

Announcer: [00:00:03] Welcome to the Science is the Best Medicine podcast with your host, Dr. Abhinav Sharma. Exploring the pressing scientific and healthcare issues of our time.

Dr. Abhinav Sharma: [00:00:12] Peer-reviewed medical journals. They are considered the highest caliber of medical knowledge. Scientists and university professors use these journals to help disseminate their scientific knowledge, but they also use it to advance their own careers. And newspapers mine these journals for interesting scientific stories. But who are the people that actually run these journals? And when we talk about medical journals, what exactly does it mean to be peer reviewed? And in this era of rapid dissemination of data when anyone can put anything online, what does this mean to be running a medical journal? To help us gain a peek behind the curtains is Dr. Joseph Hill, he's a cardiologist at the University of Texas-Southwestern, and the Editor in Chief of one of the most prestigious cardiovascular journals *Circulation*, let's dive in.

Dr. Abhinav Sharma: [00:01:13] So thank you very much for being with us today on Science is the Best Medicine podcast. A couple of questions for you. Would you mind telling us a little bit about the journey that led you to where you are today?

Dr. Joseph Hill: [00:01:23] Sure, well I'm a physician scientist and that means I spend my day to some extent taking care of patients and to some extent doing science, and moving between those two worlds such that my science is driven by and informed by the patient care that I provide and the patients I see inspire me in my science. And to get to the point, I trained as a physician, as a cardiologist, and also trained in parallel as a scientist, and have been doing this in a faculty context for about 20 years or so at a couple of different universities.

Dr. Abhinav Sharma: [00:02:02] And so with regards to your current position as the Editor in Chief of *Circulation*, how exactly did you come about this role? Did you always want to be a medical journal editor? Was it always on your horizon or your radar?

Dr. Joseph Hill: [00:02:16] No it was not. I started off exclusively as a physician scientist which I still do, and progressively have taken on administrative responsibilities, and I have to say that editing a biomedical journal was not on my radar screen until about a couple of years ago or so when a mentor of mine suggested I consider that, and the journal *Circulation*, the previous editor who did a remarkable job was sunsetting his tenure there, and I began to think about how biomedical publishing has evolved over the years, and some of the ways that a novel approach, novel technology, novel infrastructure could have an impact on a global scale in terms of the scope and direction of cardiovascular science. And as I thought about that more and more, I became progressively more and more excited, and energized by that prospect, and that's something that now that I'm doing and have been doing it for some months I'm very, very excited about.

Dr. Abhinav Sharma: [00:03:17] Well, that sounds absolutely fascinating and a bit of a change in terms of the previous work that you've done as a clinician scientist. Now just taking a bit of a step back, what exactly does a medical journal editor do?

Dr. Joseph Hill: [00:03:30] Well, there's sort of two broad categories of things. We receive something in the range of 100 papers a week, and we evaluate them in a complex process that has multiple stages to it, and of the 100 papers we receive we publish about five or six of them which are the best ones, and the process of evaluating science, working with authors to improve their science, to check its veracity, its statistical validity. Those sorts of things are a process that is at once complex, and also uniquely human in that at some level the subjective decision about what is incremental versus what is novel is sometimes not so clear and so it's an interesting process that's involved. The other half of the job is more a one of assessing the landscape of cardiovascular

medicine and biology and deciding what questions would benefit from a perspective from a thought leader. A review article, where is the science going, where are there issues of controversy or debate where the journal could reach out to thought leaders and commission content to clarify a particular part of the broad world of cardiovascular medicine.

Dr. Joseph Hill: [00:04:51] And so we subject each one of them to a internal review process to establish its veracity and novelty and importance and a subset of those will actually send out for external review where we ask people outside of the journal to evaluate the paper. They are typically content experts on the science that is being discussed and or the methodologies that are being used. And then we will select the top five papers for publication.

