Amy Lightner: What's next for IBD care—Insights from a surgeon-scientist

Lauren Fish (00:08):

This is Science Changing Life, and I'm your host Lauren Fish. Inflammatory bowel disease, commonly known as IBD, is on the rise across the globe. Despite decades of research, its exact causes still remain elusive. In the US alone, an estimated 2.4 to 3.1 million people are currently living with IBD. These patients need answers, better treatment options, and renewed hope. Today we're joined by colorectal surgeon and Scripps Research Professor Dr. Amy Lightner, where we'll explore why IBD is so difficult to treat and touch on other conditions in her area of expertise. We'll talk about how new science may finally turn the tide here, but we first started at the beginning of Amy's journey, her college years where her path toward medicine and science first emerged.

Amy Lightner (00:51):

I was actually really interested in writing. I went to college thinking that maybe I would be an English major and go into writing and maybe be a professor at a liberal arts school or something like that. And I was volunteering at the Children's Hospital up at Stanford. And on Sundays they had this bedside reading program for kids in the hospital. And so we'd go on Sunday for a few hours and we'd read to them or we'd play cards with them, play games with them. And it was a great program. And there was a cardiac surgeon that kept making his rounds on the weekend. And so he was on the floor and he would come by and round on the patients and he knew that I was an undergraduate student at Stanford. And we kind of got to talking at one point and he said, Hey, do you want to come shadow me in the OR sometime be a good experience.

(01:31):

You could see what it's like to be in the operating room and see what these kids go through so that when you're coming and reading to them and spending time with them, you kind of know what their experience has been. I said, sure, that'd be fun. It'd be great to go to the or. And so went with him once and then it became multiple times and kept going back to the operating room. And I was just fascinated. And that was the coolest thing that I had seen, that I got to be in there with this cardiac surgeon who was helping these little kids and then get to see them after their surgery and just thought the experience was amazing and felt like, wow, look what this person is doing for these kids and for their life and for their families, and what an impact he got to make. And so then I switched my major in human biology and went down the path of going into medicine,

Lauren Fish (02:17):

Quite the change. I can't believe that you were able to enter into the OR. That's amazing.

Amy Lightner (02:22):

As a student, you can be an observer. And so he allowed me to come into the operating room,

Lauren Fish (02:28):
You get on, I guess they probably have a lot of

Amy Lightner (02:30):
Pre-med students that would hopefully get that opportunity.

Lauren Fish (02:32):
That's so crazy. Was that your freshman year then? Because,

Amy Lightner (02:35):
So that was my freshman year toward the end of my freshman year. And I hadn't really been exposed before. I didn't have anyone in my family that was in medicine,

(02:43):
And so I just hadn't had that experience. And then that was the end of my freshman year. And so my sophomore year I started on the human biology tract. So we had this core program we had to take and then we had to pick an area of focus, and then it was encouraged. We do some research. So actually through that cardiac, I met an interventional cardiologist who was a professor on campus and he was doing some research that was looking at kids after a fontan operation, which is a big cardiac reconstructive surgery. And we were using this open MR where they had built a bike actually to ride and then look at under exercise what happened with different flow pulmonary arterial flow after a font operation. So after my sophomore year, I stayed and did a research project with him. And so really that initial experience of shadowing him and then him connecting me to research on the undergrad campus really changed my entire trajectory.

Lauren Fish (03:36):
Knew you wanted to do both. I can imagine too. Well, the two inform each other so much. I can imagine in the clinic you become insulated from all of the work. That's kind of more early stage, what's really at the forefront. So cool to be able to match both of those. So what led you into the colorectal space? Started out more cardiac, what led you down that path?

Amy Lightner (03:57):
So as an undergraduate, I got exposed to medicine in general and research in general and loved it. And even though I had shadowed in the operating room, I didn't really necessarily think I would be a surgeon per se. I hadn't preconceived that idea. And I went to medical school. And then in medical school I met a colorectal surgeon who I really liked and looked up to and he was really a mentor and he had some research projects that he engaged me in early on. So I worked with him a lot and kind of did extra time with him in the operating room and just really liked his patient population. So became much more interested in surgery. And then I tried to a couple other things because I feel like seeing the surgery residents, I went, oh my gosh, this is a really hard lifestyle to try to manage. Maybe won't go exactly

Lauren Fish (04:42):
How many years is that residency? Seven years? Oh my God.

