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VOICEOVER:

Welcome to ASA's Central Line, the official podcast series of the American Society of Anesthesiologists, edited by Dr. Adam Striker.

DR. ADAM STRIKER:

Welcome to ASA's Central Line. I'm Adam Striker here with Dr. Miriam Treggiari, Professor and Vice-Chair of Clinical Research in the Department of Anesthesiology at Yale University. Welcome to the show, Dr. Treggiari.

DR. MIRIAM TREGGIARI:

Uh, thank you for having me here today and for the opportunity to share my research work with you. I've also would like to acknowledge of our colleagues in medicine and science in general today for their efforts and dedication during this critical time in our fight against the COVID-19, um, both in the US and worldwide and so I believe in the importance of research now more than ever and I appreciate you taking the time, um, this time.

DR. STRIKER:

Absolutely, well said. I couldn't agree more. We wanted to talk to you today about your research, your career, and importantly about your roles and mentor to others. We're looking forward to learning about life as a physician-scientist. So, to kick things off, let's tell her listeners a little more about you and your work. Can you tell us what you're investigating now?

DR. TREGGIARI:

Um, briefly, about myself, I'm originally from Italy and I trained in anesthesiology and critical care medicine in Geneva, Switzerland. And then I trained in epidemiology at the University of Washington in Seattle. Uh, I stayed at University of Washington after, after completing my training and joined the faculty, um, in the early 2000's under the direction

of Dr. Fred Cheney, a long-standing Chair of Anesthesia at the time, and there I started developing my first research program. And later, I was recruited to Portland in Oregon under the leadership of Dr. Jeffrey Kirsch an absolutely outstanding (sic) Chair, and then more recently I joined the faculty at Yale University under the direction of another outstanding leader, Dr. Roberta Hines. And here my goal is to continue and strengthen the clinical research program at Yale.

So, um, my research focus is primarily on perioperative outcomes. Currently, we are conducting two large clinical trials, um, that both involve critically ill patients. So the first study is a multicenter trial at 10 sites in the country and investigates resuscitation end points in a patient with acute spinal cord injury. The rationale for this trial is that the guidelines regarding blood pressure management are based on very weak evidence and currently these guidelines recommend blood pressure augmentation to higher targets than those that are conventionally used for ICU patients. So in this trial, we want to determine if an augmented blood pressure target is superior to a conventional blood pressure target that would be used in the general ICU population. And we want to know if the augmented target improves long-term neurological outcomes, and specifically functional recovery. This, um, project is funded by the Department of Defense, under a particular program that is called Congressionally Directed Medicare Research Program.

The other study is a single-center trial but it's still a very large trial they will enroll over a thousand patients and it's a complex study because it's conducted under exception from informed consent. It's an ethics study, and so this is a specific situation, um, of emergency research where, uh, there's a narrow therapeutic window to start an intervention, like could be an emergency intubation of a cardiac arrest. So there is no time to ask for consent. In this situation, the FDA allows the study procedures to begin before obtaining informed consent. However, there are several, several rigorous regulatory requirements and that need to be met to conduct this type of research.

So, in this trial specifically, we are randomly assigning participants to, um, be intubated with different endotracheal tubes, um, during emergency intubation, either in the emergency department or in the ICU or in the hospital, and they will receive two different types of endotracheal tubes. One is a standard tube, and one is a special tube that is designed to prevent ventilator-associated pneumonia. And so the specifics, are um, that it, it has a polyurethane cath and a side port for aspirational (sic) secretions. So, we'll monitor the patients in the ICU for ventilator-associated events, and then we follow the patients, six months after the intervention to determine, um, if their outcomes are different. Um, specifically we're doing an airway evaluation and then we're recording and documenting the quality of life and cognitive function in these patients. So this trial is founded by the NIH, um, and specifically by the National Heart Lung and Blood Institute, so NHLBI.

