

SCIENTIFIC AMERICAN FRONTIERS
PROGRAM #1307,
"The Wonder Pill"
premieres February 18, 2003

TEASE
A DIFFERENT WAY TO HEAL
BRAINWAVES LIFT THE BLUES
EXPECTATION PAYS
SNUFFING THE SNIFFLES
HEALING RITUALS

TEASE

ALAN ALDA This may or may not be real acupuncture. And this may or may not be a real drug. Now here's a provocative question. Does it matter?

ALAN ALDA (NARRATION) Our show is about placebos - sham medical treatments masquerading as real.

ALAN ALDA I feel it. Yeah. I felt it. Have you seen people markedly improved on the placebo?

MICHELLE Yes. We've seen complete cessation of depression on the placebo.

ALAN ALDA (NARRATION) Placebos may not only help you feel better - new research suggests they can change your brain.

SEDRIC BELL It's like trickery, you know? They tell you they've given you whisky but they haven't.

ALAN ALDA (NARRATION) So if placebos work so well...

RANDREA MAJORS Oh, yeah, I'm really glad I got it.

ANDREW LEUCHTER I think it's worth it.

ALAN ALDA (NARRATION) What does it mean for how your doctor treats you?

ALAN ALDA I feel better already. I'm Alan Alda. Join me as Scientific American Frontiers investigates the power of the placebo in The Wonder Pill.

A DIFFERENT WAY TO HEAL

ALAN ALDA Imagine a scene like this: You come into your doctor's office with a problem that won't go away. You've had the usual round of blood tests and maybe some expensive scans. Finally the doctor is ready to prescribe some medicine for you. And she gives you a choice: some heavy hitting drugs with risks of side effects, or this: a pill which she says is proven effective in some one-third to one-half of patients taking it. It's been in use for years. It's been through thousands of clinical trials and has minimal side effects. No one's quite sure how it works, although some new research has been coming up with interesting ideas about how it affects the brain. Oh, and one more thing -- and she sort of slips this in there -- it doesn't actually contain any active drug. So, what do you think? Would you give it a try? The pill you were offered was a placebo, a sugar pill. Placebos are a hot topic in medicine right now. The placebo effect is the often positive response that patients get to a sham medical treatment -- not just a fake pill, but in some cases even a fake surgical procedure. Recently researchers have discovered that in some cases, placebos cause physical changes in the brains of people taking them. This has led to surge of interest in understanding the placebo effect. And while your doctor may never offer you a sugar pill instead of the real drug, there's real interest now in trying to turn the placebo effect into a useful therapeutic tool. Which is why we're starting our show here: among the graves of people who died often very young, from diseases that pre-scientific medicine was unable to cure. This is the grave of Dr. Harriet Hunt, one of the first women physicians in the country. What was it that Harriet Hunt and her mostly male colleagues in the healing profession were able to offer their patients?

ALAN ALDA (NARRATION) The short answer, obvious in the gravestones here at Mount Auburn Cemetery in Cambridge, Massachusetts, is not much. There are hundreds of graves of children - and many of the adults died in their 30s and 40s. Most of these deaths were from infectious diseases like cholera and tuberculosis that medicine was once helpless against. But as long as people have been getting sick, there have been people who claimed to be able to cure them. We invited Anne Harrington and Charles Rosenberg, both of nearby Harvard University, to help us understand what kept doctors in business.

ALAN ALDA Over the centuries, what have people actually been given to make them feel better?

CHARLES ROSENBERG Well, lots of different things. But I think there's a real continuity. People always expected if they were sick to take a drug. This book was published in 1656. And it was a very very popular English book called *The English Physician Enlarged*. It has "369 medicines made of English herbs that

were not in any impression until this." This is an herb called Allheal. It was also called Hercules Allheal and Hercules Wound-Wort. "It is under the dominion of Mars, hot, biting and choleric. It kills the worms, helps the gout, cramp and convulsion, provokes urine, and helps all joint aches. Helps a cold grief of the head, the vertigo, falling sickness and lethargy. The wind colic, obstructions of the liver and spleen. It is excellent good for the grief of the sinews, itch, sores and toothaches.

ALAN ALDA Grief of the sinews?

CHARLES ROSENBERG That would probably mean probably arthritis or something like that -- diseases of the joints.

ALAN ALDA You know what's wonderful about this? It's so authoritative, it tells you about the planets that govern it. It's a lot like saying, proven in clinical trials...