Amy Lightner (04:45):

See, have seven years of residency and then a fellowship afterwards. So I really tried to embrace some of the other medical specialties thinking that maybe surgery would be a little bit too busy to manage surgery, especially if I was going to be doing research. But I kept going back to the operat room. I loved it. That's love. The idea started of fixing things started and getting to use your hands and see a patient that has an issue and you get to actually really make a dramatic change for them and for their family and their life, and that is very rewarding. And so I just loved being in the operating room and just seeing patients before and explaining what they were going to have done and getting that trust. It's a very unique relationship with the patient when you're going to be operating on them and then being able to see them afterwards. So I ended up going into surgery because I just couldn't stay away.

(05:32):

And then in residency, I had additional mentors that were really in the inflammatory bowel disease space and colorectal surgery space and just really liked the medical part of it because inflammatory bowel disease, we still don't know how to treat it very well. So there's a medical aspect to it, a research aspect to it, a young patient demographic, an older patient demographic. Technically when we're operating, there's a lot of variability in what we do. So there's a lot of just challenges on a day-to-day basis that we get to learn every day. And so I liked all those aspects,

Lauren Fish (06:01):

All the different aspects.

Amy Lightner (06:02):

The mentorship, I think it really comes back to mentorship. It's who you meet along the way, and I think people that you gravitate toward.

Lauren Fish (06:09):

Yeah, it's such, it takes all of your time. So I can imagine having the people that can support and answer questions and kind of be there for you through that journey is super important. And I'm sure too, the IBD space has probably just changed pretty dramatically since you've been within it because I feel like in the last, I don't know, you would know better than I would, but in the last decade, two decades, it's really just become such a pervasive

Amy Lightner (06:33):

Issue. We're now up to one in a hundred in the United States with IBD, so 1% of the patient population. And we think that Canada will be there by 2030, probably the western world in general. But globally, we're seeing increase prevalence everywhere. And we're seeing countries that had never had a diagnosis of IBD now seeing this patient population. So some of it may be awareness, increased diagnostics, but there clearly is an increased disease as well and disease activity. And I don't think we have a good understanding as to why.

Lauren Fish (07:04):

But

Amy Lightner (07:05):

This is becoming more and more common. There's certainly in the gastroenterology world, there's more fellowships, there's more need for it, there's more interest in going into the field. On the surgical side, we're seeing more patients. And so it's a growing field because there

continues to be little understanding about what actually causes this disease. And we're still looking for medications and there is more and more medications that are being approved. And so the field is sort of exploding in terms of both the medical aspect and the surgical care too,

Lauren Fish (07:32):

And just the need. And that's where being on both the clinical side, the surgery side, and the research side is so important. If there's some environmental factor that's probably contributing to this. So we need the emerging research to hopefully be able to pinpoint what's kind of causing that. Have there been any early discoveries? I remember reading recently that for colon cancer, it was the bacteria that they think was causing maybe some of the early incidents. So have there been any other interesting

Amy Lightner (08:04):

Discoveries? We still have not made any true discoveries as to the underlying etiology of the disease. We've tried to look into genetics, we've tried looking at microbiome, we've tried looking at different animal models, different human organoid models, but we still really don't have a fundamental understanding as to what is the instigating event. It could be something viral that then predisposes someone down the line to developing IBD, but we have not yet figured that out.

Lauren Fish (08:30):

Yeah. So many question marks. So what does a typical day for you look like? So how much time are you able to split between the clinic and the research bench because you do so much translational work at Caliber, our drug discovery arm. So yeah, what is, or a typical week maybe if whatever you can fit in that.

Amy Lightner (08:50):

Yeah, so technically I'm 50 50 on paper. So Monday I operate, so Monday I'm in the OR all day. And then Tuesday and Wednesday I am in the clinic seeing patients. And Thursday and Friday are my research days. So after I operate on Monday in the mornings, I'm always in the hospital rounding. We need to see our patients after we've operated on them, and then I usually will head over to the lab or to clinic. And yeah, it's actually, it's fantastic. It's a really good schedule. The challenge becomes, the clinical really takes priority when patients are sick. So there may be times that we're in the lab or that we're working on a grant and you get a call that you need to see a patient or you need to operate on someone, and that can't always wait different levels of emergencies. So that becomes a challenge in terms of balancing time. That definitely makes sense.

