

An Evening with Dr. Robert Moldwin

New, Emerging Therapies for Interstitial Cystitis

**Featuring Dr. Robert Moldwin,
Associate Professor of Clinical Urology
Director, [the Pelvic Pain Center](#) at [The Arthur Smith Institute for Urology](#)
Author of [The Interstitial Cystitis Survival Guide](#)**

Moderated by Jill Osborne, President - [IC Network](#)

Date: July 11, 2006

Jill Osborne - Good evening and welcome to the 2006 IC & PBS Online Patient Conference. Tonight is our 8th special event and we are delighted to welcome Dr. Robert Moldwin to our event tonight. Dr. Moldwin is a name most of you should recognize. He is the author of the IC Survival Guide, a book which has educated tens of thousands of IC patients, family members and medical care providers on interstitial cystitis.

What you may not know, however, is that he is one of the few world experts in the treatment of urologic infectious and inflammatory diseases and has contributed tremendously to the treatment and understanding of these conditions. As the Director of the IC Center at the Long Island Jewish Medical Center, he and his staff have provided hope to thousands of patients, many of whom travel from around the world to see him.

He has published extensively in peer-reviewed journals and often serves as an advocate and expert consultant on IC in lectures and through the media. What we appreciate most about Dr. Moldwin is his kindness and compassion. He's one of the "good guys" who takes the time to listen to the needs of patients and to create resources that can help. From sponsoring IC support groups to writing the #1 best selling book on IC, Dr. Moldwin is clearly dedicated to the cause. We are so grateful that he has agreed to appear tonight. Welcome Dr. Moldwin!

Dr. Moldwin - It is an incredible pleasure to be with you all this evening and thank you for that very kind introduction.

Jill Osborne - Clearly, IC therapies have changed dramatically in the past ten years. What is your current goal in working with patients?

DR. MOLDWIN – We're always trying, of course, to find the holy grail of IC, which is to eliminate ALL symptoms for the patient. The problems that we've learned as clinicians, and as patients have learned, is that that is a very difficult goal to achieve.. The bottom line is that there is no cure for IC...YET! Therefore, for the time being, our main goal is to reduce symptoms as much as possible, thereby improving the patient's quality of life.

In this process, we try to apply one of the major medical tenets: "Do No Harm." As most patients know, some of the therapies that patients have gone through cannot be the most exciting, wonderful, or joyful experiences. Therapies can cause other problems, such as constipation, increased pelvic pain, increased daytime fatigue and other problems that can be worse than the original complaint. As many patients know, some of the medications that we place into the bladder can cause a great deal of irritation, at least at the beginning. Some of the evaluations, such as hydrodistention or placing chemicals in the bladder, can also be very uncomfortable.

Although we still have to go through some of these uncomfortable processes. Many clinicians are now pulling away from these therapies and have adopted other therapies or diagnostic methods that keep patients as comfortable as possible. For example, some of the earlier methods to help diagnose IC relied upon stretching of the bladder (i.e. hydrodistention) or the placement of caustic agents in the bladder (i.e. potassium). However, today, we have less traumatic methods of evaluation that can be used.

Jill Osborne - What I've seen in the past five years is more sensitivity towards the patient experience and the use of testing and therapies that are more soothing and designed to help the patient have a better experience.

Dr. Moldwin - I agree with that. We're trying to be nicer to the patient with more soothing therapies, etc. I also see many new, young urologists coming out of training that are much more accepting of IC, are willing to treat it and have more of an interest in the IC patient population. They seem to be more accepting of IC issues and other coexisting conditions, whether it be pelvic floor muscle spasms or IBS.

Jill Osborne - I'm curious to see if you still see any of the older treatments for IC. What are your thoughts on clorpactin and silver nitrate?

Dr. Moldwin - I don't use them at all. I don't like the concept of using caustic agents in the bladder. Firstly, they may cause scarring of the bladder wall. If any of those agents have contact with the ureter (the tube that brings urine down from the kidneys to the bladder), they can cause scarring, which then gives that patient a whole new spectrum of problems. If they were the only agents available, then maybe I would have to use them ... but now there are other agents, more innocuous chemicals that can be placed into the bladder, which can have as good, if not better, results.