ALAN ALDA (NARRATION) Some of these herbal remedies may have had consequences - acting as a diuretic, say, or making your pulse race - but it's unlikely they actually cured many diseases.

ALAN ALDA Was there anything that worked, a hundred, a hundred and fifty years ago?

CHARLES ROSENBERG Well, the issue is worked, because that sounds like a simple word, but it's a complicated word. Because when we say worked, we put a kind of physiological, modern kind of notion: does it have a physiological effect, make a disease change its course, make the body operate differently. But if you think of worked as having a patient feel differently or have the patient feel that someone was taking care of them, then medicines worked in a different kind of way.

ALAN ALDA (NARRATION) This different kind of way is what our show is about - the mysterious chemistry brewed up between doctor and patient that works even when the medicine is what today we'd call a placebo - an inert substance masquerading as medicine. While most doctors in the past would certainly not have thought as their remedies as placebos, there was a time, right before the advent of modern medicines, when placebos had an acknowledged place in the physician's medical cabinet.

ANNE HARRINGTON Back in the '30s and '40s when we lived in a more paternalistic culture, doctors would keep bottles of placebos on their shelves. In fact, they had these mail-order catalogues that advertised placebos of different sizes and shapes and colors. And there were professional conversations about the yellow ones that were particularly good for patients who were suffering from

one kind of thing. Blue would be good for sleeping pills. Red were good for pick-me-uppers. Because these things had a symbolic logic that doctors were aware of. And doctors were prepared to give these pills to patients in the 1930s and '40s because it was felt, in a sense, that doctor knows best. Patients didn't need to have full consent and information about what was going on. We live in a different kind of society today.

ALAN ALDA (NARRATION) It's a society where housecalls have been replaced by the 10-minute HMO appointment, robbing the doctor - and so his patient -- of what was once medicine's only effective treatment.

ANNE HARRINGTON I sometimes think of it as the white feather effect. In the Disney film, Dumbo needs a white feather in order to fly. He believes the white feather... you haven't seen this film, have you?

ALAN ALDA I've haven't seen it since I was five. So you're looking at a blank face here, I'm sorry.

ANNE HARRINGTON In the animated Disney film, Dumbo was an elephant with gigantic ears. And he flaps his ears and he can fly. He believes he can only fly when he carries a white feather in his trunk.

ALAN ALDA Well, that's true for me, too.

ANNE HARRINGTON And one day, the white feather falls from his trunk and he realizes he was doing it all along. So the placebo is the trick that enables us to open up things inside ourselves through mechanisms that aren't well understood but are beginning now to be elucidated somewhat in the laboratory. But we do it to ourselves.

ALAN ALDA (NARRATION) In this show we are going in search of Anne Harrington's white feather, trying to rediscover the trick that allowed 19th century physicians like Harriet Hunt to turn a placebo into a wonder pill -- and that even in the medicine of the 21st century, can perhaps still cast its spell.

BRAINWAVES LIFT THE BLUES

ALAN ALDA (NARRATION) Of my two companions here at the University of California in Los Angeles, one succumbed spectacularly to the spell of the placebo effect - while the other decidedly did not. They each answered an ad recruiting people suffering from severe depression for a study of antidepressant

medications. As is usual for such studies, some of the patients were assigned to a control group, receiving placebo pills instead of the real thing

ALAN ALDA They told you that you might be on the medication, or you might be on a placebo.

JANIS SCHONFELD M-hmm.

ALAN ALDA And you assumed you were on the medication.

JANIS SCHONFELD I certainly did.

ALAN ALDA When did you make the transition from thinking--I wonder what I'm taking. You must have thought that, didn't you?

JANIS SCHONFELD No, I never did.

ALAN ALDA Oh. It sounds like they didn't have to give you anything.

JANIS SCHONFELD No. Because I was feeling so much better, I was convinced I was on the medication.

ALAN ALDA Are these the pills that the patients take?

NURSE These are the pills, the study material.

ALAN ALDA Which pills are these?

NURSE Well, we don't know.

ALAN ALDA Oh, so they all look exactly the same.

NURSE They all look exactly the same.

ALAN ALDA Of course they would.

ALAN ALDA (NARRATION) The physician running the study is Dr Andrew Leuchter.

ANDREW LEUCHTER When somebody comes to this big imposing research institution and they see warm and caring nurse in a white coat, they have an expectation they're going to get better. They believe they're going to get helped. And since we're conditioned to believe that sugar pills can't possibly get you better, we tend to think those are real medicine.