Lauren Fish (09:37):

But hopefully you have a robust enough lab too where they can, they know what they're working on and kind of just carry on while you have. Yeah, we have fantastic

Amy Lightner (09:46):

People in the lab.

Lauren Fish (09:47):

So in the lab then you're investigating samples that you collect in surgery, and then you're able to understand the underlying physiology of what's going on. Can you tell me a little bit about that process?

Amy Lightner (09:59):

Yeah, so we're trying to really come up with new therapeutics for IBD, but also understand the disease better. And our animal models we're really limited because again, going back to we don't really understand what causes IBD. So the animal models that we used most often are DSS colitis, for example, or TMBS, and it's really a toxin, so it's not really representative of IBD. So we're trying to develop a more representative model of IBD when we do drug development and try to understand this disease. So we collect tissue both from healthy subjects through a partnership with life share, which is our organ procurement organization. So if there is an organ donor who maybe has their kidneys allocated for clinical use or their liver allocated for clinical use, would it ever is not allocated for clinical use? Often intestine is not.

Lauren Fish (10:49):

We

Amy Lightner (10:49):

Can retrieve that for the lab for research purposes if that patient was consented for research. So we get healthy tissue in that way. And then when I do surgery on Crohn's patients or ulcerative colitis patients, we can consent them for use of tissue in the lab to better understand their disease. And so in the lab, we take those tissues and we create organoids, which are just 3D representation at a cellular level in a dish of what the tissue is. And then we can use those organoids to study the disease and study different treatments that might be used to treat that disease.

Lauren Fish (11:23):

And yeah, really just kind of brings that translational model full circle.

Amy Lightner (11:27):

Yeah.

Lauren Fish (11:28):

And are we able to talk about the phase two trial that's coming up?

Amy Lightner (11:31):

Yeah, absolutely.

Lauren Fish (11:32):

So yeah, I know that there's a phase two trial coming up that Caliber is conducting the first phase two that we're able to do. So could you go into that a little bit more as well?

Amy Lightner (11:40):

Yeah, we're very excited about this. So Caliber has an asset that they've been working on a very long time, long before I got here, CLF oh six five, which is a long-acting GLP two, so a stapled peptide, which makes the half-life much longer than the previous GLP twos.

(11:55):
And they had done a lot of preclinical work largely in IBD model. So again, the DSS colitis model, and it looks as though this GLP two restores barrier function, which is very important in IBD because there's a breakdown in the mucosal lining a barrier. And so GLP two really can regenerate that. So it's really a regenerative therapeutic, and there's an anti-inflammatory component as well. And so we did the preclinical work and then Caliber ran a healthy volunteer, a phase one study, and about 106 subjects looking at safety and different dosing to come up with optimal dose. So very safe compound, very few adverse events not related to the compound itself. And so we came up with optimal dosing and the safety profile. And so now we are ready to move into phase two trial.

Lauren Fish (12:39):
So exciting.

Amy Lightner (12:40):
And so we're going to be studying this compound in patients with pouchitis. So patients with ulcerative colitis, they may undergo a surgery where we remove the whole colon and the rectum, and we reconstruct them with an ileal pouch. So the small intestine, that last part of the small intestine, we make this J pouch, which acts as a reservoir for them, and it bring that down, attach it to the anus so that patients can have continence in the way that you and I would, and they can get inflammation in that pouch that we make, which is kind of like an IBD phenotype and behaves like an IBD phenotype. And we don't have good treatment options for chronic pouchitis. And so we are studying CLF oh six five in chronic pouchitis. So amazing.

Lauren Fish (13:23):
Actually, one of my good friends had that surgery, how you're familiar. Yeah, no, I'm very familiar. I didn't even know that surgery existed before she had to get it, I think when she was 20 years old. So yeah. Oh my God, that's so cool. So that is hopefully kicking off in September

Amy Lightner (13:38):
Timeframe, right? So the fall, we are hoping to have first

Lauren Fish (13:40):
Patient in insane, and this is part of caliber's overarching regenerative pipeline where it's really focused at not just kind of halting the disease, but hopefully regenerating some of that tissue that is damaged.

Amy Lightner (13:52):
Exactly.

Lauren Fish (13:53):
And then, so a very busy time for you, but you also have a conference coming up in

Amy Lightner (13:57):
September. You're very excited

Lauren Fish (13:59):

About this. So yeah, what's happening there?

