

SPIRAL JETTY

by

AJ Dehany

Day 10 of the 29 Plays Later Challenge: find an expression, an idiom, a cliché, etc... and use it as a literal impetus for a play.

I considered 'taking a dose of your own medicine' which led me to think of Barry Marshall, who faced down the medical establishment and in order to prove that peptic ulcer has a bacterial basis infected himself with *Helicobacter pylori*. In 2005 he and Robin Warren shared the Nobel Prize.

This draft contains material derived from interviews and primary sources, including some direct quotation. The substance of the story has been dramatised, though with extensive use of quotation in the first scene, which is monologue owing to lack of time.

ajdehany@gmail.com

SCENE 1

(BARRY MARSHALL)

BARRY MARSHALL: In medical school it's quite possible to get taught that you can diagnose everybody and treat everything. But then you get out in the real world and find that for most patients walking through your door, you have no idea what's causing their symptoms. You could slice up that person into a trillion molecules and study every one and they'd all be completely normal. I was never satisfied with saying that by ruling out all these diseases, a person must have a fake disease, so I accepted the fact that lots of times I couldn't reach a fundamental diagnosis, and I kept an open mind.

Most of my work revolves around peptic ulcers. If you don't think that sounds important, ask someone who has had them how painful they are and then shield your groin from the barrage of kicks as they try to give you some idea of the level of pain. Beyond the agony and the decreased quality of life it can cause, peptic ulcers have been linked to increased chances of one getting stomach cancer.

I watched in horror as ulcer patients fall so ill that many had their stomach removed or bleed until they die. Ulcers at that time afflicted 10 percent of all adults, but there is a simple treatment.

In the third year of my internal medicine training, in 1981, I had to take on a project. Robin Warren, the hospital pathologist, said he had been seeing these bacteria on biopsies of ulcer and stomach cancer patients for two years, and they were all identical.

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The infections were distinctive. The microorganisms all had an S-shaped or helical form, and the infections coated the stomach. Warren had found them in about 20 patients who had been sent to him because doctors thought they might have cancer. Instead of cancer, he had found these bacteria. So he gave me the list and said, "Why don't you look at their case records and see if they've got anything wrong with them." It turned out that one of them, a woman in her forties, had been my patient. She had come in feeling nauseated, with chronic stomach pain. We put her through the usual tests, but nothing showed up. So of course she got sent to a psychiatrist, who put her on an antidepressant. When I saw her on the list, I thought, "This is pretty interesting."

Then another patient turned up, an old Russian guy who had severe pains. Doctors gave him a diagnosis of angina, pain that occurs when blood to the heart can't pass through a narrowed artery. It's rare, but you can theoretically get that in your gut, too. There was no treatment for an 80-year-old man in those days, so we put him on tetracycline and sent him home. He goes off, and two weeks later he comes back. He's got a spring in his step, he's practically doing somersaults into the consulting room. He's healed. Clearing out the infection had cured him. I had one more year to go,

so I did the paperwork to set up a proper clinical trial with 100 patients to look for the bacteria causing the gut infection; that started in April of 1982.

We had been trying to infect animals to see if they would develop ulcers. It all failed; we could not infect pigs or mice or rats. Until we could do these experiments, we would be open to criticism. So I had a plan to do the experiments in humans. It was desperate: I saw people who were almost dying from bleeding ulcers, and I knew all they needed was some antibiotics, but they weren't my patients. So a patient would sit there bleeding away, taking the acid blockers, and the next morning the bed would be empty. I would ask, "Where did he go?" He's in the surgical ward; he's had his stomach removed.

SCENE 2

RESEARCH AND MAINSTREAM RESISTANCE

(BARRY MARSHALL, ROBIN WARREN AND

MEDICAL REP)

MARSHALL: Nothing turned up until patients 34 and 35, on Easter Tuesday, when I got this excited call from the microbiologist. So I go down there and he shows me two cultures, the grand slam, under the microscope. The lab techs had been throwing the cultures out after two days because with strep, on the first day we may see something, but by the second day it's covered with contamination and you might as well throw it in the bin. That's the mentality of the lab: Anything that didn't grow in two days doesn't exist.