ALAN ALDA (NARRATION) Janis Shonfeld had never taken antidepressants before. But Frank Strauss had - and to be eligible for the UCLA study had had to stop taking his old medication a couple of weeks before the trial began.

FRANK STRAUSS When I get depressed, it's debilitating. I can't see it to walk downstairs; I have to hold on to the railings. I can hardly leave my apartment. I get zero sleep 'cause my heart beats all night long. And I just lay there and watch the sun come up, and it's like, the worst.

ALAN ALDA How did you feel when you knew it was a placebo?

FRANK STRAUSS You know, I thought it was a really cruel joke, is what I thought. I thought, here's my whole life in the balance, and they're giving me something that, all of a sudden I'm getting like screwier by the moment. And I was angry to say the least. It never even entered my mind that they were giving me a placebo, because, I'm like, here's this basket case, you can't possibly give me a placebo. You know, it's like, what are you thinking?

ALAN ALDA (NARRATION) Frank may not have responded, but many studies have shown that some 40 per cent of patients with depression feel better on placebo - and in this respect, the UCLA trial was typical.

ALAN ALDA Have you seen people markedly improved on the placebo?

MICHELLE Yes. We've seen complete cessation of depression on the placebo.

ANDREW LEUCHTER The patients who got better on placebo, and the patients who got better on medication, couldn't be distinguished. At the end of eight weeks, we told everybody what they were getting. So at the end of eight weeks, they knew they'd been getting either placebo or medication. The patients who got placebo, almost all of them within a month of the end of the study, had relapsed. Because as soon as they knew they were on placebo, most of them said, "you know, maybe I'm not feeling that good."

ALAN ALDA "Maybe I don't feel that good." Yeah.

ANDREW LEUCHTER Exactly.

ALAN ALDA "I'm still depressed."

ALAN ALDA (NARRATION) But while Andy Leuchter's study was unremarkable in finding that many patients - like Janis - responded to placebo, it was pioneering in what it found out about her brain. Like the other subjects in the

study -- including those taking real antidepressants - Janis came in for regular EEGs. Leuchter was trying to see if he could spot early changes in the brain waves of patients on medication. Often patients don't get any benefit from an antidepressant for several weeks, and Leuchter was hoping to find a brain wave signature that would predict if an antidepressant is going to help. Early results looked promising. Depressed patients usually have less activity than normal in their prefrontal cortex, and in the UCLA trial, antidepressants that worked lowered the activity still further. A puzzling finding, perhaps, but still potentially a useful predictor of an effective treatment.

TECHNICIAN Try to think about something that keeps you alert.

ALAN ALDA (NARRATION) But the big surprise came in the brain waves of patients like Janis Schonfeld, who felt better even though they were on placebo.

ANDREW LEUCHTER What we found was, in patients that got placebo when they got better, this same region of the brain here, actually showed an increase in activity. It was the opposite pattern. It took a little bit longer to come on. But over the span of eight weeks of treatment, there was this augmentation of activity in the front of the brain in patients who felt better on placebo.

ALAN ALDA Now wait, this is a little hard to get. They take the antidepressant pill, the real pill. And, they feel better and they get lower activity in that part of the brain.

ANDREW LEUCHTER That's correct.

ALAN ALDA Then they're given the placebo, and they feel better, but they get heightened activity in that part of the brain. Now originally I would imagine you would have thought the lowered activity was related to feeling better. How is it that--never mind that they took the placebo--how is it that they have this heightened activity here, but they feel better. How could that take place? What do you think is going on there?

ANDREW LEUCHTER As you yourself said, the brain is extraordinarily complex. I think what it all gets down to, is there are multiple pathways to improvement. There's not just one way to get better. Now, it may not be as robust an improvement as a lot of patients would get with medication. And we don't think it lasts as long. We think it's a more fragile kind of improvement. But it's important because this other way to feel better that some patients are able to activate.

JANIS SCHONFELD My mood lightened, definitely, and if you've ever suffered from depression, and I have been diagnosed with clinical depression beforehand, there's such a weight that you carry, it feels like it's on your shoulders and on

your head that, to have that lifted, it almost feels like you can run... you can run a marathon. Or you can run quickly. And that's how I was feeling.

ALAN ALDA That's amazing. And yet it was a sugar pill.

JANIS SCHONFELD Yes.

ALAN ALDA (NARRATION) Andy Leuchter's discovery that placebos can actually change the brains of people who feel better is dramatic confirmation of the fact that - while it may all be in the mind - the placebo effect is real and measurable.

