelator called deferiprone (Ferriprox®), the test should be done every 2 weeks)

Serum ferritin

Liver and kidney function (If you are on an iron chelation therapy, this test should be done every month)

RECOMMENDED SCHEDULE OF MONITORING FOR LISTED COMPLICATIONS

	Baseline	Date	Every year	Every 2 years	Date
Red blood cells formed outside of the bone marrow (extramedullary hematopoiesis)					
MRI C/T/L* spine with contrast	Monitoring frequency depends on the severity of your anemia and symptoms, such as back or upper belly pain, feeling of fullness, and loss or decrease in ability to feel things or move parts of your body				
Spleen size (physical exam/ultrasound)					
High levels of iron (Iron overload)					
Liver MRI for liver iron concentration†	●		●†		
Heart scan (cardiac T2* MRI§)	●				
Heart function					
ECHO,* including TRV*			●		
Holter monitoring or equivalent	Monitoring frequency depends on your specific health situation				
Weak and fragile bones (osteoporosis*) and bone disease					
Bone density (DEXA scan*)	●			●	
Vitamin D	●		●		
Hormone imbalance (endocrinopathy*)					
Your doctor will collect a baseline assessment and will perform exams every year if there's evidence of iron overload¶					
Low reproductive hormones* (hypogonadism)					
FSH,* LH,* testosterone, and estrogen	●		●		
Low thyroid function (hypothyroidism)					
Free thyroxine (FT4) and TSH*	●		●		
Low parathyroid function (hypoparathyroidism)					
PTH,* calcium, phosphate, magnesium	●		●		
Diabetes mellitus					
Fasting glucose or oral glucose tolerance test	●		●		

*Your doctor may perform a baseline liver MRI if you are receiving frequent transfusions or serum ferritin ≥ 300 ng/mL.

†Your doctor may perform assessments every year if you are on chelation therapy and every 2 years if you are not receiving chelation therapy.

§Your doctor may perform cardiac MRI if liver iron concentration is ≥ 10 mg/g dry weight.

||Your doctor may perform this test every 2 years or every year if an abnormality is detected.

¶Exams may be referred to an endocrinologist or performed independently.

*Key Terms and Abbreviations

Chelation therapy: Medicine that binds to iron in your bloodstream so it can be eliminated via the digestive or urinary tract. **Complete blood count:** Assesses many elements to get a more complete picture of the health of your blood and typically includes, among other measures, hemoglobin, hematocrit, and white blood cell levels. **Endocrinopathy:** A condition where your glands or organs do not produce the right amount of hormones. **Extramedullary hematopoiesis:** Occurs when your body starts making red blood cells in places outside the bone marrow, such as in other organs or the spine. This happens because thalassemia lowers the number of red blood cells in your body, causing it to try to produce them in other areas to compensate for the shortage. **Hormones:** Chemicals that travel throughout your body via the bloodstream. They help regulate growth and development, metabolism (changing food into energy), mood, sexual function, and reproduction. Hormones are part of the endocrine system. **Osteoporosis:** A condition where your bones become weak and fragile, making them more likely to break.

C/T/L=cervical/thoracic/lumbar; **DEXA**=dual-energy X-ray absorptiometry; **ECHO**=echocardiogram; **FSH**=follicle-stimulating hormone; **LH**=luteinizing hormone; **MRI**=magnetic resonance imaging; **PTH**=parathyroid hormone; **TRV**=tricuspid regurgitant jet velocity; **TSH**=thyroid-stimulating hormone.

OTHER DOCTORS WHO MAY BE ADDED TO YOUR CARE TEAM

Get a referral to meet with a cardiologist	Get a referral to meet with an endocrinologist	Get a referral to meet with a reproductive endocrinologist
When ECHO* with TRV* or MRI* scans show possible issues with your heart or high blood pressure in your lungs (also known as pulmonary hypertension). When heart monitoring shows irregular heartbeats or other problems with your heart's electrical system.	When blood test results indicate: • Low levels of reproductive, thyroid, or parathyroid hormones, or diabetes • Abnormal results on a DEXA scan* You can also get a referral to see a bone health specialist when DEXA scan results are abnormal.	If you're considering having children, you may want to learn more about your fertility and explore possible support options.