When I see a patient, I need to assess where they are clinically RIGHT NOW; but I also have to think about where that patient will be ten or twenty years from now. As we're seeing so many more young patients in our practice, this is even more on my mind. Every time I do a hydrodistention or a fulguration, I am always concerned about possible ramifications in the distant future. I'm concerned about causing scarring that could limit the patients bladder capacity further. So, I try to limit these procedures as much as possible. In the case of IC, often "less is more."

Jill Osborne - What's your position on DMSO???

Dr. Moldwin - DMSO is, as you know, one of the two FDA approved medications for IC, DMSO & Elmiron. I still use DMSO but it's not my first line agent at this time. But, I believe that although it can be very irritating to the bladder initially, many of its features can provide benefit to the IC patient. There is data to support its use. I generally use a "DMSO cocktail" which is comprised of DMSO, heparin, an antibiotic, a steroid, and sodium bicarbonate. Each one of those agents has some theoretical role in reducing symptoms.

The main problem with DMSO is that it can hurt or cause frequency, at least with the initial instillations. Patients need to be counseled about this before they start treatment. They need to understand that they will probably get worse before they get better. Often patients can hold DMSO in their bladder about fifteen seconds before they need to urinate it out the first time. We hope to see improvement in holding it and a slow improvement of their symptoms with continued use.

In my opinion, *after* the third instillation, I expect to see some improvement in symptoms. If the improvement in symptoms is not evident by the fourth instillation, we usually stop and switch to another agent. In my experience, if you haven't improved in that time, the only thing that will occur is the patient being frustrated, and I very much don't want to see that occur. I like to see patients

progress and improve within a reasonable period of time. There is nothing more depressing and frustrating than sitting around for a month with an unsuccessful therapy.

The bottom line is that we pick and choose the medications on the basis of what we think will work best but it is, in reality, a great deal of hit and miss. If one therapy is not working, we need to move on to another therapy. Ultimately, it's the rare patient, the very rare patient, who does not improve somewhere along the way.

Jill Osborne - What therapies have you found to be the most successful or helpful??

Dr. Moldwin - Let's start with the simple stuff. Evaluation! Before we can discuss therapies, I believe that it's extremely important for patients to understand that most IC patients have multiple pain generators, such as IBS (that cause abdominal or pelvic pain), fibromyalgia, pelvic floor spasms or pelvic floor dysfunction. 70-80% of IC patients will have some degree of pelvic floor dysfunction or spasm that may account for even more pain than the bladder pain. Of course, vulvodynia is also frequently found. So, one of the most important parts before we get to therapy is to try to dissect apart all of those different conditions.

I can tell you that between a good history and a good physical examination, a good clinician can pull these specific problems apart and decide on which one merits therapy first. In my opinion, it is unreasonable to attack everything at once because you won't know what is helping what. Our methodology is to try to eliminate one variable at a time, and that can be frustrating, but it is, in my opinion, the best way to begin.

Now supposing I feel that a patient has IC but the majority of their pain, pelvic pressure and even frequency is coming from pelvic floor spasms, I will start a program of pelvic floor muscle relaxation. This usually consists of avoiding straining with urination, aggressive control of constipation, warm baths, local heat applications and, usually, muscle relaxants. This may be supplemented in some instances with physical therapy.

I should also mention that there is a rapidly expanding interest in the Physical Therapy community to get involved in this specific area ... which is absolutely wonderful to see. In the past ten years, there has been an explosion in the number of physical therapists dedicated to treating pelvic floor dysfunction (PFD). I don't believe that these PTs would be involved in the field if they weren't seeing positive results. I constantly see positive results.

Jill Osborne - Do you ever have patients who just don't believe that their muscles can be contributing to their pelvic pain?

Dr. Moldwin – Absolutely, however I can usually prove it to them. We first look at symptoms. Many patients complain of urinary hesitancy associated with pain or discomfort. They need some time to start the urine flow. They sometimes need to push to get the urine moving along. Some patients have constipation. Each one of these issues may be associated with pelvic floor dysfunction. Essentially, in each of these instances, the body wants to move something out (either urine or stool) but the muscles are just not relaxing properly; hence, these symptoms occur. Stress can often worsen these symptoms, much like a tension headache.