Amy Lightner (14:01):

Yes. So IBD cutting edge. So the idea with this conference is a lot of our meetings are really clinical. So we have scientific meetings that generate activity from basic scientists and interest from basic scientists, and then we have clinical meetings where we're really talking about clinical practice, but we have very few meetings where we create a story arc where we can go from the basic science and translational science into the clinical trials and then into how we manage patients. So the idea around this meeting was to bring everyone into the room together, so all the way from basic science to clinicians to understand this disease better. So the meeting will start out with translational science, basic science, what are we doing in IBD, what's at the forefront right now? And then it will move into what are our challenges with clinical trials, both from the GI standpoint and the surgery standpoint is what are we learning from the trials? How are we applying these clinical trials to practice? And then it will move into pearls of clinical practice and multidisciplinary care. And so the goal is to be able to have all those people in the room together so that we can crosstalk between the science and the clinical practice and understand where are the questions in clinical practice, what do we really need to work on so that can drive the scientific questions and vice versa.

(15:14):

So very excited. Can everyone in one room

Lauren Fish (15:15):

Together? That's so

Amy Lightner (15:16):

Cool. It's like the

Lauren Fish (15:16):

Whole Scripps model, but in a conference setting.

Amy Lightner (15:20):

So we have joined forces with Scripps Clinic and UCSD, and then we got sponsorship from echo, which is the European Crohn's and Colitis organization. So this is the first actually US meeting that is sponsored PET Echo. Wow. So very excited about that. The largest organization for IBD

Lauren Fish (15:36):

Globally.

Amy Lightner (15:37):

And then we have sponsorship from the Crohn's and Colitis Foundation as well. And so Gary kti, she's a gastroenterologist at Scripps Clinic, and Sid Zing is a gastroenterologist at UCSD, have been helping to co-chair this meeting. And so it's been a very collaborative effort. It's been a lot of fun. Its so exciting. Again, I don't know how you managed

Lauren Fish (15:55):

To, it's this all in a one week span in addition to clinic and then research and then also, yeah, event planning. But yeah, hopefully, like you were saying, that's the kind of dialogue that needs to happen to really kind of uncover what's happening here and expedite

Amy Lightner (16:11):

The research forward and just prioritize where do we move next. I mean, there's a lot of unanswered questions, but I think when the science and clinical worlds don't talk to one another, sometimes science is doing something really interesting, but perhaps it's not really the unmet need clinically and vice versa. The clinicians may not really be understanding the basic science to understand how to ask the questions. And so I think creating that dialogue and that crosstalk of the two worlds will be hopefully very, definitely very good

Lauren Fish (16:37):

Meeting. What would you say

Amy Lightner (16:39):

The biggest misconceptions around IBDR? That's tricky. There's a lot of misconceptions. I think one thing that faces IBD patients is I feel like they feel very alone oftentimes in their disease. So trying to create community for them so that they can reach out to other patients to understand, because some of that aloneness, I think comes from, they may be walking out in the world. We may know patients or may know people who have IBD and to someone else, they wouldn't know it. Their appearance is good, they're at work, they're doing whatever it is that they're doing. And you would never know the chronicity of the disease that they have and what they're facing every single day.

Lauren Fish (17:18):

Just the extreme pain, the severe toll it takes on your

Amy Lightner (17:22):

Quality of life. Yes, quality of life, the pain, the fatigue, how it affects just every aspect of their life. And so

Lauren Fish (17:28):

You can socially too, right?

Amy Lightner (17:29):

Socially. Professionally, yeah. Yes. And so it's quiet in some ways. And so I think that that can generate some feeling of aloneness. So I think that maybe there's not always awareness. Some diseases are very visible and you can see them much easier. And so people know that that person is sick, whereas patients with IBD sometimes carry that and have to carry that burden of it.

Lauren Fish (17:52):

And

Amy Lightner (17:52):

So I think that leads to some of the misconceptions as to how much their life is being affected,

Lauren Fish (17:58):

How painful it is. And I can imagine there's probably a historical aspect to that too, where because it hasn't been as diagnosed more readily and people just don't know as much about it. So I can see that contributing to it as well. But hopefully with so much efforts being put into this, hopefully that's the tide to shifting there.

Amy Lightner (18:17):

Exactly.

Lauren Fish (18:18):

Yeah. What would you say is the most rewarding aspect of your

Amy Lightner (18:21):

Work? I love my job. I'm really lucky. I love being back in San Diego where I grew up too. Oh, you grew up here, grew up here. Where did you grow up? Grew here in Coronado. So my whole family is here. Me too.