Dr. Joseph Hill: [00:05:20] So that's probably about half the job. The other half of the job is to canvass the cardiovascular space for areas of debate and controversy or new developments that are emerging rapidly and commission review articles, point counterpoint pieces, debates perspectives, opinion pieces to help clarify an area that's evolving rapidly, or that is subject to controversy. Help to sculpt the direction that we believe important, we think that this area of science should be emphasized, so we bring in content that points in that direction, so that second type of activity where we are in a more creative way trying to evaluate the future of cardiovascular medicine globally and broadly and helping to sculpt the direction that it moves.

Dr. Abhinav Sharma: [00:06:13] So in your role as editor you must be seeing journals from hundreds of researchers from across the globe. I'm actually very curious, are you receiving articles from predominately North American sources European sources, from Asia? Where exactly are you getting your articles from?

Dr. Joseph Hill: [00:06:31] Well most any country you can think of. The number one submitter to *Circulation* is the U.S., I believe number two is UK, number three is China, and there are probably 20 or 30 countries that submit regularly and then we will get a rare paper from some other countries, but it is quite an international scope.

Dr. Abhinav Sharma: [00:06:50] And so now you are someone who's been on both sides, you are a clinician scientist, and as that role you've submitted journals or submitted articles to journals, and now you're on the other side receiving articles as well. Have you noticed things are changing over the years with regards to how articles are either perceived or received through a journal?

Dr. Joseph Hill: [00:07:10] Well, I mean science is evolving very, very rapidly and the methodologies and the techniques have facilitated many, many things, we can generate a knockout mouse in a matter of weeks. Now whereas before it took two years. You know the ways in which clinical trials are developed, the number of novel approaches to adaptive trial design are there emerging improvements in registries, meta-analytics strategies.

Dr. Joseph Hill: [00:07:33] So across the entire spectrum there are entirely new ways to accomplish the science, and the questions that are being posed across that spectrum are also changing in many ways. We've seen enormous successes in taming the acutely lethal manifestations of atherothrombotic heart disease. There are still many challenges, it hasn't gone away, but new problems are emerging, for example the dramatic changes in obesity and obesity dependent diabetes that are exploding around the world is changing the face of cardiovascular medicine and we are working hard within the journal to do our best to get out in front of those questions and facilitate research to help prevent what I fear will be a major advent of new disease around them.

Dr. Abhinav Sharma: [00:08:19] So in addition to I guess all of these changes that you've seen from a scientific aspect, are you seeing a lot of changes with regards to how papers are

disseminating some of this information? So for example, is *Circulation* utilizing social media Twitter or other avenues to really get the message out there, get the science out there as well as opposed to traditional articles that are in the paper itself?

Dr. Joseph Hill: [00:08:43] Of course we have a print journal and we've engineered a whole new look to the journal, but on many occasions I've asked audiences how many people actually physically touch a journal. And the answer is almost always a very small fraction, probably less than 10 percent. So people interact with journals like this very differently, some exclusively online. Others get electronic tables of contents and then print out PDFs and track journals on social media. I've been unable to discern a consistent pattern or frankly any age related markers for who interacts with journals in a given way, some young people like paper journals some older folks only follow electronically and vice versa. So we do it all just like many journals, we print a very attractive paper journal we have a very user friendly web site now. We have a quite spectacular podcast called *Circulation on the Run*, weekly that is hosted by our associate editor in Singapore named Carolyn Lam.

Dr. Joseph Hill: [00:09:43] We have Twitter feeds and we have a Facebook page. The AHA, American Heart Association Press Office, releases our content that we recommend to them to two newswires and so forth, so a multi-disciplinary strategy of disseminating the information.

Dr. Joseph Hill: [00:10:01] Well that sounds absolutely fascinating, although very interestingly in one of our previous episodes we've had some discussion on medical fraud and journal retractions. There was some statistics that show that medical fraud has been increasing over time, and the submission of articles that have falsified information has also increased over time as well. Have you come across any of this in your own time as an editor or with any previous work in journals, and if you have, how have you approached the circumstance when you've fraudulent data in submitted journals?

Dr. Joseph Hill: [00:10:33] Well I'll start off by saying that our job at some level are the gatekeepers of novel and new information, and that is a heady responsibility that we take very seriously. And I have seen fraud before, probably much, much more commonly I've seen inadvertent mistakes where people you know have a paragraph that they pulled over from one article into another, inappropriately but it was more at the level of an innocent mistake than something that was nefarious. That happens much, much more commonly.