DR. STRIKER:

That's fascinating and two studies that I know are quite valuable as, as uh, contributions to the field. Things, um, things that we all do in all our practices each and every day so, um, excited to see how those turn out. But I'm curious, why did you pursue perioperative research, specifically?

DR. TREGGIARI:

Thank you for asking this question, Dr. Striker. So my training is in anesthesiology and critical care medicine and therefore perioperative medicine, uh, and perioperative research aligns with my interest and with my expertise, and ultimately my research efforts are about improving patient care, uh, improving patient outcomes in the perioperative period, and contributing. My intent is to contribute with something that makes a real difference in the care of patients that we treat every day. Um, and therefore, this way, I feel with my, the impact of my research extends well beyond individual patients I can personally see, and so I can achieve a larger goal of improving patient care for many more patients than the ones I can actually can care for.

DR. STRIKER:

When did you know research interested you? For instance, while in medical school were you exposed to the idea of a career in research?

DR. TREGGIARI:

Uh, yes, I, I knew really early in medical school that I was attracted and fascinated by research, and this emerged for me from the understanding that, um, there were many topics where there was not a single answer to certain problems. And so it was often unclear to me, which one would be the best approach that would most benefit the patient and also will protect the patient from harm. And so, um, my first experience and exposure to research as a medical student was, uh, in my last year of medical school. I was an exchange student in Europe and I completed my last year in actually Scotland in Dundee at Ninewells Hospital. And um, and there is where I conducted my first research project, and where I really, um, felt excitement and was really energized about research and discovery. At the time, um, my first mentor was, um, now a good friend, too, Dr. Jim Lange, who was helping me conducting this project and allowing me to, um, present the project in Paris. And then helped me writing the manuscript that was successfully published. And that really helped me, um, getting really excited about, uh, a career in research.

And later, when I was an anesthesia resident, um, I was in, in the equivalent of a scholar program. So I did an extra year during the residency, um, that was dedicated to conduct research work. And so during that time, I really, uh, conducting one of my first studies and I remember this work being heavily criticized by the review worse because of weaknesses in the study design. And so at that point it was still early in my career, I realized that, um, to become a solid researcher, I needed more rigorous training, and that is what really prompt me to later on to, um, to search, uh, for a more formal training, and brought me to University of Washington in Seattle, uh, which had a highly-regarded Institution for, um, for Public Health. And they had excellent faculty, um, for me to receive, um, really strong training. And, uh, and so at University of Washington I earned a Masters in Public Health, and later a PhD in epidemiology, uh, under the direction of my mentor, Noel Weiss um, and I was really fortunate to be able to work with him because he's an excellent methodological thinker and an exceptional mentor.

And so I was able to develop, uh, and learn research methods formally, and I learned how to design study, how to carefully and properly analyze and interpret data, and also, how to become good, skills of technical writing, so how to write grants, how to write manuscripts. And so the, really the training was very rigorous with Dr. Weiss' guidance. And also I was very fortunate to be able to be exposed to outstanding faculty through the Department of Biostatistics there. And it was really, I was really thrilled when I was in a class with Thomas Fleming going about clinical trial design, and for example, learning about the O'Brien-Fleming Stopping Rules for clinical trial, or, um, learning from um, Norm Breslow, um, longitudinal analysis and learning about the Breslow Estimator. So it was really exciting to learn methods from the very people that invented them. And so I was really, you know, fortunate to receive outstanding training and having, you know, these amazing experience.

DR. STRIKER:

What resources have been the most valuable to you in becoming a successful physician scientist?

DR. TREGGIARI:

Uh, so I would say that my immediate supervisor has been by far, my greatest resource, along with, you know, a good dose of self-determination. Uh, so my mentors were really invaluable my early career at University of Geneva, and I want to name, Dr. Peter (sic) and (sic). Uh, they really encouraged me to travel to the US to train and strengthen my skills. Uh, subsequently, uh, along my path, I, you know, met Dr. Fred Cheney, Jeff Kirsch, Roberta Hines, who provided me with really that balanced mix of clinical duties and protected time to be able to develop the research program, uh, that I, you know was

working on, and also mentor junior faculty. And so I think for, um, emerging research scientists, it takes hard work, self determination, uh, being resourceful and also, have an inquisitive attitude and lots of dedication to learn new areas in that. And that can take up a lot of nights, weekends and vacation time to achieve.