Secondly, we can show patients alterations in their urination pattern using a simple test called uroflowmetry. This test displays the urine flow pattern graphically. This test can be performed along with special measurements of the pelvic floor muscle activity, a test called electromyography. Very frequently, we see that the urine flow increases and decreases in speed based upon inappropriate muscle activity in the pelvis.

On physical examination, we often find painful, uncomfortable *trigger* points in the muscles, themselves.. With all of this information, patients usually realize that something is amiss. Finally, patients ultimately see that therapy dedicated to pelvic floor relaxation really helps....So, I rarely

have a patient that walks out the door who isn't a "believer."

Jill Osborne - Is pelvic floor rehabilitation a short or long-term therapy??

Dr. Moldwin – I feel that pelvic floor dysfunction is akin to having a bad back. Some people get a little back strain and it goes away and they don't need physical therapy. Other patients may be completely debilitated and need long term, chronic therapy. So there is a wide spectrum of severity and patient need.

Jill Osborne - What therapies have you found to be successful for someone with symptoms associated with the bladder rather than the PFD??

Dr. Moldwin - The very simplest of therapies is diet modification. We just finished a research study this year which supports the notion that diet can cause bladder irritation and pain. Thus, learning to avoid those trigger foods is important.

With respect to treatments, the big three that I still use a great deal of are Elmiron, tricyclic antidepressants and hydroxyzine, I tend to use the hydroxyzine as the last agent in that group many because the tricyclics already have some have antihistaminic properties.

There was a recent study in Germany a double blind placebo controlled study was recently performed and published in the Journal of Urology that clearly demonstrated that amitriptyline (Elavil) was beneficial in reducing IC symptoms. The good part is that this medication can help patients sleep, reduce their nighttime voids, decrease their pain levels and even decrease problems associated with allergic phenomenon.

Unfortunately, the tricyclic antidepressants have their downsides, which is why not everyone can tolerate this medication. Patients can develop constipation, dry mouth, dry eyes, palpitations, and weight gain. It can decrease sex drive and their ability to orgasm. If a patient already has cardiac problems, it needs to be used with some caution perhaps under the consultation of a cardiologist. So, it's not perfect, which is why I sometimes use Pamelor (nortriptyline), a different tricyclic but which often has fewer side effects. Also, nortriptyline comes as a capsule which can be opened. I've had some patients who couldn't tolerate the lowest doses (10 mg) able to tolerate the medication when opening the capsule and just sprinkling a tiny bit onto their food.

Elmiron is a very reasonable medication. It's actually the only FDA approved oral agent for IC. I find that patients with food sensitivities seem to respond the best. I usually combine Elmiron dosing with amitriptyline. Both medications theoretically affect two different abnormalities that are seen in IC, namely bladder surface changes and nerve changes of the bladder wall.

The fact is that not everyone will tolerate all of these meds and it is always nice to be able to offer patients alternatives, keeping in mind that most are not FDA approved specifically for IC.

Anti-seizure medications may improve patients' symptoms. A common medication that has been used is the antiseizure agent, Neurontin (gabapentin). The difficulty with this medication centers upon fatigue. Another antiseizure agent that I am personally having a great deal of success with is Lyrica (pregabalin). I find it to be easier to dose with less associated fatigue. Another medication that has been found useful for pain management includes the SNRI, Effexor ([venlafaxine](#)). The newest SNRI that has been helpful for pain has been Cymbalta (duloxetine). Unfortunately, Cymbalta can slow down the urine stream; therefore it should be supervised closely. I suspect that many more medications in this class will be arriving within the next few years.

The audience should also understand that the prevalence of IC seems to be increasing, most likely due to more patient and clinician awareness. Many pharmaceutical companies are becoming interested in the development of medications for this condition. I can tell you that I've

been consulting with several companies who are developing intravesical (medications instilled directly into the bladder) and completely new oral therapies for this condition.

Jill Osborne - What are your thoughts on cyclosporine as a possible therapy for IC?

Dr. Moldwin - I think that it has potential based upon some of the known pathologies of IC. There is some data to support the use of other immunosuppressants, such as prednisone, in IC. But my biggest concern are the complications that can arise from them. In the case of cyclosporine, the biggest concern is kidney malfunction. So, I believe that even if it does show some efficacy one would have to carefully weigh the risks and benefits of that therapy.