WARREN: We discovered that Helicobacter is slow-growing. After that we let the cultures grow longer and found we had 13 patients with duodenal ulcer, and all of them had the bacteria.

MEDICAL REP: You haven't managed to infect the animal model. You have some interest and support from a few but widespread rejection and significant delays on publication of your work. Your conclusions are premature and not well supported. Your work is typically disputed and disbelieved. It simply can't be

true. Noone could replicate your results. The bacteria are obviously either contaminants or harmless commensals.

MARSHALL: It's not true. We have been successfully experimentally treating patients who have suffered with life threatening ulcer disease for years. Some of my patients postponed surgery which became unnecessary after a simple two-week course of antibiotics and bismuth. I've developed a hypothesis that these bacteria were the cause of peptic ulcers and a significant risk for stomach cancer. If I'm right, then treatment for ulcer disease can be revolutionized. It will be simple, cheap and it will be a cure.

MEDICAL REP: It is accepted by the medical community that ulcers are caused by a combination of stress, spicy food and too much stomach acid being produced.

MARSHALL: Millions of people are suffering. How many have lost chunks of their stomachs via wholly unnecessary surgery?

WARREN: I discovered that the gut can be overrun by hardy, corkscrew-shaped bacteria called *Helicobacter pylori*. Biopsying ulcer patients and culturing the organisms in the lab, Marshall has traced not just ulcers but also stomach cancer to this gut infection.

MARSHALL: What we have realized is that there is a readily available cure: antibiotics

MEDICAL REP: All gastroenterologists agree that ulcers are caused by

stress.

MARSHALL: You say ulcers are caused by lifestyle: stress, diet, alcohol, drugs, or it's genetic. The doctor who can't cure you is blaming the patient for having the ulcer! It takes the pressure off - very comfortable!

WARREN: We have studied the presence of spiral bacteria in association with gastritis and performed the initial culture of H. pylori and developed a hypothesis related to the bacterial cause of peptic ulcer and gastric cancer.

MARSHALL: We need this theory proven quickly to provide curative treatment for the millions of people suffering with ulcers around the world.

MEDICAL REP: Ridiculous! No bacteria can live in such an acidic environment as the stomach!

MARSHALL: I know I'm right. People have been finding bacteria in the stomach since 1893, and there's plenty of evidence that antibiotics clear ulcers right up.

MEDICAL REP: This is career suicide. Why don't you accept what everyone knows?

WARREN: As a hospital pathologist I have been seeing these bacteria on biopsies of ulcer and stomach cancer patients for two years, and they are all identical.

MEDICAL REP: Times are difficult, and there isn't money for research.

MARSHALL: The drug companies are making a billion dollars a year for the antacid drug Zantac and another billion for Tagamet. You could make a patient feel better by removing the acid. Treated, most patients don't die from their ulcer and don't need surgery.

MEDICAL REP: Think about it. These treatments are worth \$100 a month per patient, a great deal of money. In America 2 to 4 percent of the population had Tagamet tablets in their pocket. There is no incentive to find a cure. You want to undermine a \$3 billion industry, not just the drugs but the entire field of endoscopy. Every gastroenterologist is doing 20 or 30 patients a week who might have ulcers, and 25 percent of them do. It's a recurring disease that you could never cure, the patients keep coming back. And here you are trying to hand it on a platter to the infectious-disease guys. So forget about bacteria. They don't cause ulcers or stomach cancer. The concept of a germ causing ulcers is like saying that the Earth is flat.

SCENE 3

DRINKING HELICOBACTER (BARRY MARSHALL &
ROBIN WARREN)

MARSHALL: There has to be an easier way of making this work. Having to wrestle fifty pound pigs on a daily basis. I'm not a wrestler. These pigs just won't get infected!