ANDREW LEUCHTER The importance of this work, from my perspective, is, we can help figure out what leads to healing. That's really what this is all about is healing. There's something that some patients are able to activate, just by coming into treatment, getting inert treatment, taking a placebo pill. Some patients are able to feel better. What is it that is leading to that placebo effect? Is it a stronger bond between those patients and their doctors? Is it they have more positive expectations? They come in believing they're going to get better? If we can distill that out and apply it more broadly, maybe we can help all treatments be more effective. And that's really one of the goals of this is to tease out something about the placebo effect that we could apply more broadly.

ALAN ALDA (NARRATION) Leuchter's hunch is that this something -- the essence of the placebo effect -- lies in that most ancient of a doctor's skills: the healing power that flows from a caring physician to a receptive patient.

ANDREW LEUCHTER Hi, I'm Dr Leuchter.

ALAN ALDA Hi.

ALAN ALDA (NARRATION) Which is why I'm in his consulting room, playing the role of a patient with depression.

ANDREW LEUCHTER So how are you doing today?

ALAN ALDA Well, I feel a little low.

ALAN ALDA (NARRATION) Leuchter is shortly to begin a new study in which as well as getting either a real antidepressant or a placebo, patients will also be randomly assigned to either a detached and businesslike physician, or - as Andy is here -- a warmer and more empathic one.

ALAN ALDA I still don't sleep well. I wake up and then I can't go back to sleep.

ANDREW LEUCHTER I'm sorry to hear that. Okay. Are you having a problem sleeping every night?

ALAN ALDA Yeah. Every night. Yeah.

ANDREW LEUCHTER Okay. I'm going to go down a list of some questions that I have to ask you here to see how you're doing, okay? Would you say you feel the depression everyday?

ALAN ALDA Oh yeah, yeah.

ANDREW LEUCHTER Okay, okay.

ALAN ALDA You know, I wake up with it. Wake up.

ANDREW LEUCHTER Right. Is there any time of day it's worse than other times of day?

ALAN ALDA Ah--I think in the evening.

ANDREW LEUCHTER Okay, okay. Do you feel that the treatment has been helping you?

ALAN ALDA Not to much, no.

ANDREW LEUCHTER I'm gonna jot down a couple notes here if that's alright.

ALAN ALDA (NARRATION) In his "old doc Brown" persona, the doctor in the new study will strive to build a bond with the patient, asking open-ended questions, maintaining eye contact even when making notes, and generally being as supportive as possible.

ALAN ALDA It doesn't seem to be working.

ANDREW LEUCHTER I'm sorry to hear that. Sometimes people do feel that way. It's important to remember that sometimes the medication can take a little while to work. So you might not notice the effect right away, but you may notice in the next week that you start to feel a little better.

ALAN ALDA But you know, it feels like nothing helps.

ANDREW LEUCHTER Let me just ask you a couple more questions here before we close. How has your appetite been?

ALAN ALDA Well, I eat when I'm depressed. I also eat when I'm feeling good.

ANDREW LEUCHTER Okay. You still have some sense of humor.

ALAN ALDA Well, yeah.

ANDREW LEUCHTER I think that you should stick with this. I think this is something that can help you. I hope you're willing to continue. And give it more time and see if, in fact, this treatment can help you.

ALAN ALDA Well, if you think so.

ANDREW LEUCHTER I think it's worth it.

ALAN ALDA Okay. I feel better already.

ANDREW LEUCHTER Okay!

ALAN ALDA (NARRATION) In his brisk HMO-doc persona, the doctor in the new study will still be polite.

ANDREW LEUCHTER Hi, I'm Dr. Leuchter.

ALAN ALDA Hello.

ANDREW LEUCHTER Good to see you. I've got a few questions for you today. I have to take some notes and see how you're doing.

ALAN ALDA (NARRATION) But this doctor will be focused on getting the clinical information he needs rather than trying to discover the needs and concerns of his patient. He'll make less eye contact.

ANDREW LEUCHTER So your mood's been down, depressed?

ALAN ALDA Yeah. I feel like nothing matters...

ALAN ALDA (NARRATION) His questions will be more pointed.

ANDREW LEUCHTER Appetite?

ALAN ALDA Well, I eat. But I'm not....

ALAN ALDA (NARRATION) Over the course of the study, patients will have their brain waves measured to see if there's a difference between the brains of the patients who get the warm doctor and those who get the cooler one.

ANDREW LEUCHTER Okay. Sleep?