Dr. Joseph Hill: [00:11:06] There certainly are examples of absolutely egregious behavior. And like many I follow Retraction Watch, and that blog points out some shocking tales of people doing stuff that is absolutely out of bounds. I've not encountered that, I've seen a number of instances where one author or someone will reach out to us and claim to have had his or her data co-opted into somebody else's paper, or that there was a dispute between two people about whose role was what, most of that I believe is at the level of interpersonal interactions and human error. I'm not the slightest bit naive about the fact that there are people in this world who are gaming the system and doing inappropriate things.

Dr. Joseph Hill: [00:11:55] But frankly I wouldn't want people to think that that's rampant, that it's happening all the time. I think if you spend all your time on Retraction Watch you might come away thinking that it's extraordinarily common. It definitely happens and we should be mindful of it and watchful and thank goodness those people there do it. But I wouldn't want young people to think that the system is stacked against them because there are cheaters out there who are going to eat your breakfast and get way ahead of you because they're cheating. That is in my experience the minority for sure.

Dr. Abhinav Sharma: [00:12:28] So you mentioned the concept of gaming the system. What exactly do you mean by that?

Dr. Abhinav Sharma: [00:12:33] Well, there are people who take inappropriate shortcuts to get their work out fast. They will manipulate data, they will falsify their methodologies and so forth. And that certainly does happen. I've seen terrible examples of where people I believe would review a grant, or a paper and take an idea from that and use it in their own research, or realize that something that they were doing there are others out there who are going faster, and that they're about to be scooped and so they will change the direction or even worse manipulate their own data because they know that they're about to be scooped by someone who's gotten ahead of them.

Dr. Abhinav Sharma: [00:13:13] So now taking a bit of a turn in terms of our discussion here, you mentioned that you're still doing clinical work and you still are doing research as well. Can you tell us a little bit about your research? Do you predominately work with humans or animals or what type of research you do?

Dr. Joseph Hill: [00:13:28] Well, the vast majority of my research is preclinical. We study in my lab for different diseases, we study the effects of high blood pressure on the heart, on the cardiac myocyte which involves a complex remodeling responsive cell growth and metabolic shifts and cell signalling advance and transcription of control many different things occur in the cardiac MI site exposed to high blood pressure.

Dr. Joseph Hill: [00:13:51] We study ischemia reperfusion injury, that which derives from a heart attack which again is a complex biology triggered by the ischemic phase, and another set of events in the reperfusion phase. We are studying now for some years the effects of obesity on the heart, that the diabetic is toxic to the cardiac MI site with fluctuations in a variety of signaling molecules, and adrenergic neurological activation and many things that are impinging on MI site in the setting of a diabetic individual that are toxic to the myocardium, and we're working on trying to understand those in hopes of blunting them, or blocking them or even reversing them. And finally the fourth disease that we've only been working on for a year or so now is heart failure with preserved ejection fraction which accounts for about half of people with heart failure. In other words tens of millions of people, but for which we have no therapies whatsoever none. And we are working to develop a preclinical model that we hope recapitulates the human phenotype. And with that to define the underlying mechanisms.

Dr. Abhinav Sharma: [00:14:58] And so how did you end up in this particular field of research? Was it something that you've always been interested in since your early clinical days or were you introduced to this particular lines of research through some mentors of yours? How did you come to do research in these particular fields?

Dr. Joseph Hill: [00:15:14] Well without that question the reasons we've selected these areas is because these are where the problems are. Hypertension is the number one killer on the planet and that's why we studied hypertension the effects on the heart for more than a decade. Obesity is rapidly expanding and that's where the problem is, and that's what we study. Heart failure with preserved ejection fraction affects millions of people for which we have no therapy. So the way I approach my science has always been, where are the pressing clinical problems? And we will drill down and try to define underlying molecular and cellular mechanisms, but we start with a disease.