Lauren Fish (18:33):

No way. Wait, did you go to Coronado High School? I did. My mom is the calculus teacher there. That's been there forever. No way. Yeah, I had her, I'm assuming you have your maiden name, right? Yeah, yeah. Fish. Yeah. Oh my God, I

Amy Lightner (18:52):

Did not make that connection.

Lauren Fish (18:53):

What a small world. Very small

Amy Lightner (18:54):

World. Yeah. So I love being back here. And then I think most rewarding, I feel like being able to do both science and medicine is a really unique position to sit in, especially as a surgeon. I feel like I see these patients that are really sick. You have this unique relationship with them where they really trust you and you're in the operating room, and you can actually feel the disease and really understand how destructive, for example, Crohn's is and what it actually is doing to the tissue. And then you can translate that into the science in terms of what we need to do. So I feel lucky that I get to have these unique relationships and ideally affect in a positive way, the one patient at a time, and they can go back to the lab and think about how can we create something that is going to affect thousands of patients at a time. And so wearing both those hats, I feel like I'm very lucky that I get to be able to do both, and really being able to do both

Lauren Fish (19:50):

And just get energy from it, right? Yes. I mean, I think you would have to be energized by it, just given what you're doing in each area and how much you're doing in each area. But yeah, I can imagine seeing, hopefully the change you're able to impact is so rewarding. That's incredible. What would you say is the most challenging part of your job?

Amy Lightner (20:08):

Challenging is trying to balance. There's never enough hours in the day. So I think it's feeling like you're pulled in different directions, and sometimes it's not always predicted what the day is going to look

Lauren Fish (20:18):

Like. You

Amy Lightner (20:19):

Try to make it as predictable as possible, but sometimes it's not. And so I think it's feeling like you want to be able to devote more time to the science, something really interesting, and you want to develop it further. And then there's the, oh, I'm in the clinic and I want to learn this new surgical technique, and I want to be really good at it, so I need to do it over and over again. And so I think it's just the juggling, maximizing

Lauren Fish (20:38):

Every hour that you can. Luckily here, hopefully everything is so close, too close that you can kind of jump between and next door run across the street and Okay. Yes. That hopefully makes it easier too. Yeah, where the spacing really makes a difference.

Amy Lightner (20:52):

Yes,

Lauren Fish (20:52):

Yes. So when you're not juggling everything, what are some of your hobbies and interests outside of the clinic and the lab? Are you still writing? Well, I still

Amy Lightner (21:01):

Write some, but not enough. I do mostly now scientific writing. Yeah, I still really enjoy riding, so I love the water. So I grew up swimming and playing water polo and then played water polo and undergraduate, so I still swim. And the coach that's, I swim with the UCSD Master's group, and he's actually been there since I was in high school.

Lauren Fish (21:20):

Oh my gosh. Fantastic coach.

Amy Lightner (21:22):

He's wonderful. I was created a really fantastic community. Cool. So I really enjoy that. And then I have twins that are 12 years old. Oh my God. So I spend a lot of time with the kids and we have great fun together. So that's where I spend most of my

Lauren Fish (21:35):

Time. Final question that we ask everyone, if you could give a piece of advice or wisdom to an up and coming scientist or surgeon, what would it be and why?

Amy Lightner (21:43):

So I think it's just finding what you really are passionate about, what you really love, because especially in science along the way, there's a lot of failures

(21:51):

And a lot of times things don't work and it can be very frustrating. Well, you spend so much time doing it right, so much time, and then something doesn't work as you expected it to, and you have to pivot. And so I think you have to really love the why of what you're doing, what you're doing. So I think it's just making sure that what you're doing, there's something that really resonates with you that drives kind of the intrinsic motivation, because someone from the outside is not going to be telling you, keep going, keep going. You're doing a great job. So there's just something has to resonate with you that really drives you forward. And so I think finding that thing will be very helpful as you go through along the way, because there's ups and downs in every career. And so I think that carries people forward if they have some kind of personal connection that they're really excited about what they do.

Lauren Fish (22:41):

And that's all for this episode. Many thanks to Dr. Amy Lightner for joining us and sharing her insights into IBD and where the future of treatment could lead. Thanks so much for listening today, and we'll see you next time on Science Changing Life, where listeners come curious and leave informed.