

ScoliScore AIS Prognostic Test Personalizes Treatment for Children With Spinal Curve

BY BOB CARLSON, MHA, Senior Correspondent

Twenty-six states mandate that schools screen children between the ages of 10 and 12 for scoliosis. New York is one of those states, and after 11-year-old Marissa did the Adam's Forward Bend Test at her school on Long Island in 2009, the school nurse referred Marissa to her pediatrician for follow-up.

That referral marked the beginning of a stressful time for Marissa and her family — but Marissa's story has a happy ending. A 24-degree right thoracic curve in her spine reversed itself to 10 degrees, and Axial Biotech's ScoliScore AIS Prognostic Test helped to predict that the remaining curve likely would not get worse.

Marissa no longer has to wear the back brace that scoliosis specialist Vasantha L. Murthy, MD, at Scoliosis Associates in Manhattan, had prescribed two months after the school screening, when it appeared that her spinal curve had increased. The improvement in Marissa's condition also meant that follow-up appointments with Murthy would be scheduled every six to nine months instead of every three or four months.

"She had another follow-up just a couple of months ago and she's very stable," says Marissa's mom, Tara, who also was diagnosed with mild scoliosis at about the same age and at the same practice. Tara had to wear a back brace but stopped growing before her scoliosis could progress.

A sizable population

Adolescent idiopathic scoliosis (AIS) is an abnormal lateral curva-

ture of the spine that can limit a young person's range of physical activity, reduce respiratory function, and diminish self-esteem.

Seven million children in the United States have AIS. The condition is often undiagnosed until the spinal curve is more noticeable — shoulders, ribs, hips, or waist may be uneven; one arm may hang lower; or one shoulder blade may protrude and, as a result, back pain may develop. Of the 100,000 children diagnosed with scoliosis annually, the disease will progress in a quarter of them; i.e., the spinal curve will increase. Scoliosis in girls is 8 times more likely to progress than in boys, which is why scoliosis specialists recommend

that girls be screened at age 10 and again at age 12, but boys only once at age 13 or 14.

The etiology of AIS is unknown, but a child has a 20 percent chance of inheriting the condition if an immediate family member has scoliosis. Marissa is at risk because both her mother and brother were diagnosed with mild scoliosis. Treatment depends on a family history of scoliosis, the child's age, and on the location and severity of the spinal curve as measured on an X-ray of the spine using the Cobb method. A curve of less than 20 to 25 degrees is monitored by a clinician every three to six months. A body brace is fitted for a curve of more than 20 to 25 degrees to support the spine and prevent progression. Spinal fusion surgery to straighten the spine and prevent pro-

gression is indicated for a curve of more than 45 degrees in a growing child. Combined with diagnostic information and the physician's clinical judgment, ScoliScore test results can help provide more informed, personalized treatment for patients.

Getting personal

"We thought we were trying to develop a test for scoliosis, but three years after we had started gene discovery, the light bulb went on and we realized that nobody needs a test for scoliosis — what they need is a test for scoliosis progression," says Kenneth Ward, MD, chief scientific officer and a founder of Axial Biotech, a privately held company in Salt Lake City,



Kenneth Ward, MD

Utah, that was incorporated in 2002 by a group of internationally recognized spine surgeons and geneticists.

That was the first of two eureka moments in the development of the saliva-based ScoliScore AIS Prognostic Test.

Board certified in four specialties, including clinical medical genetics and clinical molecular genetics, Ward was wearing his OB/GYN hat when one of his patients mentioned that her husband, a spine surgeon, was interested in identifying genetic markers for scoliosis. Ward learned about new, minimally invasive "fusionless" scoliosis treatments that could be initiated early in the disease process for those patients whose scoliosis would likely progress.

"Without a prognostic test to figure out who needs it, the whole de-

vice development in this area was stalled,” Ward recalls. “There were things that could be done, but we didn’t know who to do them for.” Scoliosis specialists had no choice but to treat all their AIS patients as if their disease would progress.