Jill Osborne - AUA had yet another study on hyperbaric oxygen and IC? Your thoughts?

Dr. Moldwin - A limited study was performed in Germany and was presented at last year's American Urological Association annual meeting. It showed that patients who received hyperbaric oxygen had some improvement in their symptoms. They underwent 30 sessions, 90 minutes each time and unfortunately, although there was improvement in some patients, the improvement in those patients was typically very mild. However, the nice part was that if improvement did occur, it usually lasted for a long duration (6-9 months).

I wonder whether subpopulations of IC patients, particularly those with Hunner's ulcer disease (IC with visible inflammation of the bladder wall) and patients who suffer from Raynaud's phenomenon (Raynaud's phenomenon is a condition that affects the blood vessels in the extremities—generally, the fingers and toes. It is characterized by episodic attacks, called vasospastic attacks, in which the blood vessels in the fingers and toes constrict, usually in response to cold temperatures and/or emotional stress.) might have a better chance of responding favorably to this therapy.

Jill Osborne - what therapies have been found to be the most successful with patients who have Hunner's Ulcers?

Dr. Moldwin - I find that the most successful therapy is surgical. Patients with Hunner's Ulcers which we treat (burn) with either a laser or an electrical cautery generally do extremely well as a group, providing that their ulcers are well defined and relatively small. The key is a deep fulguration (burning), since the specific regions of inflammation tend to be very deep seated and can go through the full thickness of the bladder wall.

Patients often experience many months of no pain whatsoever but, unfortunately, the ulcers usually return proving to me that this still is a medical condition that needs to be managed with not only a surgical approach but also with all the other facilities that we have available. For example, most of my patients with Hunner's Ulcers will be on medical therapy, Elmiron, Elavil, and any other medications that might help their general discomfort.

We will often also treat these patients with intravesical therapy. The most common that we have been using has been "anesthetic cocktails" (aka rescue instillations) which is comprised of a short AND long term anesthetic (marcaine and lidocaine jelly) along with heparin, an antibiotic (usually gentamycin), and a steroid (triamcinolone). Patients can instill these themselves or we can do this in the office setting. The frequency of use depends upon the clinical situation.

If someone comes into my office with diffuse Hunner's Ulcers, I won't take them into surgery first. I'll use the rescue instillations to help reduce that inflammation and then possibly perform the surgery afterwards. Obviously, if the patient is feeling well after the intravesical therapy, there's no reason to do the surgery. 70 to 80% of IC patients will have a greater than 50% decline in symptoms when we instill the cocktail and over 90% of IC patients with Hunner's Ulcers will have a positive result.

We have used this therapy to help diagnose IC as well.

Jill Osborne - Does anyone know what causes Hunner's Ulcers?

Dr. Moldwin - No, we don't know however, anecdotally I can tell you that many patients who have them have significant allergies. I have one patient that is allergic to every tree in the north east and that is precisely why I tend to treat these patients with higher doses of antihistamines.

Jill Osborne - Can you explain the use of liposomes in IC treatment?

Dr. Moldwin - Liposomes are essentially fat molecules around a center that may be as simple as water or more complex, like a drug. A recent study that was performed at the Univ. of PA showed that one could calm an irritated bladder down by placing a liposome solution into that inflamed bladder. This study was performed in rats but it does suggest that this might be a reasonable therapy, ultimately, for human use.

Jill Osborne – Your thoughts on RTX and BCG???

Dr. Moldwin - I was never a big fan of BCG because it can cause inflammation. It's one of those therapies that may be able to help a patient now, but I don't know if there are negative consequences 10, 20, 30 years from now. That's why I believe in keeping therapies as simple as possible. RTX (resiniferatoxin), which is a very hot chemical in the hot pepper family, just didn't produce the benefit that we were all hoping for. I have a feeling that we might see better results with some changes in the doses and timing of the doses, but I don't expect that medication to be evaluated again in the near future.

Jill Osborne - Do you have any comments about Cystistat or Uracyst, bladder coatings used in Canada and Europe??