Dr. Abhinav Sharma: [00:15:48] So a lot of your research is clearly very clinically focused. A lot of other researchers that are out there are often doing research in a sense for the sake of doing research where it may not have a direct clinical applicability. Do you feel that all research should have some sort of immediate clinical aim or clinical goal or should people be doing research just for

the sake of gaining that knowledge , and gaining an understanding of the world around us?

Dr. Abhinav Sharma: [00:16:12] Well without question science should be accomplished to explore the fundamental nature of biology. Without question the CRISPR Cas9, which is a technology that will revolutionize biology, emerged from people studying acquired immunity in bacteria. People who studied slime molds discovered micro RNA, the retrovirus worked from the 1970s emerged with clinical relevance in the 80s with the HIV epidemic. So there's a great deal of benefit and merit doing fundamental science for his own sake. That said, given that my starting point is as a physician I can bring unique perspectives to my science as a doctor. Hence it only makes sense for me to be studying clinically relevant questions.

Dr. Joseph Hill: [00:16:58] And so given your time as a clinician scientist what do you feel are some of the challenges that young scientists and young research are facing today, and have these challenges changed from when you were just starting out in your research career?

Dr. Joseph Hill: [00:17:15] Well there has been over the last decade a retrenchment in societal investment in fundamental biomedical research, the last two years excepted, we have seen a decline in NIH funding on real term dollars to the tune of something around 20 percent or so, and that is very, very, very unfortunate in that it has done many things. First of all it's slowed and even eliminated some areas of investigation. It's very difficult to conduct research in an on again off again funding environment.

Dr. Joseph Hill: [00:17:48] You need a five or 10 year timeline in order to do anything productive, and to know that if I start this there'll still be support for me to continue down the road. It has almost certainly eliminated the careers of some people at that transition phase from training into independence where that jump is a difficult one. And I know quite well that some people have decided it's just too risky. I'm going to go work on Wall Street or do something different instead. And so that that is unfortunate and I will argue strongly that as health care expenditures the United States are going to bankrupt our nation eventually, Medicare is broke.

[00:18:29] The only way we're going to be able to deal with these incredible financial challenges is by attacking the problem at the root by understanding the mechanisms of obesity induced heart disease, or Alzheimer's disease, things like that, that if we can understand those and find ways to trim and mitigate their effects we will save many, many fold at the far end when these people would otherwise be debilitated with heart disease neurological disease and so forth. The way to bend the cost curve in healthcare expenditure in our country is at the level of discovery science at the root of the problem rather than trying to clean up the mess down the road when people have severe disease.

Dr. Abhinav Sharma: [00:19:14] So then given these challenges in research that you mentioned for young career scientists, what are some of the challenges that you're facing right now as someone who is more advanced into their career?

Dr. Joseph Hill: [00:19:25] Well you know I have a large lab and we're doing what I think is exciting work and you know it's my responsibility to maintain that lab financially viable and so I spent a lot of time writing grants and on one hand it is arguably not the most productive use of one's time to be spending a large swath of their effort writing grants but it is the reality and interestingly funding in the US is better than a few places, like Canada. It's worse than many places like some places in Europe and in Asia.

Dr. Joseph Hill: [00:19:59] There are other countries that are investing in the sorts of things that I'm talking about here to a degree that outstrips the United States, and we are seeing many of the bright young people who have trained in the US, who are moving to China or to Singapore and

places like this that have decided that not only is investment in biomedical research a worthwhile goal, but frankly it is an economically viable way to develop novel industries and novel drugs in the pharmaceutical world. Many things like that, so the return on societal investment to research is a robust one. But right now in the very complicated and acerbic political environment that is the United States, that message is not being heard by many lawmakers in Washington.

Dr. Abhinav Sharma: [00:20:49] Now you mentioned that some young scientists may be potentially leaving to go to other countries. Is there a brain drain essentially then of clinicians scientists to areas where they can have successful labs or get more funding for their research?

