

KNOWLEDGE IS POWER FOR SYMPTOMATIC CARRIERS

BY STEPHANIE STEPHENS

Lara Palermo was 19 years old when she delivered her first child, Natalia, in 1996. Instead of going home after a few days, like most mothers, she was hospitalized for a month. She had severe postpartum bleeding that required five blood transfusions.

“My doctors thought I had a lazy uterus,” Lara recalls. With this condition, the uterus does not contract adequately after delivery to expel intrauterine contents and places the mother at a high risk of bleeding.

Lara, now 30 years old and living in Rochester, New York, says that there was no prior history of bleeding disorders in her family. While growing up, she experienced nosebleeds, but dismissed them as harmless. She was never tested for a bleeding disorder.

In July 1998, Lara’s mother had another child, Justin, who was diagnosed with severe hemophilia A following circumcision. At that time, Lara was pregnant again. On her mother’s recommendation, she sought advice at the Mary M. Gooley Hemophilia Center in Rochester, where Peter A. Kouides, MD, is medical and research director.

“When [Lara] saw us while pregnant with her second child, we thought perhaps she could be a carrier,” says Kouides. Since Lara’s brother Justin did not have a detectable genetic mutation, genetic testing was not performed on Lara, Kouides says. “We were left to just measuring her factor VIII level in her third trimester, which was ‘normal.’” In most women who are carriers, however, the factor VIII level typically rises during the third trimester.



THOMAS BARWICK/GETTY IMAGES

Lara underwent a planned Cesarean section for her second delivery. Her postdelivery factor VIII level was a low 45%, so she was treated with synthetic hormone DDAVP (desmopressin acetate) to suppress postpartum bleeding. The birth went smoothly, and Lara’s son Darrell was born in April 1999. Soon after the birth, Darrell was diagnosed with severe hemophilia A, like his uncle. Darrell’s diagnosis confirmed Lara’s status as a carrier.

Lara’s experience is not an isolated case, according to Kouides. Although few published studies exist, he cites a 2006 Netherlands study published

in the journal *Blood*, in which health-care professionals are urged to pay closer attention to symptomatic carriers like Lara. A symptomatic carrier is a person who carries the gene for hemophilia and is thus symptomatic with regard to potential bleeding under certain circumstances.

“The study showed that approximately one-third of women who are carriers can also have low clotting factor levels,” explains Kouides. It suggested a higher risk of bleeding in carriers of hemophilia, especially after medical interventions (including childbirth) or procedures like a dental extraction. It also emphasized the

importance of clotting factor level measurement before interventions in all carriers and potential carriers.

Defining a Symptomatic Carrier

Family history and assessment of clotting factor VIII and IX levels were once the sole methods of identifying carriers, before the advent of genetic counseling and carrier testing commonly used today. “The most accurate, gold-standard way to identify a female carrier is to do genetic testing on her blood, assuming that her relative with hemophilia has had genetic testing and has an identifiable mutation,” says Kouides. Sometimes the mutation cannot be identified because the relative’s insurance wouldn’t pay for full sequencing.

“Hemophilia carriers can present all manner of levels of clotting factor VIII and IX, depending upon whether the normal gene is dictating a normal amount and what the defective gene is dictating,” says Andra James, MD, assistant professor of obstetrics and gynecology at Duke University Medical Center in Durham, North Carolina. She is also a member of the National Hemophilia Foundation’s (NHF’s) Project Red Flag Women’s Task Force.

“We consider a level below 60% of factor VIII or IX to be low,” James says. “But people may function completely normally with a level of just 40%. Most hemophilia carriers have a level around 50%—half that found in individuals who are not carriers.” Bleeding symptoms can vary and are not always predicted by factor VIII or IX levels, which can have a wide range. Generally, the lower the level of factor, the more bleeding symptoms a carrier exhibits.

Carrier testing is necessary for several reasons. “A woman may show no symptoms until she undergoes a medical procedure that challenges her clotting system,” Kouides says. Carriers experience more sponta-

neous and provoked hemorrhages than noncarriers, the *Blood* study showed. Their clotting factor levels may not be measured or, as with Lara, they’re unknown.

Kouides and James concur that a fine line exists between diagnosing a symptomatic carrier versus an individual with mild hemophilia. “The terms are interchangeable,” says Kouides. “If you’re a symptomatic carrier, you do have mild hemophilia.” Then again, some men have mild hemophilia, but are not carriers. Mild hemophilia is defined as having a factor VIII or IX level ranging from 5% to 40% of normal blood levels.

Be Informed

It’s vitally important for women who might be carriers to first ask questions about their own symptoms as they relate to other family members’ bleeding disorders.

“Rarely do we make a carrier diagnosis without someone in the family having hemophilia—it’s possible but unusual,” James says. She says heavy menstrual bleeding is the number one symptom in women with bleeding disorders.

Both hematologists, who are also members of NHF’s Medical and Scientific Advisory Council, caution that a family doctor or obstetrician/gynecologist may be tempted to say there’s nothing to worry about when a woman is a symptomatic carrier. Participating in an open dialogue with healthcare providers can help alleviate confusion, frustration and possible health problems.

“A woman needs to be informed not only about the risk of her own bleeding symptoms, but also about the risk of having an affected child,” says James. Following a definite diagnosis, strategies can be devised to reduce risk, which include being seen by a hematologist in a facility equipped to manage carriers during and after delivery.

Women need more informa-

tion about symptomatic carriers. Kouides, also co-chair of the Female Universal Data Collection Working Group of the Centers for Disease Control and Prevention UDC project, reports that a companion study is under way to identify and collect data from as many carriers as possible, with results expected to be available in the next few years. This effort is another positive step forward in recognizing a segment of the bleeding disorders community that has been historically underserved.

“If I’d been checked for things outside the norm, we would have known I was a carrier,” says Lara. “If you think something’s wrong, don’t be afraid to demand an answer from your doctor.” ●

To Learn More

- Read the study: Plug I, et al. Bleeding in carriers of hemophilia. *Blood* 2006; 108:52–56.
- Contact HANDI, NHF’s information resource center, at handi@hemophilia.org or 800.42.HANDI.