

## Type 1 Gaucher Disease Signs & Symptoms

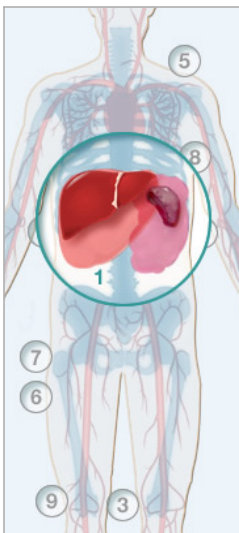
Type 1 Gaucher disease is heterogeneous, presenting with a wide array of signs and symptoms throughout the body, with particularly painful and debilitating skeletal pathologies associated with bone marrow infiltration. These signs and symptoms may be classified in four areas: visceral, hematologic, skeletal, and biochemical. Physicians may find these groupings useful in narrowing the diagnostic investigation and ordering appropriate tests.

Since these signs and symptoms also appear with many other conditions, physicians may not always immediately consider Gaucher disease as a diagnosis,<sup>1</sup> often creating an interval between symptom onset and diagnosis.

Other symptoms primarily include fatigue caused by an increased resting energy expenditure (unusually high metabolism) and delayed growth development in children.<sup>2</sup>

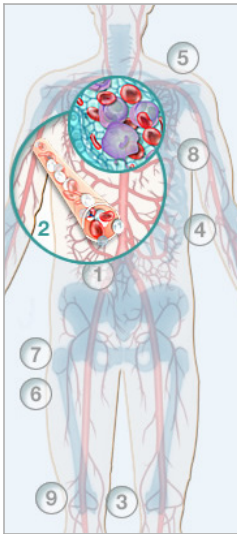
<sup>1</sup> Beutler E, Grabowski G. Gaucher disease. In: Scriver CR, Beaudet AL, Sly WS, et al, eds. *The Metabolic and Molecular Bases of Inherited Disease*. 8th ed. New York, NY: McGraw-Hill; 2001.

<sup>2</sup> Data on file, Genzyme Corporation.



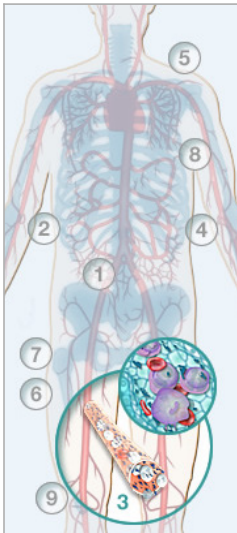
### 1: Hepatosplenomegaly

Gaucher patients may have protruding abdomens, from enlarged liver and/or spleen, due to accumulation of Gaucher cells. The spleen can swell to 5-75 times its normal size, while the liver to 1.25-2.5 times its normal size. The involvement of these organs can have many other effects on patients, including suppressing the appetite (because the swelled organs press on the stomach, creating a full feeling after eating very little), blood problems related to an overactive spleen, more serious liver disease, and low self-esteem related to appearance.



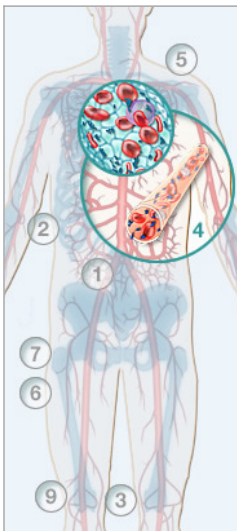
## 2: Thrombocytopenia

A build-up of Gaucher cells in bone marrow may cause fewer blood platelets to be produced. In addition, an enlarged, overactive spleen (caused by accumulated Gaucher cells) may break down blood cells faster than they are produced, contributing to an overall lower platelet count. As a result, Gaucher patients may experience excessive bruising and bleeding, including after even minor trauma. There may also be abnormalities in clotting and fibrinolytic factors.



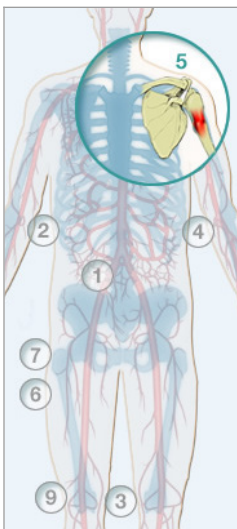
## 3: Anemia

When the spleen is enlarged from accumulated Gaucher cells, it may become overactive and break down red blood cells faster than they are produced. As a result, Gaucher patients may suffer from anemia. The resulting fatigue may also be exacerbated by fatigue and low stamina caused by a higher-than-normal metabolism found in many Gaucher patients.