Dr. Joseph Hill: [00:21:03] Yeah I'm not sure I would call it quite a brain drain but there certainly are people who have benefited from training in the U.S. or in Europe who are returning to China and Singapore and so forth. And that's probably a good thing. I'm not saying that's a bad thing it's a good thing, that there are many questions as I mentioned earlier that the obesity epidemic in China is something that needs to be addressed ultimately in Asia. And I'm certainly in favor of that. But the career path of the physician scientist has always been a challenging one. It's always been an incredibly exhilarating one. But right now in the last few years when we're in an ebb of societal support through the National Institutes of Health and so forth it is more challenging now than it has been at some other times in the past.

Dr. Abhinav Sharma: [00:21:48] And so what would then be some of the strategies for scientists to really push for getting more research funding, or to try and convince these lawmakers, is that we should be lobbying more aggressively? Should we be putting this forth to our congressmen and congresswomen that we need more funding? What can scientists do at the frontline to really bring forth that this is an important investment in our society?

Dr. Joseph Hill: [00:22:11] Well most definitely getting that message out, getting involved in organized medicine and advocating on Capitol Hill that's what I was doing yesterday just yesterday before I came here to Durham. I was in Washington doing just exactly that.

Dr. Joseph Hill: [00:22:25] It's incredibly important. That said it's interesting that lawmakers across the entire political spectrum, everybody would like to see heart disease cured. There's not a single person in Congress who wouldn't like to see Alzheimer's disease cured. The difference is, how are you going to pay for it? Some on one end of the political spectrum will say, you know what, I'm willing to tax people more to invest in these disease cures. Others will say we will never tax more. We will just cut someplace else. Tell me what you want to cut. 'Yes, I agree with you we should cure heart disease. Tell me what you want to cut to get there.' So that's where the conversation obviously becomes difficult.

Dr. Joseph Hill: [00:23:04] And, to the extent that we sit in someone's office and try to convince them that heart disease is a terrible thing that ought to be cured is I think talking the wrong conversation because they get that, everybody gets it. The question is convincing them that it is a worthwhile investment that there is a societal return on that investment, and that taking money either out of taxpayers' pockets or out of the military, or somewhere else, those funds will return with a robust investment return. So in other words speaking in economic terms with these people not so much with biological terms but rather that it is a worthwhile economic endeavor.

Dr. Abhinav Sharma: [00:23:44] So in speaking to some of these lawmakers, what has been their reception? I mean it seems that they all agree that cardiovascular disease and dementias need to be cured and there appear to be differences in opinions as to how to go about funding some of these endeavors. But is there a political initiative to do this or is there just a lot of inertia? Do these politicians not want to move forward because it's just too complex and too difficult to actually move

forward on some of these very important scientific endeavors?

Dr. Joseph Hill: [00:24:15] Well I would say in the last two years for the first time in more than a decade there has been bipartisan support to increase NIH appropriations. Some would argue that's because they don't agree on anything else and it's at least one thing that they can actually do to show the world that they accomplished something and so that's a positive sign. I will tell you that in the 1990s when the NIH budget was doubled with Bill Clinton as president, Newt Gingrich who politically was way at the other end of the spectrum from Bill Clinton agreed with him. In fact Newt Gingrich who is very conservative has argued that the way to bend the cost curve in healthcare expenditure is to increase the NIH budget fivefold. He's advocated for quintupling the NIH budget. So that's someone who on the conservative end of the political spectrum understands the economic side of this conversation.

Dr. Abhinav Sharma: [00:25:08] And do you get the sense that lawmakers today also understand the economic aspect of things, or are you finding that there's some stumbling blocks or are people just not quite understanding that potential return on scientific investment to society?

Dr. Joseph Hill: [00:25:24] Many of them don't understand and frankly we've not done a good job of explaining it to them. We've not done an adequate job of explaining understanding what is that return on investment because it is not uniform there's some areas that have been less productive and other areas that have been hugely productive.

Dr. Joseph Hill: [00:25:38] It's estimated the Women's Health Initiative which basically put the kibosh on estrogen replacement therapy for women that the return on investment there was something like 143 to one. I mean that's spectacular, unbelievable return on investment to that multimillion dollar study. Obviously not all research has had that kind of return, but I personally believe that we need to do a better job of understanding and articulating the economic argument because many of the folks in Congress are business people, their attorneys they have no biological training at all. And that's how they think, they think in terms of dollars and cents, and that explaining it to them in those terms I believe is the most productive strategy.