WARREN:: We know that these bacteria cause stomach ulcers, but we can't legally test the theory out on humans. I'm out of ideas.

MARSHALL: What if... There's no law that can stop me testing the theory on myself though.

WARREN: You'd rather infect yourself than wrestle pigs? It doesn't sound legal. Is it?

MARSHALL: It's perfectly legal. In fact it's ethically principled. The Nuremberg Code requires that no experiment be conducted that an experimenter wouldn't conduct on himself.

WARREN: You're not a pig, Barry. Pig-headed maybe.

MARSHALL: People are bleeding in my practice and dying from ulcers in my hospital. There's a huge urgency to solve this dilemma.

WARREN: The ethics committee will never pass it.

MARSHALL: We need to fast track this. Without the ethics committee. If we got rejected by the ethics committee I'm sure I'd go ahead anyway, but then we wouldn't be able to publish it and I'd get the sack life would basically be over.

WARREN: Phew!

MARSHALL: I'm gonna need some moral support here, Robin.

WARREN: You're crazy, Barry.

MARSHALL: There's no other way! Lab mice don't work cos Helicobacter pylori only affects primates, wrestling pigs isn't working, we can't experiment on people. The only person I can ethically recruit is me.

WARREN: What'll your wife say?

MARSHALL: Adrienne? She's already convinced about the risk of these bacteria. I'd never get her approval. This is one occasion when it would be easier to get forgiveness than permission. It could take months, or years, for anything to develop. She might not find out. I suppose she would notice if it works and I get stomach ulcers. Or even cancer.

WARREN:: Barry, you have to tell her. You don't need to be a scientist to know that upsetting your wife is worse for your health than

stomach ulcers, even when factoring in the potential increased risk of getting stomach cancer.

MARSHALL: I'm desperate, Robin. We'll do a baseline endoscopy, I'll skip breakfast and take 400mg of cimetidine to lower my stomach acid level so the infection takes. We'll get Neil Noakes to scrape an inoculated culture of Helicobacter and disperse the bacteria in alkaline peptone water.

WARREN: Meat broth! Tasty!

SCENE 4

MY WIFE'S REACTION (BARRY MARSHALL AND
ADRIENNE MARSHALL)

ADRIENNE: Barry!

BARRY: Just a bit out of puff.

ADRIENNE: Are you going to tell me what's going on? I've watched your condition deteriorate for over a week and I've kept my mouth shut, but this is it.

BARRY: It's something we discussed a few months ago, in general terms. The self experiment. You agreed we needed to fast track the research. I didn't know if it would work.

ADRIENNE: You've infected yourself?

BARRY: I got the bacteria the patient with gastritis, and cultured them, then worked out which antibiotics could kill his infection in the lab-- bismuth plus metronidazole. I treated him and did an endoscopy to make sure his infection was gone. After that I swizzled the organisms around in a cloudy

broth and drank it the next morning.

ADRIENNE: Just like that.

BARRY: I got to waking up in the morning and vomiting. Once I got it off my stomach, I would be good enough to go to work. I'm so tired though. Today I had an endoscopy. The bacteria are everywhere. There's all this inflammation, and gastritis has developed.

ADRIENNE: You pick your moments don't you - it's only three weeks since the car accident. I've got cracked ribs and I'm still sore from whiplash and now I'm caring for four children as well as a husband who's getting worse by the day. And what if you transmit the bacteria to me or the children.

BARRY: I didn't really think about it.

ADRIENNE: We're getting older. In our thirties now and you still have this belief that you're invincible!

BARRY: It was selfish of me. Especially after the crash. But you agreed.

ADRIENNE: In principle! Saying something in theory isn't the same as doing it. You don't seem to grasp this basic fact of scientific method though do you? No, you go ahead and, what did you do, drink it, drink a load of helicobacter and give yourself God knows what, ulcers and cancer. Are you going to make me a widow?

BARRY: Adrienne...

ADRIENNE: And your children orphans. For science. For what?

BARRY: Adrienne, think of the difference this could make to our lives! The grant applications are going to fail more than likely.