Dr. Moldwin - I believe that any medication that has the ability to coat or augment the bladder surface might be beneficial. This is the concept of placing heparin in the bladder as well as Elmiron. Cystistat theoretically works as a bladder coating agent. Studies in the US did not demonstrate efficacy of this agent, but most clinicians who see IC patients have seen patients respond favorably. Could it be placebo effect?... perhaps. On the other hand, I always worry that medications that directly affect the bladder, like cystistat, may not do well in clinical trials because much of any given patient's pain may be coming from the pelvic floor or other sources. When the pain doesn't go away in an impressive way, we assume that the medication isn't doing a good job for the bladder when that may not be true at all.

Jill Osborne - Do you see any complications with the long term use of DMSO?

Dr. Moldwin - I don't have any experience using this long term. I think it would be prudent to have periodic blood work performed, i.e. complete blood count, liver function, electrolytes, kidney function, etc. A concern has been raised about the development of cataracts. I recommend yearly ophthalmologic exams, but have never seen a patient develop this problem.

Jill Osborne – Do you suggest hormonal therapy or the use of birth control pills?

Dr. Moldwin - I believe that most female IC patients have some relationship of their symptoms to their menstrual cycle. In patients that the cycle has a profound impact upon their symptoms, I refer them to their gynecologist to consider placing them on BCPs, changing their BCPs or even to consider BCPs that limit the number of menstrual cycles per year.

Jill Osborne - Do you believe that IC is an autoimmune disease?

Dr. Moldwin - The last studies that suggested this were performed over twenty years ago when they looked for specific bladder auto-antibodies. There was some evidence that this was occurring but I'm not certain that this is the scenario for every IC patient. IC may be a whole host of different diseases that have common symptom complex. That may be why not every single patient responds to the identical therapy. I hope that, in the future, we'll be able to distinguish one patient group from another patient group.

Jill Osborne - What do you think is the most promising line of research currently under study?

Dr. Moldwin - One of the most encouraging and potentially helpful findings is that of increased levels of APF (antiproliferative factor) in the urine of most IC patients. We've been waiting for many years for some commercial testing to be developed and we're hoping that this comes to fruition within the next two to three years.

Jill Osborne - What would you recommend for immediate pain relief for someone suffering from an IC flare up?

Dr. Moldwin - Well, it depends upon the cause of the flare. When there is a flare and there is burning, you still have to go back to the urology basics. This happened today... a patient was quite upset because she thought she was having an IC flare but it turned out to be a UTI. Is it a flare, a UTI or is it because of a terrible pelvic floor spasm due to sex or stress?

Ultimately, if it's just a bladder having a problem, I often suggest using vicodin or tramadol to control pain. For other patients, Pyridium might be helpful. Some patients may come into the office for an anesthetic cocktail (rescue solution) that can often stop the flare in its tracks. .

Jill Osborne - Many patients struggle with quality of sleep or nighttime frequency. What can suggest that would help them get a better nights' sleep?

Dr. Moldwin - First off, evaluation is again important. Important questions which may make a difference in your care include: are you just a bad sleeper (well known to be a big problem in patients who have co-existing fibromyalgia)? Do wake up because of bladder pressure or pain? Are these large or small volumes that you void at night? Do you go right back to sleep or do you stay up until the next void? Are you taking medications or foods that can stimulate voiding before you sleep (diuretic/caffeine)? As you can imagine, the answers to these questions might prompt different possible helpful therapies that could run from dietary changes to fluid intake or medication changes to sleeping pills.

If it is related to the bladder, I think it's good to use the two birds with one stone philosophy, that is to take care of the IC and sleeping issues using the same therapy. The typical medications used are the tri-cyclic antidepressants and/or the antihistamines, such as hydroxyzine.

Other medications that I've mentioned previously may also have the side effect of fatigue. We can use that fatigue to our advantage when it comes to sleeping problems by simply taking these meds at night. Patients should understand that they can have a "hangover" effect the next morning and that the best way to manage that specific problem is by dosage adjustment or taking the medication earlier in the evening.

Jill Osborne - Do you have a specific plan for men with IC?