Um, I do have a few stories about this, but one that I fondly remember when I was a, um, there, I was leaving for a planned vacation to Bali while a grant deadline was looming for my spinal cord injury, um, trial. And so, I had planned on finishing the work from, you know, a room with a view from the villa that we were renting, with actually my initial mentor from Scotland, Dr. Jim Lange and his family. But, on the way there, we were, uh, there was a volcanic eruption in Indonesia, and we were stranded in Singapore airport for a couple days and then later our flight to Bali was diverted to Jakarta. And so as the deadline is fast approaching, I remember finishing the submission after borrowing an adapter from a passenger and standing next to a column with the only plug in the airport. So we were able to submit just in time and while I would have preferred avoiding this stress of this last-minute situation, I was really thrilled when I learned later that the application was funded.

So, I would say that it's important, uh, for research scientist that embark on their careers to prepare to be resilient, and because there are going to be bumps in the road and, uh, unexpected issues and problems, but you should not be discouraged easily from those. And so I have been fortunate to work with very talented people in, in the past and currently and I found even so, I found it even more the exception that a grant is funded on the first submission, or a manuscript is accepted without rejection of needing revision. And so, while it's really tough to be rejected, there is a lot of important lesson to learn from the review persons so these are actually great opportunities to improve and become better.

DR. STRIKER:

I used to think that struggling for an outlet on a deadline was mainly only something for journalists. I didn't, I hadn't really thought of for a researcher. I don't think a lot of us appreciate just what kind of pressure you're on when you're trying to submit these things.

DR. TREGGIARI:

Yes, yes, there is definitely a lot of moments, uh, you feel like you're on call all the time when you, when a deadline is getting closer, for sure.

DR. STRIKER:

Well, you know, one thing I am always fascinated with when it comes to any physician, I should say, but especially physician scientists, but mentors, and the role they play in your career path. Um, talk a little bit about, did mentors play a role, and how so in your specific career path?

DR. TREGGIARI:

Oh, definitely, I, I think I can't emphasize more how my mentors have been enormously influential in my career, and I've been incredibly fortunate and really blessed to have and opportunity to learn from truly exceptionally, dedicated, talented and hard-working role models.

Um, I've learned very, very much, uh, and what's important is that they not only taught me about research, but I learned about leadership skills, life lessons and, you know, many other things that go well beyond just the research itself. Um, so initially, at least for my early career, my mentors helped me guide to find resources and opportunity. And I wouldn't, probably never achieved what I have done, without their help and guidance.

Um, I can also, later in my career, I can make, give you other example, for example, a story I recall, also related to a grant deadline. I was working very intensively on, on a grant. The deadline was fast approaching, and I had clinical duties in the OR and so I was busy in there while taking care of patients and I didn't have, really lot of time, to work on the grant. And at the time, you know, Dr. (sic), she was my chair. She came in my room and said, I'll take, I'll take over your cases, so you can focus on your grant and finish it up. And the ground was funded, so, you know, the people like this, um, and the support, and the working as a team, is, is really what makes you successful. And receiving support from others is really very, very important.

So to me, mentors have much more than just colleagues advising me on you know how to advance my career. They really have been lifetime mentors and great friends to date. And so, I do have developed a, a strong relationship with my mentors and consider this to be a very special gift. Um, it's been very enriching personally, and I wish for everyone to have these experiences, as well.

DR. STRIKER:

Absolutely. It's so important, not only to, um, to have mentors, but act as mentors as well. Is there specific advice, uh, that you've taken away from your mentors? Or some degree of wisdom that has been passed on to you that you hold dear?