“Unless you live down the street from a spine surgeon, that usually means taking off work, sometimes driving for hours, sitting in a waiting room, and then being told, ‘Well, nothing’s changed, so we’ll see you again in three or four months,’” Ward says. Visits could also include an X-ray of the spine from brain stem to tailbone, a dose of radiation equivalent to approximately 30 chest X-rays.

These insights led to the second eureka moment in the development of the AIS prognostic test.

“We realized that even more important was a negative predictive value test that would make it possible for spine specialists to do fewer X-rays and have fewer office visits with patients who didn’t need a lot of medical care and to focus on those who do,” says Ward. “It’s the perfect personalized medicine story.”

One couple from England

Launched nationally in 2010, the ScoliScore AIS Prognostic Test is designed for Caucasian male and female patients, 9 to 13 years of age, diagnosed with mild AIS (Cobb angle 10 degrees–25 degrees) to help predict which children are likely to progress to a severe spinal curve (Cobb angle of 40 degrees or more).

Scoliosis occurs at the same rate in all races, but 94 percent of patients who are monitored and treated for mild scoliosis are Caucasian. According to Ward, data are being collected to further develop and validate the test for patients of other races.

In developing the ScoliScore test, Axial Biotech researchers collected DNA samples from more than 9,500 individuals at more than 100 clinical

sites throughout the world. “We started with a very simple experiment,” says Ward. “We took the last hundred patients that had been operated on for scoliosis, and we asked what do their family trees look like?” It turned out that 70 percent of the children in Utah whose scoliosis was severe enough to require surgery were descendants of one couple in England who emigrated to Utah in the 1800s. Descendants of that one family — along with a higher prevalence of scoliosis — are now found around the globe.

The ScoliScore AIS Prognostic Test can help reduce care for low-risk patients. The annual cost saved? About \$2,000 per kid.

Using their proprietary genealogic database of 30 million ancestors and descendants of the original Utah pioneers, Axial Biotech researchers searched for other overlapping family lines with a high rate of scoliosis. The Axial team sifted through nearly one million potential DNA markers to identify the 53 single nucleotide polymorphisms associated with scoliosis progression. The ScoliScore AIS Prognostic Test was subsequently validated in three studies of 800 patients with AIS. Ward estimates the total cost at \$45 million.

At Axial Biotech’s laboratory, which Ward directs, an algorithm converts the results of TaqMan genotyping into the Risk of Progression Score, a numerical value ranging from 1 to 200. Scores from 1 to 50 are classified as low risk, 51 to 180 as intermediate risk, and 181 to 200 as high risk. A score in the low-risk range is clinically proven to help physicians predict with 99 percent probability that scoliosis will not progress to a severe curve. The test does not help predict an individual’s susceptibility to inherit the condition

or the final outcome of a patient’s progression.

Saving money

Bracing one AIS patient costs \$2,500 to \$4,000 annually, and two or three braces are typically required over the course of the adolescent growth span. An estimated 30,000 children are put into braces, but only 5 percent progress to a degree that requires surgical intervention. Scoliosis patients make more than 600,000 visits to physician offices. Annual costs associated with the care

of one child with progressing AIS average about \$24,000, according to the National Scoliosis Foundation. The list price for the ScoliScore AIS Prognostic Test is \$2,950.

“Based on the way spine specialists have changed in how they take care of low-risk kids, they may save \$2,000 per child just by being able to identify those who need less care,” says Ward.

Marissa is one of those low-risk kids. She and her mom now make the 50-mile round trip from Ocean-side to Manhattan, at most, only twice a year. But for Marissa, the best part of having a ScoliScore of 11 is losing that back brace. “It was torture trying to get her to wear the brace,” says Tara. “It’s devastating to a preteen girl.”

“It’s sorta like bulky and stuff,” says Marissa.

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