ADRIENNE: What if your little experiment had failed? What if the bacteria didn't take, what if gastritis didn't develop - your whole hypothesis could be wrong.

BARRY: It'd make it harder to convince the skeptics we've found something important sure. I could get jobs in clinical medicine, maybe interview for a placement in private practice, somewhere where my theories are less well known.

ADRIENNE: Somewhere less eccentric?

BARRY: But what if it works? A successful infection with *Helicobacter* would point towards a career in clinical research.

ADRIENNE: Exciting, but not financially secure, Barry.

BARRY: We can talk about it when the family settles down a bit. Hey? Look, when I vomited it was just like water. As a medical student I know what vomit's like. Dad still hasn't forgiven me for my twentyfirst - though I still claim it was the dog. Seriously, like water. There was no acid in the vomitus, which is the key: *Helicobacter* is a pathogen!

ADRIENNE: Promise me you'll stop this now, and take the antibiotic. You're sick!

BARRY: Just give me two more days, Adrienne. Then I'll take the antibiotic.

ADRIENNE: Now, Barry!

BARRY: I need the extra time. Just two days. And I'll get an endoscopy and a biopsy too, to make sure you and the kids haven't picked up the Helicobacter infection.

ADRIENNE: You've only just thought of that, haven't you. Risking infecting your family just to prove a scientific point.

BARRY: To build a life for us! Everyone already has the infection, Adrienne. You know that Helicobacter infection starts in childhood. When you're toddling around, eating dirty things and playing with your dirty little brothers and sisters. You don't remember getting it because you get it before you can even talk.

ADRIENNE: My ribs are aching. Unfortunately not from laughing, though maybe I should laugh. This is ridiculous. Why did I marry a scientist?

BARRY: It'll win us the Nobel Prize, believe me. Just give me till the weekend.

ADRIENNE:

You really believe you'll win the Nobel Prize. I'm just shocked that you'd do this without telling me, risk your life and ours, just for your career. Maybe think about that. You can have until the weekend.

SCENE 5

THE NOBEL PRIZE (BARRY MARSHALL AND
ROBIN WARREN)

MARSHALL: But why did noone tell me I had bad breath? I didn't know until my own mother had to tell me. I told the old bird she was imagining it. Then my wife told me I had "a putrid breath". The embarrassment is worse than the gastritis. No wonder I was depressed with everyone avoiding my bench.

WARREN: You could have worked it out, Barry. Halitosis due to the achlorhydria: no acid to kill bacteria in the stomach, and their waste products manifested as bad breath.

MARSHALL: I might have been a bit preoccupied with feeling nauseous, vomiting my bloody stomach up, and then when the biopsy showed massive inflammation from developing gastritis as the precursor to an ulcer, vomiting and halitosis, sickness, clamminess, exhaustion, and all the while working extra hours and weekends and having to do grant applications.

WARREN: The life scientific.

MARSHALL: Whose birthday was it when we confirmed the spiral bacteria in the gram stain of the first biopsy?

WARREN: Ross Glancy? Or was he working on the pathology specimen?

MARSHALL: Yeah, teeming with Helicobacter and pus cells, proving Helicobacter was a pathogen. That was some party that anyway, whether or not I've got the time all wrong.

WARREN: The article in the Medical Journal isn't doing very good business. Give it a decade eh? Some interested that you didn't develop antibodies to H. pylori, the suggestion that innate immunity can sometimes eradicate acute H. pylori infection.

MARSHALL: They can't ignore the evidence forever. Soon, Robin, they'll announce it writ large: the key to treatment of duodenal and gastric ulcer is the detection and eradication of Helicobacter pylori.

WARREN: My wife keeps asking when we'll get the Nobel Prize. Last year we said 1986, and now it's 1986....

MARSHALL: I'd say the same thing, 1986. Next week.

WARREN: Always trying to fast-track everything.

MARSHALL: You should try it some time, Robin. It's infectious.

[CURTAIN/END]