ALAN ALDA Yeah, I don't sleep much.

ALAN ALDA (NARRATION) Andy Leuchter is the first to acknowledge that a study like this is fraught with problems, not the least of which is that the doctor-patient relationship is a two way street. For instance, for whatever reason, I find myself slightly preferring this more detached doctor than the one who was supposed to be warm and fuzzy.

ANDREW LEUCHTER Well, I think that taking this medication is an important part of your recovery. It can help you stay well, so we need to continue with what we're doing right now.

ALAN ALDA (NARRATION) But what's most fascinating about Andy Leuchter's planned study is that it will be one of the first to try to bring the tools of research medicine to the study of medicine's art - to try to quantify what has always been regarded as mysterious and beyond quantification.

ANDREW LEUCHTER Okay, very good. Thanks for coming in.

ALAN ALDA Okay. I don't know. What do you think? You think the other guy was better?

ALAN ALDA (NARRATION) When the original UCLA study was over, patients on the placebo were offered a real antidepressant, free of charge. Janis Schonfeld took up the offer and made a full recovery from her depression. Frank Strauss never made it beyond the first few days on placebo.

FRANK STRAUSS I say this sort of in jest, but I was too screwy to even stay with the study. So they sent me down the road to another place. They said, we can't help this guy, go down here. So I went down--.

ALAN ALDA You finally want to get a positive ending to this. You finally did get on a medication that helped you.

FRANK STRAUSS I did, yeah, right. Down from another organization. Finally I balanced it out and I've had the best years of my life since then. It's amazing what all that's happened. It's totally changed.

ALAN ALDA So it sounds like two different testimonials to say about placebos. Yours isn't so bad, but you don't seem to be a fan of placebos.

FRANK STRAUSS No. It's kind of like being in the desert, thinking you're getting a bottle of water, instead you're getting sand or something.

JANIS SCHONFELD It almost sounds like, really, one of the things that effects your reaction is your expectation going into it, don't you think? I mean, you had another need and want it than I did. Yeah.

FRANK STRAUSS I was interested in finding something that was a little better than the ones I was taking. So I thought this new--whatever it was would be the miracle drug that would fix me up. All of a sudden I get rich and find the girl of my dreams. All over night, you know.

ALAN ALDA The have a pill for that?

FRANK STRAUSS I was looking for it, you know?

EXPECTATION PAYS

ALAN ALDA (NARRATION) We're in Vancouver, British Columbia, where Sedric Bell is renewing a love affair with the latest version of a car he first drove over 40 years ago. Back in his native England in the 1960s, Sedric had great success racing Minis on some of Britain's major circuits. He emigrated to Canada 20 years ago. But then Parkinson's Disease stuck, stiffening his limbs and making movement difficult. Now it takes 16 to 20 pills a day to give him control over his body - and the dosage has to be tuned precisely.

SEDRIC BELL If it cuts in good, I'm as fit and agile as anyone. I can run, jump, anything like that. But when you're stiff, you're just as stiff as a board. If you're a little bit over my head's flopping all over, there's no control over my muscles. People say, "relax." I can't relax. There's no connection. My head can't tell my arm and leg to relax. It's just lock solid until the medication works through.

JON STOESSL Just relax your head, let it go loose. Okay, very good. Now just open and close your hands, would you please?

ALAN ALDA (NARRATION) Sedric was recently one of the Parkinson's patients volunteering for a study conducted by Jon Stoessl and his colleagues at the University of British Columbia Hospital.

JON STOESSL Now open and close your left hand.

ALAN ALDA (NARRATION) Like Andy Leuchter at UCLA, Jon Stoessl planned a study of real drugs - but ended up instead with startling new evidence about how placebos affect the brain. The tests Sedric's going through are standard for assessing the severity of a patient's impairment due to Parkinson's. His right side is more affected than the left, showing up mostly in his slow and difficult movements, but also - especially when he's stressed - in the tremor most of us associate with Parkinson's.

JON STOESSL The tremor is often not a prominent feature, even though it's a very common feature, it's often not the most prominent feature for people and, in fact, it is very uncommon for it to be the disabling feature of Parkinson's. The disabling feature is the poverty of movement, the slowness of movement.

SEDRIC BELL It's rare that I shake. See. It's very rare. The only time I notice it is on the transition of the medications when it's coming on and going off. I may get a little bit of --. It could be any part of the body. And then it just settles down when it goes in. And generally I should be good for three hours with the medication I take.

