BERNARD GERSH: Hello. I'm Bernard Gersh from the Mayo Clinic. And with me today, and it's great pleasure to have him, is Dr. Juan Bowen, who is Chief or Director of the Marfan and Thoracic Aorta Clinic. And, Juan, this is a multi-disciplinary clinic.

JUAN BOWEN: Yes, it is. It involves a cardiologist, a geneticist, and of course imaging specialists, cardiac surgeons. I'm a general internist, but it is a multi-disciplinary clinic. And we use all the disciplines.

BERNARD GERSH: How frequent is Marfan syndrome?

JUAN BOWEN: Well, I'm glad you asked that question, because this is an important condition. It affects about one in 5,000 people. And we're discussing it today because the cardiovascular aspects of it, although not the most visible, are the potentially lethal aspects of it.

And it's also interesting that it's estimated that perhaps half of the people in the United States with Marfan syndrome have not been diagnosed. They don't know they have this potentially lethal condition.

BERNARD GERSH: And that includes a fair number of athletes, because they're very tall.

JUAN BOWEN: Yes. And every few years, something bad happens, and that's in the newspaper. So the most visible aspect of it is the musculoskeletal aspect, where people are very tall and thin, very long fingers, very long limbs. But in 2010, the diagnostic criteria were revised, because a lot of some Marfanoid-appearing people do not have the Marfan syndrome. And using the new criteria, these criteria emphasize the cardiovascular aspects, the aortic root, and they also emphasize the newer, better, more available genetic testing.

BERNARD GERSH: Before getting onto the cardiovascular aspects, as you were talking it, I thought of an analogy with hypertrophic cardiomyopathy, also very often undiagnosed, does affect athletes, may cause sudden death. You read about it in the newspapers. How often does Marfan's cause sudden death? I know you'll get into the cardiac details, but actually sudden death.

JUAN BOWEN: Oh, with reasonable frequency. It is not one of the most common causes of sudden death, but patients who experience dissection, unfortunately even aortic rupture, may die very fast. That would be the main mechanism.

BERNARD GERSH: So what do we need to look for as a cardiologist?

JUAN BOWEN: Well, first of all, I think to recognize the musculoskeletal features. That may not be the job of the cardiologist, but I think sometimes it will be. Usually, the patients will have been referred.

And I think the importance of echocardiography and other imaging, the central issue of the aorta and the aortic root, in particular-- most patients with Marfan syndrome have disease of the proximal aorta and a few of the distal aorta. Interestingly, now that Marfan patients live a lot longer, newer problems are arising-- distal aortic conditions. Their musculoskeletal and ocular problems get worse as they get older. So the natural history of the condition is changing because of the success of medical and surgical treatment.

BERNARD GERSH: I want to get on to that in a moment. But just to bring you back to the heart itself, mitral valve prolapse I know is very common. But how common is chordal rupture and severe mitral regurgitation?

JUAN BOWEN: It's interesting that that aspect of the Marfan syndrome has not been fully studied, not as much as it should be. Right around 30%, 40% of the Marvin population will have mitral prolapse. And because it is a generalized connective tissue problem, the people who have mitral prolapse tend to have bileaflet prolapse, and they tend to have more progressive mitral regurgitation than the usual person with mitral prolapse.

BERNARD GERSH: Oh, they do? When I've heard you and your colleagues present-- and what is striking and, I have to say, very exciting is, here is a disease where the natural unnatural history really has been strikingly changed--

JUAN BOWEN: Dramatically so.

BERNARD GERSH: --in the last 20 years.

JUAN BOWEN: Dramatically so.

BERNARD GERSH: How?

JUAN BOWEN: Well, the primary improvement was the realization in the 1970s that the aortic root could be repaired effectively using the Bentall or composite graph technique.

BERNARD GERSH: Let me just interrupt for a moment. 20, 30 years ago, what was the average lifespan of a Marfan's patient?

JUAN BOWEN: Most patients died in their 40s.

BERNARD GERSH: And now?

JUAN BOWEN: They can be expected to live a normal life expectancy.

BERNARD GERSH: That's amazing, in 20 years. Carry on.

JUAN BOWEN: Well, yes. With the development of this operation by Hugh Bentall from London, then all of a sudden the repair of the dilated aorta became possible. And then with increasing experience and time, the thresholds for when that repair should be done prophylactically have progressively lowered. So today, it's routine to have an operation prophylactically when the aortic root reaches 45 to 50 millimeters, in certain cases. Formerly, it was 60 millimeters.

BERNARD GERSH: Yeah. And do you ever weigh it beyond five centimeters or 50 millimeters in a Marfan's patient?

JUAN BOWEN: Most of the time, no. There's little reason to wait. And in fact, operations are done sooner than the usual threshold in certain circumstances-- an adverse family history.

BERNARD GERSH: Pregnancy.

JUAN BOWEN: Yes. And particularly rapid growth of the aorta.

BERNARD GERSH: And so then you would go between four and 4.5?

JUAN BOWEN: Yes.

BERNARD GERSH: What else has contributed to the improvement in longevity?

JUAN BOWEN: Well, medical therapy is on the threshold of major improvements, we hope. For some time now, the medical therapy has been directed at the protection of the aorta.

BERNARD GERSH: Beta blockers?

JUAN BOWEN: Beta blockers, to reduce hemodynamic stress, but also lifestyle changes. Some Marfan patients are taught that they should not do certain things, like contact sports or extreme exertion. So that's part of it.

Beta blockers have been still our standard therapy. Interestingly, the trials that have shown the benefit of beta blockers involved relatively few patients, but they are still the standard treatment. But now, because the fibrillin molecule, which is the cause of the Marfan syndrome, is a regulator of TGF beta signaling, now there's a brand new potential therapy, which is down-regulation of TGF beta signaling.

This has been proven in laboratory animals in the mouse model. And as we speak today, there are 10 trials going on around the world studying losartan in human beings, and we anticipate that some of these will be reported in the next year to two years.

BERNARD GERSH: This has really been a fascinating and a striking example of a genetic model being translated to the clinical laboratory or the clinical setting. Because it is an ARB, and it doesn't apply to an ACE inhibitor. It's very specific.

JUAN BOWEN: Yes. At least in the mouse model, blockade of the AT1 receptor seems to be very important.

BERNARD GERSH: Now, at this stage, should we be using losartan or an equivalent clinically? Or should we be entering patients into trials? And what should we do if we can't enter them into a trial?

JUAN BOWEN: I think the prudent thing to do, and what we do today, is to stay with the standard therapy, which is beta blockade. Many patients have heard about losartan and request losartan. And I think particularly in patients with elevated blood pressure-- after all, it is a standard anti-hypertensive-- I feel comfortable adding losartan. And I think after a discussion with the patient and informed consent, I think it's OK, but I don't feel comfortable using losartan alone just yet.

BERNARD GERSH: Fine. Well, just to wrap up, what can we look forward to in the next 10 years? I mean, it's been pretty dramatic the last 20 years. But what do you think is around the corner?

JUAN BOWEN: Well, it's very exciting, because for the first time there is the potential for treatments which affect the pathogenesis of the condition. And the basic science laboratories are busy around the world studying more than just dissecting the TGF beta pathway. So I think there will be new molecular targets, there will be specific molecular therapies, and I think we'll find also improved ways to assess the health of the aorta beyond just diameter.

BERNARD GERSH: Juan, thank you very much. Thank you for joining us.