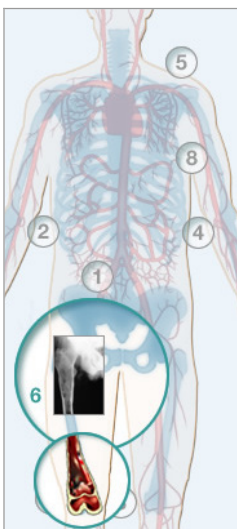
## 4: Leukopenia

When the spleen is enlarged from accumulated Gaucher cells, it may become overactive and filter white blood cells faster than usual. As a result, Gaucher patients may get sick more frequently than other people.



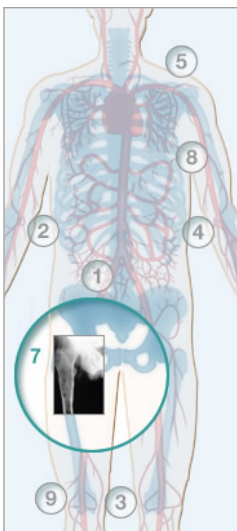
**5: Bone crisis**

Gaucher patients may experience severe bone pain, or “bone crisis,” as a result of bone infarction (with insufficient blood flow and delivery of oxygen and nutrients to the bone) due to infiltration of Gaucher cells in the intramedullary space and local release of chemical factors. The pain is intense, often accompanied by fever, and can last from a few hours to a few days or even weeks, usually rendering patients bedridden during this time.



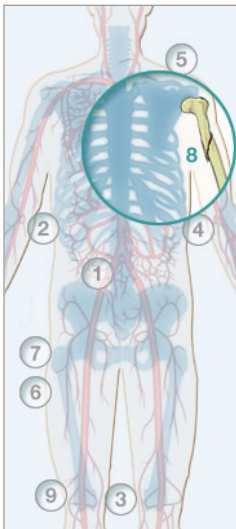
**6: Osteonecrosis / avascular necrosis**

As Gaucher cells accumulate in bone marrow, they can restrict normal blood flow and thus delivery of oxygen and nutrients to the bone -- sometimes leading to bone infarction and ultimately bone death. This causes severe pain and potentially leads to weakened bones, subject to fractures and joint collapse.



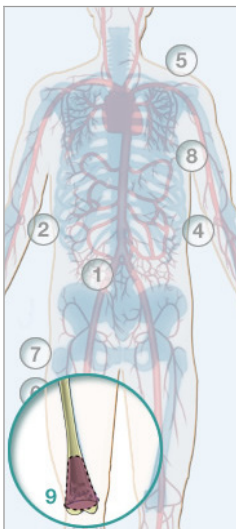
**7: Osteopenia**

Adult patients with Gaucher disease may have lower bone mass than expected for age and sex due to generalized demineralization, loss of trabecular bone and cortical thinning. This reduced bone density causes thinning and weakening and thus greater susceptibility to fractures.



### 8: Pathological fracture

Weakened bones due to osteonecrosis, avascular necrosis and osteopenia are susceptible to pathological fractures from normal activity.



### 9: Erlenmeyer flask deformity

Gaucher disease includes osteoclastic dysfunction and bone remodeling abnormalities. The most common among Gaucher patients is the Erlenmeyer flask deformity, in which the ends of the bone (most commonly the femur and tibia) develop a flared, flattened shape rather than the normal rounded form.

## Metabolic disturbances and constitutional signs and symptoms

Fatigue<sup>3</sup>

Pubertal delay<sup>3</sup>

Temporary growth retardation<sup>3</sup>

### Other possible manifestations

Pulmonary<sup>3</sup>

Lymphoproliferative disorders<sup>3</sup>

<sup>3</sup> Cox TM, Schofield JP. Gaucher's disease: clinical features and natural history. *Bailliere's Clinical Haematology*. 1997;10(4):657-689.

### Quality of life

Gaucher disease may have an impact on a patient's quality of life. Pain and fatigue may hamper his or her ability to perform daily activities. In addition, these encumbrances and other disease effects such as hepatosplenomegaly and delays in growth and development can cause considerable concern among Gaucher disease patients.<sup>4</sup>

<sup>4</sup> Verderese C, Graham O, Holder-McShane C, et al. Gaucher's disease: a pilot study of the symptomatic responses to enzyme replacement therapy. *J Neurosci Nurs.* 1993;25(5):296-301.

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