ALAN ALDA (NARRATION) The medication is levodopa, which in Sedric's brain helps replace dopamine, one of the brain's communication chemicals, and essential for controlling movement.

JON STOESSL When we start treatment for Parkinson's, people get a good response for a few years, or several years. But after a few years, they get into the trouble, often with the benefit of the medication wearing off before the next dose is due. So we were doing studies to try and better understand why that might occur, and those studies involved looking at the amount of dopamine that's actually available to the nerve cell.

ALAN ALDA (NARRATION) Measuring how much dopamine is released in response to medication involves a trip to the hospital basement...

NURSE Her we are at Positron Emission Tomography.

ALAN ALDA (NARRATION) Where Sedric has spent long hours lying in the PET scanner.

SEDRIC BELL The bed knows me.

NURSE It does. Yes.

ALAN ALDA (NARRATION) During this time, his head must be perfectly still. A mask that's flexible when warm and can be molded to his face dries into a rigid head restraint.

TECHNICIAN And as it cools it's going to harden to the shape of your face.

ALAN ALDA (NARRATION) Parkinson's is one of those conditions - like depression - that in many patients can be alleviated - at least for a while - by a placebo. So it was especially important to include in the trial of active dopamine-releasing drugs a placebo control.

JON STOESSL They were told explicitly that they would be receiving three or four injections of drug. One of which would be an inert substance. They were not told in which order those injections were to be given.

ALAN ALDA (NARRATION) As expected, the PET scans showed an increase in dopamine release in the brains of subjects receiving an active drug. But what was not expected was that there was just as big a dopamine release in the brains of some patients - like Sedric Bell - when the injection was of an inert placebo, a saline solution.

JON STOESSL It was initially, certainly a big surprise, and then when we stopped to think about it it became somewhat less of a surprise in that it's been recognized for many years that dopamine is somehow involved in reward mechanisms in the brain. So when we have things that we enjoy or that we look forward to....Drug addicts, for instance, get their reward related to dopamine release. So if you think about it, the placebo effect has everything to do with the expectation of benefit and that, I think, could be very analogous to reward.

TECHNICIAN Okay, we're going to bring you out now. You did well. Good job.

ALAN ALDA (NARRATION) Making the Vancouver study even more remarkable was the fact that the placebo released dopamine in precisely the same place in the brain as do the real drugs - just where it's needed to activate the pathway that controls movement. And to top it off, volunteers like Sedric whose PET scans revealed dopamine release in response to placebo also improved when run through the standard test battery - again, just as you'd expect if he'd received active medication.

NURSE So you're a little better than you were earlier.

JON STOESSL I think this is really a tremendous example of the mind controlling the body. Those of us who work in neuroscience regard these as closely linked. We don't really think that there's something different about the mind. But this is

really the classic example of how your expectation of something, your attitude towards something can materially affect the physical outcome, that it's not just loosely how you think about whether or not you responded. But there is actually a physical explanation.

SEDRIC BELL It's like trickery, you know? They tell you they've given you whisky but they haven't. It's great surprising that things turned out like that. To take something that activates your dopamine cells. And it isn't supposed to do anything like that at all. It's truly amazing.

SNUFFING THE SNIFFLES

ALAN ALDA (NARRATION) We've seen how the expectations aroused by placebos can affect the brain. Those same expectations can make drug research an often very messy business. These volunteers, whose noses are being rinsed out with a saline solution, are being paid to catch a cold.

ALAN ALDA If you wash his nostrils out he'll have a better chance of catching cold?

BARBARA WRIGHT Mm, mm. 'Cos the nose'll be nice and clean.

ALAN ALDA This is a horrible thing to learn first thing in the morning. OK, go ahead. I mean I would have thought that getting your nose clean -- like, you know, they say, keep your nose clean -- I would think that would help.

ALAN ALDA (NARRATION) The man dispensing the colds is Ronald Turner. What he's carefully placing up the nostrils of his volunteer subjects here in Charleston, South Carolina, is a strain of rhinovirus, one of the commonest causes of the common cold.

ALAN ALDA Now you already had one of these?

ANNE SANDERS I had one. I had one already.

ALAN ALDA So how many do you give?

RONALD TURNER Two. We just go around twice.

ALAN ALDA You really want to make sure you make these poor people sick.

RONALD TURNER OK, this is the same as before.

ALAN ALDA (NARRATION) Actually, Ron Turner is hoping some of his volunteers won't get sick...

RONALD TURNER Here we go again.