OTHER COMPLICATIONS TO WATCH FOR

Complication and/or condition	Details
Hemolytic crisis A sudden and often severe anemia that occurs when the body cannot produce enough red blood cells to replace the ones that are being destroyed.	If you have alpha-thalassemia and experience an infection with a fever, your doctor may discuss the risk of a medical emergency, known as a hemolytic crisis. Tell your doctor if you experience signs and symptoms of fatigue, yellowing of the skin, or dark-colored urine.
Before and after a splenectomy Splenectomy is a surgical procedure that removes the spleen.	You will get vaccines before and/or after a splenectomy. Talk with your doctor about which vaccines are most appropriate for you based on CDC* recommendations. After a splenectomy, it is important to talk with your doctor about the risk of infections and what to do in case of a medical emergency. People who have their spleen removed may have high platelet counts, leading to the formation of blood clots.
Thrombosis and vascular events Formation of clots inside your blood vessels, which can interrupt or block the flow of blood.	Talk with your doctor if you experience signs and symptoms of: • DVT*: swelling, pain, warmth, tenderness to the touch, or redness in the leg • PE*: shortness of breath, chest pain, and cough
Liver fibrosis, cirrhosis, and HCC* Long-term liver damage can cause reversible (fibrosis) or permanent (cirrhosis) scar tissue. HCC is a type of liver cancer that can develop from cirrhosis.	If you suffer from long-term, severe iron overload or hepatitis, talk with your doctor about measuring a baseline AFP* and performing imaging scans (such as ultrasound and FibroScan*).
Gallstones Forms in the bile ducts because of anemia and the breakdown of red blood cells (hemolysis). This is different from when there is too much cholesterol in the body.	Talk with your doctor if you experience signs and symptoms of: • Pain in the upper right side or middle of the stomach, nausea, vomiting, and worsening yellowing of the skin and eyes. You may be given blood tests to assess your liver and imaging scans.
HCV, HBV, and HIV* While the chances are very low, HCV, HBV, and HIV can be spread through blood transfusions. HCV and HBV damage the liver, while HIV weakens the immune system.	If you have received blood transfusions in the past 12 months, talk with your doctor about obtaining an antibody and/or antigen test to assess your blood for HCV, HBV, and HIV. If the test results are positive, have your doctor perform a PCR* test to confirm the results.
Leg ulcers Open sores or wounds on the lower legs that do not heal properly.	Talk with your doctor if you experience signs and symptoms of: • Pain or discomfort, swelling, and redness in the affected leg. Have your doctor check for leg ulcers at every visit.

SHARE THE IMPACT OF THALASSEMIA WITH YOUR CARE TEAM

At every visit, be sure to talk to your care team about how you're feeling, especially if you're experiencing any changes in your symptoms, ability to complete daily activities, and mental health.



Physical well-being

Feeling fatigue and/or tiredness
Feeling weak or washed out
Lack of energy



Functional well-being

Ability to work
Ability to do usual activities
Ability to tolerate exercise
(eg, walking up stairs)



Emotional well-being

Depression
Anxiety and/or stress

*Key Terms and Abbreviations

ECHO: An echocardiogram, or "echo", is a scan used to look at the structure of the heart. **DEXA**: An X-ray scan of the bone density in a particular area of your body.

FibroScan: A special ultrasound technology that measures liver stiffness (hardness) and fatty changes in your liver.

AFP=alpha-fetoprotein; **CDC**=Centers for Disease Control and Prevention; **DVT**=deep vein thrombosis; **HBV**=hepatitis B; **HCC**=hepatocellular carcinoma; **HCV**=hepatitis C; **HIV**=human immunodeficiency virus; **MRI**=magnetic resonance imaging; **PCR**=polymerase chain reaction; **PE**=pulmonary embolism; **TRV**=tricuspid regurgitant jet velocity.



Connect with a myAgios® Clinical Nurse Educator (CNE), who can walk you through this monitoring guide and help you prepare for your doctor visit. A CNE works closely with patients, families, and care teams to offer you individualized support; educational resources, and community connections. Call 1-877-77-AGIOS (1-877-772-4467) or visit [RethinkThalassemia.com](https://www.RethinkThalassemia.com) to get started.

*CNEs are employees of Agios Pharmaceuticals and do not provide medical advice. For medical advice or treatment-related questions, please talk to your healthcare team.