Dr. Abhinav Sharma: [00:26:18] So, hypothetical scenario: You're a lawmaker, you have the ability potentially to make these changes. What would you do if you had that ability in terms of moving some of these initiatives forward. What would be some of the strategies that you would implement?

Dr. Joseph Hill: [00:26:31] Well, people have done studies where they've compared the amount of investment in research relative to the impact of a disease process. And the two that come out on the short end of that stick are heart disease and diabetes, where society invests a certain amount on research. But yet the problem is much, much, much greater. At the other end of that spectrum is a terrible disease process, that being breast cancer where society invests a more on research on a problem that in fact the clinical impact in terms of economic terms is much, much smaller. I'm not here to suggest that we shouldn't be working hard to address mechanisms and cures for breast cancer, we certainly should, but the amount that society invests in breast cancer research relative to the scope of the problem is many fold greater than the small amount of money invested in heart disease and diabetes relative to the magnitude of the problem. And I would rebalance those sorts of distributions.

Dr. Abhinav Sharma: [00:27:35] Well that's absolutely wonderful insight from someone like yourself who's had experience in the clinical world, and from your experience as a medical editor seeing research across the spectrum of cardiovascular diseases.

Dr. Abhinav Sharma: [00:27:46] So with that we're just going to ask a quick rapid fire couple of questions, our Sign See section really just get to know a little bit more about you.

Dr. Abhinav Sharma: [00:27:53] So when you're not spending your time doing research and seeing patients, and reviewing hundreds of articles what are we going to find you doing?

Dr. Joseph Hill: [00:28:01] Well I enjoy working out, I am reading a biography of Elon Musk right now. I'm a certified sommelier, and I enjoy wine and reading about wine tasting wine.

Dr. Abhinav Sharma: [00:28:11] That's fantastic. And if we were to take out your phone and look at your music playlists what are we going to find on that?

Dr. Joseph Hill: [00:28:19] It would be classical and jazz largely, although I have to say when I'm writing something depending on my mood, sometimes Pandora will migrate to the Beatles or Weezer or who knows. Never Justin Bieber, never, never just never.

Dr. Abhinav Sharma: [00:28:34] Fair enough.

Dr. Abhinav Sharma: [00:28:35] And has there ever been a time when you're just to do clinical work to pick up the scope, and just see patients all the time, or have you always had in you that you've always wanted to be that scientists, and see patients and the medical editing at the same time.

Dr. Joseph Hill: [00:28:48] Well, I always wanted to do the research and the clinical together and that was clear in college for me. The editor business came on 20 some years later, many years later, but I cling to my roles as a physician and as a scientist and that that has been my bedrock for you know throughout my career.

Dr. Abhinav Sharma: [00:29:05] Well that's fantastic. Dr. Joseph Hill thank you so much for your time, we really appreciate your comments and your thoughts today.

Dr. Joseph Hill: [00:29:10] My pleasure. Thank you.

Dr. Abhinav Sharma: [00:29:15] On wrapping up with our conversation with Dr. Joseph Hill, I feel like we've navigated through the dizzying world of medical journal editing, politics and even academic fraud, while the peer review process is far far with a capital F from perfect. It serves as one of the best ways to ensure quality and integrity of scientific results. Now a new way of doing things is coming. Whether this means crowdsourced reviewing of scientific journals, to completely opening up entire databases, but you know what, whether these gain traction in the scientific community remains to be seen. So the next time you feel like brushing up on the latest and greatest in scientific knowledge, grab a tea, open up your laptop, head to a peer-reviewed scientific journal in the field you're interested in and soak it all in.

Dr. Abhinav Sharma: [00:30:07] Thanks to all of those who have made today's episode possible. I'm your host Abhinav Sharma and I hope you've enjoyed your dose of the Science is the Best Medicine podcast.

Announcer: [00:30:23] You've been listening to the Science is the Best Medicine podcast with your host, Dr. Abhinav Sharma. This episode is brought to you by the Duke Clinical Research Institute.