ALAN ALDA (NARRATION) ...because for the last two weeks some of them have been taking twice-daily doses of one of those herbal extracts that a lot of us believe helps fend off or shorten a cold.

RONALD TURNER Some are getting active medication, some are getting placebo. Everybody gets the virus.

ALAN ALDA Now do you know, are you aware of who's getting the placebo and who's getting the medication?

RONALD TURNER No, we're all blinded.

ALAN ALDA You don't have any idea?

RONALD TURNER No.

STEVE SCIBELLI This is what they look like.

ALAN ALDA The famous ju-ju bead medication. So what do you think is in there?

STEVE SCIBELLI I'm really not sure. Hopefully some medication that will take care of me. But for all I know it could be just sugar pills.

ALAN ALDA (NARRATION) This need to ensure no one knows who's getting what is absolutely critical in a trial like this. It's especially important that the volunteers aren't picking up any clues from how the pills taste or make them feel.

RESEARCHER Do you think you were getting the active medication or the inactive medication?

ANNE SANDERS I think I was getting the inactive.

ROBERT BOZARD I have no idea. I really don't. I had no side effects, no symptoms of any kind either way, so...

RESEARCHER OK, give me a guess.

ROBERT BOZARD Active.

RANDREA MAJORS Inactive.

DAVID MIN I think I was getting inactive.

EDDIE GORDAN Active.

RESEARCHER And why?

EDDIE GORDAN I don't know. It was just that whenever I took it I felt, like, fuller.

MIKE LEWIS I would have to say the active medication.

RESEARCHER Why would you say that?

MIKE LEWIS It'd kind of depress me if I was having the other medication.

LINDSEY DUGAN I would say the inactive.

RESEARCHER Why would you say that?

LINDSEY DUGAN Just because I didn't feel any difference.

ALAN ALDA Do you think it matters whether or not you believe you're taking the active ingredient?

LINDSEY DUGAN Yes. I think if I thought I was on it, I would definitely experience a placebo effect and feel better than maybe I should. And thinking that I'm not on the medication I might be more inclined to feel the symptoms more severely.

ALAN ALDA (NARRATION) Lindsey's right: if people are able to figure out what they're getting, then it could dramatically influence the results of the trial.

STEVE SCIBELLI I'll go with active.

RESEARCHER Why do you say that?

STEVE SCIBELLI I'm hopeful.

ALAN ALDA (NARRATION) In fact, in Ron Turner's opinion, the placebo effect - and in particular the difficulty of eliminating it - is why we're all so confused about popular cold remedies like echinacea or vitamin C. Take one of my favorites, for example, zinc lozenges.

ALAN ALDA Is it true that, even when you're not in a study, when you're just sick and taking this lozenge, the fact that it tastes funny, might increase the placebo effect for you and may help you feel better sooner. Is that possible?

SCIENTIST Yeah, I think that's the old-It's gotta taste bad to be good-concept. You know-good medicine has got to be, in some way-onerous. There's got to be some penalty for getting better faster.

ALAN ALDA If we in fact believe that on some deep level, then it might be a self-fulfilling prophecy. Is that right? Is that the way it might work?

SCIENTIST Sure. I think clearly that's a possibility. And, in fact, you might say, "well, so what?" If that's the benefit you get, that's good.

ALAN ALDA Alright, okay, I'm desperate now. What did you put in the study today? Maybe I can take that. I mean even before you find out in your study that it's no good, I'll have a couple of colds that I can use it on and get the placebo effect.

CAROLINE SWAIN Definitely have the cold. The cold, I have it.

MIKE LEWIS I don't feel ill at all. If I'm supposed to be ill right now, I'm not ill.

UNKNOWN I have the cold.

ALAN ALDA (NARRATION) Three days have passed since our volunteers were infected with the cold virus. They've been reporting in every morning since.

RESEARCHER It's been about 72 hours since the inoculation. Do you think you received a cold?

STEVE SCIBELLI Yeah, I do. I definitely had it yesterday.

RESEARCHER OK, I want you to rate your symptoms this morning, based on the severity since your last visit. Any symptoms of sneezing?

STEVE SCIBELLI I'd say about a two.

RESEARCHER OK. Runny nose?

STEVE SCIBELLI One.

RESEARCHER Nasal stuffiness or obstruction?

STEVE SCIBELLI Two.

ALAN ALDA (NARRATION) There are a dozen symptoms on the list -- enough to get a pretty objective measure of the severity of the cold.

RESEARCHER Definitely getting a little bit worse, huh?

STEVE SCIBELLI Yeah.