DR. TREGGIARI:

Uh, yeah, so, this, how, I have lots of stories, but, um, I would say that, um, in early career, um, probably the mentors are more influential, and for me particularly, uh, so my mentors from Switzerland really changed my life. Uh, so they had insisted on the importance of training in the US for example, and they told me, uh, they wanted to keep me on the faculty of University of Geneva when I finished my fellowship, and, uh, and they said, uh, that you know, for you to stay on the faculty so you need to leave, go in the US and learn something that you don't know, or that we didn't taught you, and then bring it back. And they made themselves, as example, like they both trained in the US, on in UCSF and my other mentor in Pittsburgh. And so they really stressed the importance of, uh, having an open mind and all things outside, you know, your narrow vision.

And, so, um, originally I think I was a little naive thinking that I already learned enough, and I had at the time, but thanks to my mentors they convinced me that I needed to broaden my knowledge even more. And so that's what brought me here to the US um, and initially, I had the goal of acquiring knowledge training, return to Geneva two years later. And then, uh, and that was, um, those two years were 20 years ago. And so I ended up staying in the US, for me, um, the rest of my career. So, um, I felt like, um, I wanted to be grateful to my mentor as well. So when I decided to stay in the US, I did try to bring my knowledge back by running my trials in Geneva so others could learn what I had learned.

Um, so I do want to emphasize also that I've been particularly lucky to have had exceptional mentors all along my career. So from the early times in Geneva, but also when I, um, started developing my career in the US, again I mentioned during my PhD training, um, I had this stellar mentor, Dr. Noel Weiss, and I was very fortunate. He, he accepted me as a mentee, and, um, is a person with a great mind from whom I really wanted to learn how to think. And, uh, later in my career, you know, Dr. Jeffrey Kirsch, and Roberta Hines have been really phenomenal mentors, and advisor in many, in many areas for me as well.

DR. STRIKER:

What advice would you give to someone thinking about a career in anesthesia research?

DR. TREGGIARI:

Uh, ok, so my first advise given that we are talking about mentors, is to explore and seek out great mentors, and also, and really establish strong relationships with them. So it's a, it's a relationship that is very important that there needs to be some, um mutual

understanding, um, and interest in the matter of advancing the career of the mentee, and mentee contribute to find some ways to the knowledge and the program of the mentor. But my stronger also advice, on a personal, you know characteristics, is to persevere. I find that that, uh, there are, you know, there is great satisfaction when projects are successful, or you see the impact of your work on practice change and improvement of care, but there are also a lot of tough moments and frustration before you get there. And so it's important to stay focused on the overall objective, uh, don't get discouraged by unexpected challenges, and so it helps to keep an open mind trying to avoid missing the forest for the trees and, and sometimes you'll find that there are many solutions to a single problem.

DR. STRIKER:

Uh, the transition from mentee to mentor, tell us a little bit about your experience with mentoring younger scholars. What kind of advice do you give them? What kind of wisdom do you like to impart?

DR. TREGGIARI:

Uh, sure, of course, and thank you for asking this question. Um, so one advice that I often give to, to my mentees is, um, it goes along the line of perseverance, so one important thing is I always tell them I personally always finish what I started and, um, I make sure that my mentees do that too. I do want them to, if they start embarking on something that, I, uh, bring, you know, their work to the end. Um, so now for me, I enjoy using my knowledge and my experience to get mentees along the path, and trying to, to teach them things to avoid. Especially you know, I don't want younger investigators to repeat errors that I've done in the past. So, um, for junior investigators, I think obtaining initial funding is a challenge you face, because the investigators need to prove themselves and success with early funding, can determine the future career path. So there is an important selection process that takes place at the beginning stages. So, um, I think, um, helping your investigator is where I feel mentorship has the biggest role in the biggest influence on the future career.

Um, so one of the, um there are many mechanisms to, um, advance career or to start in early career, and I wanted to mention, um, the FAER program, which is it, really a strong program to allow early developing clinician-scientist to get started towards, uh, establishing longer-term programs that are more substantial and, and typically federally funded.

