The importance of early detection of these autoantibodies in the fetus is underscored by the fact that once third-degree, or complete, heart block has developed, it is irreversible with current therapies, according to Dr. Buyon, professor of medicine, department of rheumatology, New York University, New York City.

Moreover, anti-Ro/La congenital heart block carries a 20% mortality, and at present the majority of children who survive need a pacemaker.

Intense research interest therefore is focused on identifying markers of early cardiac injury, at a point before fibrosis and scarring are permanent, and on the potential for therapeutic interventions to reverse early changes.

The use of cardiac monitoring to detect prolongations of the PR interval greater than 150 milliseconds was recently evaluated in the observational PR Interval and Dexamethasone Evaluation (PRIDE) study of pregnant women who were positive for anti-Ro and/or anti-La antibodies. The study also attempted to provide some data on outcomes following the administration of steroids. Fetal echocardiography was performed weekly between weeks 16 and 26, and then biweekly between weeks 26 and 34, according to Dr. Buyon, one of the study investigators.

She and her colleagues were looking for prolongation of the PR interval, evidence of tricuspid regurgitation, and unexplained atrial echodensities. Among the 88 patients who completed an evaluable course, there were three cases of third-degree heart block.

One of these patients had a normal PR interval, but some tricuspid regurgitation was noted at 17 weeks and atrial echodensities at 22 weeks. A week later the fetus was in third-degree heart block and, despite treatment with maternal dexamethasone, 4 mg/day, the fetus developed and the pregnancy was terminated.

The second fetus had a normal PR interval between weeks 16 and 18 along with mild tricuspid regurgitation at week 17. The mother missed an appointment and, by the next time she was seen, third-degree block had developed in the fetus. This persisted despite administration of dexamethasone, and the child continued to be followed after birth (Arthritis Rheum. 2006;54:S689).

The third fetus also had a normal PR interval with mild tricuspid regurgitation later in the first trimester of pregnancy. The pregnancy was terminated at 20 5 weeks.

First-degree block was detected in an additional three fetuses. In one, the PR was normal at weeks 16-18, was prolonged at week 19, and normalized within 7 days of dexamethasone treatment. The second had a prolonged PR interval at week 22 that resolved within 3 days of dexamethasone treatment. These two patients both had normal electrocardiograms at birth.

The third fetus had normal PR intervals throughout gestation but an electrocardiogram at birth showed first degree block that has persisted to age 3 years. Dexamethasone was also used in nine cases of second-degree block. Of these, four fetuses progressed to third-degree block, four remained in second, and one was born in normal sinus rhythm. “This was a little disappointing,” Dr. Buyon said. Of the 79 neonates for whom birth electrocardiograms were available, 78 were normal, and all 46 for whom 1-year follow-up electrocardiograms were available were normal, she said.

In conclusion, the study suggests the following, according to Dr. Buyon:

- First-degree block in utero is reversible with dexamethasone, but if present at birth, close observation by a cardiologist is needed because of the possibility of later progression.
- There has not been evidence of conduction abnormalities developing later in neonates whose electrocardiogram was normal at birth.
- Advanced cardiomyopathy can occur within 7 days of a normal PR interval, so even a weekly evaluation may not always be sufficient.
- Tricuspid regurgitation may be an important early marker of injury.

Dexamethasone treatment poses significant hazards to both mother and fetus, with maternal risks including diabetes and hypertension, and fetal risks including intrauterine growth retardation, adrenal suppression, and decreased brain growth. Moreover, as was seen in PRIDE, efficacy is hardly guaranteed.

Accordingly, other therapeutic approaches are currently being investigated, including inhibition of transforming growth factor β to limit fibrosis and progression of intravenous immune globulin (see box).

Watch Fetus In Presence of Anti-Ro/La Antibodies

Medical Therapies Stabilize, but Not Cure, Peyronie’s Disease

BY NANCY WALSH New York Bureau

MONTREAL — There is no cure for Peyronie’s disease, but management can offer patients stabilization in as little as 12 months, Dr. Laurence A. Levine said at a congress sponsored by the Canadian Society for the Study of the Aging Male.

The condition, first reported by Francois de la Peyronie in 1743, is characterized by the development of a penile plaque in the tunica albuginea caused by deposition of collagen. Deviation, shortening, and an hourglass-like shape can result. During the early inflammatory phase of the disease, patients can experience pain with erection.

Peyronie’s disease is a disorder of wound healing that occurs in a genetically susceptible patient, probably in response to minor trauma, Dr. Levine said.

A proliferative fibrotic reaction results in an inelastic scar. Disruptions of collagen and elastin are seen, along with upregulation of cytokines such as transforming growth factor β and imbalance of nitric oxide and nitric oxide synthase.

The standard treatment is surgery, but that must wait until the disease stabilizes and pain ceases. In the interim, and for patients unable to undergo surgery, therapies based on current thinking about pathogenesis can help.

To survey the medications used in Chicago, the most commonly used remedies were vitamin E and Potaba, said Dr. Levine, of the department of urology at Rush Presbyterian-St. Luke’s Medical Center, Chicago. Yet studies have found no benefit for vitamin E and only reduction in plaque size for the antifibrotic drug Potaba (aminobenzoic acid powder). Colchicine, tamoxifen, and carbamazepine have also been reported.

Intralesional interferon has been used with some benefit, but “it does not appear to be as robust as what we see with vera- pamil,” he said.

Topical verapamil is popular. Manufacturers are making substantial claims about its efficacy, but there is no published evidence of benefit, according to Dr. Levine.

It does not penetrate into the tunica albuginea, he said.

Medical therapies also can be used in conjunction with mechanical stretching. Since studies have shown 50% of patients worsen with no treatment, it’s important to treat early, Dr. Levine added.

Next: IVIG for Heart Block Prevention?

Intravenous immune globulin (IVIG) has a history of safely being used in pregnancy, primarily for autoimmune thrombocytopenia and immune deficiency syndromes. A few cases of successful use in congenital heart block have also been reported.

To determine if this prophylactic approach could reliably decrease the placent al transport of anti-Ro/SSA and anti-La/SSB antibodies, the Preventive IVIG Therapy for Congenital Heart Block (PITCH) trial is now enrolling patients. Sponsored by New York University School of Medicine and the Alliance for Lupus Research, the trial aims to enroll 19 women who are antibody positive and have already had a child with congenital heart block or a rash that might have been neonatal lupus. Such mothers are at much higher risk of having another child with congenital heart block than are mothers positive for anti-Ro/SSA who have not already had an affected child.

Participants will be given 400 mg/kg of IVIG every 3 weeks for a total of five treatments between weeks 12 and 24 of pregnancy. If fewer than three fetuses develop second- or third-degree heart block, another 35 women will be enrolled.

“Then, if there are fewer than six cases of heart block out of 54, we will be on the way to having a prophylactic therapy,” said Dr. Buyon, who is principal investigator for the trial.

Additional information about the PITCH trial is available online at http://clinicaltrials.gov/show/ NCT0046928.