What led you to specialize in bladder dysfunction?
As opposed to a lot of chronic conditions, many bladder problems can be treated with dramatic improvement. During my training, I saw a lot of patients who had bladder problems, and when they had an improvement in their condition they had a remarkable improvement in their quality of life. The average person has no idea of the severity of the impact of bladder problems on quality of life. For instance, if a patient has incontinence, even with no neurological problems, the psychological issues can be very detrimental, causing embarrassment, social anxiety and fear of leaving the home. This ranges from women who know every bathroom on the way to the mall, right up to patients who literally cannot leave their home at all because they are in diapers. When you can fix that, or even improve it, the quality-of-life improvement can be substantial: that is what attracted me to the field.

What is the current focus of your research?
I do a lot of work with neuromodulation. Neuromodulation involves using electrical impulses to modulate bladder function. It is thought that a lot of what causes things to go awry in the bladder is a failure in messages running from the spinal cord or the brain down to the bladder (e.g., in multiple sclerosis), or messages coming from the bladder back to the spinal cord, which can get confused and then cause problems. Alternatively, you could have a patient (e.g., with a spinal cord injury) where there are no messages at all. By using electrical stimulation to stimulate the various nerves that are involved in bladder function, in many of these situations you can help the bladder to function more normally. By using electrical stimulation to stimulate the various nerves that are involved in bladder function, in many of these situations you can help the bladder to function more normally.
Another area that I am involved with is the use of botulinum toxin for bladder dysfunction. Botulinum toxin injected into the bladder can calm an overactive bladder, by partially paralyzing the muscle. Also, there are patients with detrusor sphincter dyssnergia: this is when the bladder contracts and the patient tries to void the urinary sphincter muscle, which should relax to allow urine flow, but contracts instead, making it very difficult for them to void. By injecting botulinum toxin into the sphincter muscle, you can paralyze the muscle just enough to allow urination. For example, I had a patient with multiple sclerosis who could not urinate at all and had to be catheterized; it was a horrible situation for him. Now he comes in every 5 months for a 10-min injection and he has no bladder problems.

Tell me a bit more about the process of neuromodulation. How is this carried out in practice?
Currently there is one device available in most countries: InterStim® (Medtronic, MN, USA). With this system, we first pass a small wire through the sacral area and next to the nerves that lead to and from the bladder. We then thread that wire out through the skin and send the patient home with a small external stimulator box for a trial period. The procedure can be carried out in the office or under sedation in the operating room. A positive aspect of this technology is that you have a chance to test whether it works. The patient goes home with the device, with the external stimulator box, and lets us know whether it works. If there is a greater than 50% improvement, we will go ahead and implant the permanent stimulator under the skin.

This device can work both for patients with urge incontinence and urinary frequency, and paradoxically, patients with idiopathic retention, where they cannot urinate at all. The basic reason is that in many patients the underlying cause of bladder dysfunction is thought to be abnormal messages from the bladder itself or the pelvic floor that cause the bladder to be overactive or switch off. Sending electrical stimulation through these nerves can actually block the abnormal messages that are coming to the spinal cord: this allows the normal messages to get through.

As well as the sacral nerves targeted by InterStim, other groups have looked at stimulation of the pudendal nerves, and we have carried out a study looking at stimulation of the dorsal genital nerve (clitoral nerve). Stimulation of this nerve gives a strong inhibitory message to the bladder, so we reasoned that by using the same technique of neuromodulation, we could inhibit the bladder. We performed a feasibility study in women with urge incontinence who had failed all other treatment options and got some very positive results, so we are now looking forward to a multi-institution study to test this more thoroughly.

What other forms of treatment, surgical and medical, do you use at present for patients with neurogenic bladder disorders?
First, it is important to understand that neurogenic bladder is a broad term, applied to any bladder dysfunction related to a neurological problem. In the most severe cases the patient may have a completely nonfunctional bladder, where the bladder acts as a reservoir but cannot contract to allow urination. Alternatively, one of the most common problems that these patients have is that the bladder becomes stiff and can not hold as much as it should. This can lead to incontinence or, if pressure in the bladder builds up, the back pressure can force urine back into the kidneys, causing kidney damage. In some of those patients, we have to perform a bladder augmentation, where we take a portion of the bowels and reconstruct it into a dome that can be used to reconstruct the bladder and increase its volume to reduce pressure. Another surgical procedure that can be used to help those whose limited mobility prevents normal catheterization is to create a tunnel to the skin, so that they can self-catheterize more easily.

So what we do runs the gamut from patients who we simply teach to carry out intermittent self-catheterization, those who use medication, neuromodulation, and all the way up to major reconstructive surgery. In the last 10 years, the number of reconstructive surgeries we carry out has dropped significantly due to the development of botulinum toxin and some of the neuromodulation techniques, and I expect that...
this decrease will continue. In the USA, the botulinum toxin is not approved for neurogenic bladder indications and so can only be administered through study protocols. Once this is readily available, I think this will impact our treatment quite significantly.

What other changes do you expect we will see over the longer term? Do you think there is a role for regenerative medicine?

I absolutely feel that there is a role for regenerative medicine. One of the reasons that we shy away from some of the bladder augmentation surgeries I mentioned earlier is that in order to try to improve the function of one organ (the bladder), you have to carry out major surgery on another (the bowels). That is a major surgery: it is easy to work on the bladder, it is very forgiving, but once you start operating on the bowels, that is where you can get real problems. There are studies now being carried out, for example, at Wake Forest University (NC, USA), where they are working on growing sections of bladder tissue. If we could just get that tissue ready-made out of the fridge, without involving the bowel, we could probably operate with less morbidity and surgery would be a lot easier.

The other thing people are looking at is producing bladder cells, which could be injected into the bladder wall to regenerate portions of the bladder. There might also be ways to regenerate the urinary sphincter in patients with incontinence, in order to augment its ability to contract.

There is a lot of interesting work being carried out in the field of regenerative medicine, and over the next 20 years it will probably change how we treat these problems significantly.

What do you anticipate focusing your own research on over the next 5–10 years?

There is still a lot of work to be done with neuromodulation. At the moment, we have a general nerve target, but there is a lot of uncertainty. We are not even sure how much electricity to use or in what patterns to apply stimulation. It is still a shotgun approach to some degree. As we learn more about it we will be able to target nerves much more specifically and know much better what sort of stimuli patterns are needed in order to make the nerves work as we want them to. I perform a lot of research with the Department of Biomedical Engineering at Case Western University in Cleveland, OH, USA. They have a huge center focusing on this technology, and we have been discussing the possibility of placing tiny cuffs on individual nerves, so that we can stimulate very specific nerves in order to get very specific bladder activity. I think we will become a lot more refined and specific with our neuromodulation, and learn a lot more about botulinum toxin. We are also starting to look at using stem cells. I think these are areas that are really going to blossom in the future.

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