DR. STRIKER:

I'm glad you brought FAER up, but before we go any further, can you just clarify for our listeners who may not be as familiar, what FAER is, what it stands for, and what its mission is?

DR. TREGGIARI:

Sure, so FAER is the Foundation for Anesthesia Education and Research. It provides funding opportunities, which are specifically dedicated to members of the anesthesiology community. And so, um, these are crucial mechanisms to support investigators within our own specialty. Um, so FAER support is critical for a wide range of candidates with different level of training, ranging from medical students to junior faculty. And so medical students, uh, for example, don't always know much about anesthesiology because they're exposed to many other specialties during their training, and so this program helps bringing highly interested people into the specialty. So I feel, I feel like it's a great screening mechanism for selecting and directing strong medical students to our specialty.

Uh, so, uh, the program also targets, or helps support residents and fellows to have, uh, protected time or supported time for an extra year to do a, additional research, so like a scholar program. And lastly, junior investigators also can benefit and this is probably, uh, the, the target population, so to speak, that is the most important to target, um, and because obtaining support to launch a research careers challenging in the early stages, especially for anesthesiologists due to the structure and scope of our profession, um, where it's very easy to get distracted and taken away from other priorities.

DR. STRIKER:

Let's talk about grants. Is there anything you wish you would have known before diving into the grant application process? What's your best advice?

DR. TREGGIARI:

Well, one, one piece of wisdom I learned that may be later than I should have, is that it's important to ensure that research goals aligns with the priorities of the funding agency. Um, for example, let's assume that an investigator has a question with a hypothesis to test, and the investigative team believes that the question is important. I think it's also critical to know what the sponsor priorities are. And then when the study questions or goals align with the funding institution priorities, this is really key to success. And so I found, uh, funding to be mostly successful when those uh, priorities are aligned.

Um, and the other advice I have is that, the way you tell a story and present your work really matters. Um, and so the way you present the application need to be clear, linear, precise. So I strongly discourage rushing because it's hard to do high-quality work without giving adequate time. It takes time to plan and design a study, uh, it takes time to try with accuracy. So my recommendation is just, you know, slow down take the times and do it right and just trying to present your work as perfect as it can be.

DR. STRIKER:

Well, let's uh, delve into the specific types of grants that are available through FAER. Can you talk a little bit about those?

DR. TREGGIARI:

Sure, there are several, and I would say ever-expanding opportunity within FAER. And, and so I was start talking about the mentor research grants, because, we, uh these are the ones that uh, are of interest to junior faculty, and these are great opportunities for them, uh, if they want the embark in a research career because, um, they, this mechanism is not only support the research project, but importantly supports that clinical time to work on the project and to learn the skills that would be relevant to their career path. So, uh, in some ways allow the departments to provide that your investigators protected time to work on their projects and, and they are, and skills that they need to develop before their careers.

Uh, and another interesting mechanism is the transition, the transition to Independence Grants and this is really sort of a bridge and fund us for the time between the end of the FAER grants and the achievement of securing of funding from a federal agency. And so if an investigator (sic) completes the FAER as a grant that has been scored but didn't reach the pay line for funding, he can receive this bridge funding and uh, allowing them to perfect their application, you know, collect more primary data or put the application in the position that will be successful for funding.

I also wanted to highlight the fact that FAER is partner with other societies to a larger portfolio and for example, and more, very recently there was a grant deadline for the Anesthesia Patient Safety Foundation for grants oriented toward patient safety. Also FAER is partnered with the National Institute of Health, for example, the Jumpstart program. Also, it's a matching plan that we did with the National Institute of Aging, and then also with the ABA for grants that are more oriented toward education. So the education grants are more focused on education, uh, and also, uh, they also available not just to junior investigators, but also to senior faculty. So uh there is a little bit broader target for, for that particular grant.