Dr. Moldwin - I don't treat men with IC differently than I treat women with IC. Unfortunately, men often go through a long misdiagnosis process, including the use of multiple antibiotics and therapies directed towards prostatitis. Ultimately, I tend to treat each patient the same, including workup, evaluation, etc.

One thing that I have noted in with men with IC is that if they have pelvic floor problems they can suffer tremendously.

Jill Osborne - Do you have any tips for making catheterizations more comfortable for those with sensitive urethras?

Dr. Moldwin - Tip #1 - Like sex, you need lots of lubrication. I am extremely liberal with lubrication and the use of an anesthetic jelly. There are some studies that show no difference in discomfort between regular jelly and an anesthetic jelly. All I can say is that if you're going to catheterize me, please use the anesthetic!

Tip #2 - The most difficult part of the catheterization is where it passes through the external sphincter. It is very easy for a doctor to say "just relax." It's not so easy to actually do that, however, if one really focuses and does some deep breathing and a bit of meditation through that area, it can be done with the least amount of discomfort possible. The tendency is to tighten up when the catheter passes through that region. By doing breathing techniques, like those used with Lamaze, the discomfort can clearly be minimized.

Tip #3 - Is the size of the catheter. I used to believe that there was no specific difference in tolerance between sizes but, now, I fully believe that the smaller diameter catheters pass with much less discomfort. The downside in a man is that passing a small catheter through the urethra is that there must be some stiffness for advancement. Smaller catheters are floppier. My suggestion, in general, is the use of a ten French catheter.

Jill Osborne - Do patients really have to take Elmiron for the rest of their lives??

Dr. Moldwin - I don't think that's necessarily true. I am a very big proponent of experimentation. I believe that if a patient is stable on a medication for a reasonable length of time, perhaps one to two years, then it would be reasonable to decrease or discontinue the medication as a trial. In the case of a medication such as Elavil, a relatively rapid taper and ultimate discontinuance can occur. If symptoms were to recur they may do so anywhere from one to three weeks later. If symptoms do return, the medication can be started again. I have never seen an instance where a patient did not go back to their improved state.

Elmiron, as you know, can take three to six months to become effective and, therefore, when I elect to reduce or discontinue this medication, I will usually be more hesitant. In most cases, I will recommend that patients decrease their dose by one capsule per month. If that patient has a worsening of symptoms with this gradual reduction, I've found it much easier to get them back to where they were before. Of course, that's just my anecdotal experience.

Jill Osborne - Do you see IC occurring in different ethnicities??

Dr. Moldwin Yes. I think that our biggest gap when trying to understand the demographics of IC relates to socioeconomic. Like many other illnesses, IC is underrepresented in lower socioeconomic groups probably, in part, because they don't have adequate access to health care services.

Jill Osborne – What are your thoughts on the use of BOTOX??

Dr. Moldwin - We have used BOTOX as a treatment for overactive bladder with injections into the bladder wall and have had extremely encouraging results. The question is whether injections of BOTOX into the bladder wall can improve the symptoms of patients with IC. BOTOX not only relaxes muscle but also seems to disrupt the transmission of pain in the nerves when injected into the base of the bladder.

However, there are still some concerns. My biggest concern is that BOTOX will decrease the

bladders ability to contract. Any patients with IC that receive BOTOX would have to understand that there is a slight possibility that the bladder wouldn't be able to empty properly. The patient might need to catheterize, at least temporarily, to empty the bladder completely.

Jill Osborne - Can acupuncture be helpful??

Dr. Moldwin - I've found acupuncture to be moderately helpful for IC patients. Fortunately, this is very "operator dependent" technique and I've noted that sending ten patients to ten different acupuncturists, they will have ten different results with different needle placements, etc.

Jill Osborne - One last question on Chinese herbs. There is an acupuncturist on the West coast who is treating IC patients with Chinese herbs, yet refuses to tell the patients what herbs are being used? Your thoughts on this?

Dr. Moldwin - I would not use that practitioner. It makes no sense to me why anyone would ingest any unknown agent on the advice of anyone. It's preposterous. Why would you take any medication or food that you have no idea what the ingredients are? I would have to wager that if their doctor gave them a pill without any information, it would be very unlikely that they would take it.

Jill Osborne - Thank you for your time tonight! Thank you so much for you time and wisdom tonight!