And then as we mentioned earlier, there is a research fellowship grants for residents and fellows that can receive an extra year of training in research and being funded for that. And finally, the medical student grants that we also already mentioned, that allows summer research project and all exposure to anesthesia research with (sic) opportunity. And, I had a lot of students over the years, and found that, um, this program is very successful. These students are very highly motivated and in just a few weeks can achieve and complete, um, you know, a self-limited project. So it's a really, really nice program.

DR. STRIKER:

Excellent, well, let's talk little bit about your daily life. What was, uh, the most surprising unexpected thing you learned or found about your day-to-day role that you currently have?

DR. TREGGIARI:

Uh, so I've learned that everything takes longer that, than you expect. So clinical trials take years before you see the results. So there's always challenges, and unanticipated issues as you implement projects. And so again, I, uh, I go back to the concept that it takes, um, perseverance and determination to achieve your goals and it really helps going through challenges by focusing on long-term goals and the important reasons that drive you forward. Um, and again, so it's really important to, um, you know, work by the principal that you need to finish what you started. It's a commitment to yourself. It's a commitment to the funding agency, and it's a commitment to your patients because, you know, this is um, this is the benefit that the patient receives we can, if we can improve care, if we can improve their outcomes. Um, so I think with these objectives in mind, it's easier to overcome any challenges.

DR. STRIKER:

Has being a physician scientist in anesthesiology met your expectations?

DR. TREGGIARI:

Absolutely, uh, so I have been very lucky to have achieved what I dreamt for my career. And I do love what I do. Um, as I mentioned earlier, as a junior resident, I've wrote my first tactical. Um, it was an important study about nitric oxide. This was in the mid 90s where we were describing the effects of exposure in humans of nitric oxide in patients with acute respiratory distress syndrome. And so we knew it was an important study, um, but it, it was, um, I required on a lot of activation before it was published but

eventually it was published in Anesthesiology. Um, and so the process was challenging, uh, and um, again, I realized I could not address some of the concerns because you cannot rescue a poorly designed study after the study's done. And, um so it was an eye opening experience. It makes me understand that I needed to learn how to design a study correctly. And so that's what really pushed me and prompted to pursue more formal study and put me in the current career path.

Uh, and now, I feel like I can pass along my knowledge and my lessons learned to those I mentor. And so also I had the opportunity to use my own skills for the funding and the work I want to do so, there, um, is a lot of investment in the early stages. Um, before everyone starts, um, you know, for me for in particular, I knew I had a goal, and I was clear what I wanted to go. I just needed to find the right way to get there. And so, um, with my mentors are both very lucky to be given the opportunity and now my hope is to be that mentor for my mentees.

DR. STRIKER:

Well, this is been a really great talk. Fascinating to get some insight into your daily life and where you started and what got you interested into your research. But before I let you go, I wonder if there's anything you'd like our listeners to know? Anything we haven't touched on yet?

DR. TREGGIARI:

Uh, yes, I would like to mention a couple of more things. So, um, we spoke about grant and (sic) scientist, but I do want to, um, say that there are several ways to do research. For example, in an academic setting, uh, so not all influential research is funded by large grants, and everyone or every um, single anesthesiologist or clinicians can contribute to advance knowledge in our field. And so, um, smaller project can make big, big contributions and there are many ways to contribute to research and so my message is that I would like to encourage everyone to be part of a research team.

And finally, for my last point, I mentioned earlier that doing the research requires hard work and takes time. I mentioned this not to intimidate, um, you know, younger investigators, but to advise them that, um, when you can see the research areas, it's important to have a passion for it. Um, it's far easier to spend time working on something that inspires, um, than working on something that you're not, you don't have much interested in.

DR. STRIKER:

Well said. That's a great place to leave it. Dr. Treggiari, uh, thank you so much for your time, for your uh, insight, the stories, and I really appreciate you taking the time to talk to us on, um, ASA's Central Line.

DR. TREGGIARI:

It's been my pleasure. Thank you for having me.

DR. STRIKER:

Absolutely, this is Adam Striker and we will see you next time on Central Line. Take care.

(MUSIC)

VOICEOVER:

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