RESEARCHER OK, you can go on back and get your nasal wash.

ALAN ALDA (NARRATION) The nasal wash will reveal how strongly the virus took hold. Meanwhile we wondered how our volunteers feel now about whether they are on the test medication or the placebo.

ANNE SANDERS I think I'm receiving just a placebo.

DAVID MIN I think it kind of got better because I was taking... I'm not sure whether I had that medication or not, but I think I did.

EMILY WORREL I believe I had the inactive medication. Because otherwise I think I wouldn't have got the cold or it wouldn't have been as severe.

KATHERINE HOEFT Based on how mild my symptoms are, I think maybe I did get the active.

RANDREA MAJORS Oh, yeah, I'm really glad I got it. Otherwise I'd be walking around with tissues hanging out of every pocket, and just not a pretty sight.

LINDA MIELCAREK I think I got the inactive medication because I've been getting worse as the days go on.

LINDSEY DUGAN I guess I got the active medication, 'cos all I've had is a runny nose and that's it.

ALAN ALDA (NARRATION) Surprise, surprise -- most of those with the worst colds thought they were on the placebo, while most subjects with mild colds guessed they had the medication. But in fact it was all in their heads. Later, when who got what was matched up with the severity of their infections, there was no difference between those who got the test substance and those who got placebo. That's right, the mystery herbal ingredient in those big brown pills did no better - and no worse - than the placebo -- a judgment Ron Turner also makes about most other popular cold remedies.

ALAN ALDA You know what's funny about this? And this is just totally personal. I'm going to keep taking this stuff, because I haven't got any other feeling of control over the cold. And for me getting a cold, because I have to use my voice in my work, is something that... I'll clutch at straws. How does that strike you as a scientist?

RONALD TURNER Well, I guess I don't have any problem with that. As I said, my job here is to try to figure out whether there is a biologic effect. Whether people choose to use that information or whether they get some benefit -- whether it's psychological or mental -- that's fine. You know, the saying is of course that if you take this medication you'll get over your cold in 7 days and if you don't it will take a week. So...

ALAN ALDA That's the best you can come up with? After all these years?

RONALD TURNER Well, I think we're doing better than that. I think we're doing better than that.

HEALING RITUALS

ALAN ALDA (NARRATION) One of the most mysterious of medical treatments is acupuncture. Thousands of years old, still practiced widely in China, it has in recent years edged into mainstream medicine even here in the United States.

ACUPUNCTURIST The patient is suffering from insomnia. Maybe due to stress, maybe due to heart Qi deficiency. Because he is a student he has a lot of stress.

ALAN ALDA (NARRATION) Acupuncture's growing popularity comes despite its striking contrast to conventional western medicine. Its theoretical underpinnings, involving the manipulation of a force called Qi through energy channels in the body, has no known basis in how Western medicine believes the body to work. People go to acupuncturists for one good reason -- many feel better as a result. But while some scientific studies suggest acupuncture may relieve pain by releasing natural painkillers in the brain, the power of acupuncture to heal some people of some conditions remains mysterious. Mysterious, exotic and tantalizingly different from establishment medicine - just the formula to entice a 1960s student radical to China to study traditional Chinese medicine. Ted Kaptchuk spent several years there, returning to the United States skilled in herbal medicine as well as acupuncture - which he practiced here with a success that surprised even him.

TED KAPTCHUK I said to myself, I'm not as good as practitioner, I'm not as good as acupuncturist as my teachers. But I kept seeing people get better much quicker than I saw in clinics where I worked in China. And it occurred to me that maybe the exoticness, the ritual, the complexity, talking about mysterious forces may indeed elicit a ritual response, or elicit a kind of magical capacity for self-healing that's actually greater.

ALAN ALDA (NARRATION) Ted Kaptchuk, now firmly back in the medical establishment at Harvard Medical School, wondered if this "magical capacity for self-healing" has more to do with the placebo effect than with Qi. So he's designed an elaborate study of RSI - repetitive stress injury, or carpal tunnel syndrome - the pain many people experience after hours spent at a keyboard. Some of the patients in the study will get a pill - either a real drug or a look-alike placebo. Others will get acupuncture - either real or a placebo, sham acupuncture. What Kaptchuk really wants to find out is how the two placebo treatments stack up against each other: is the placebo effect of sham acupuncture - with all its rituals and mystery intact - more effective than the placebo effect of simply popping a pill?

TED KAPTCHUK And that's what's unusual about this particular experiment. It's saying, no longer do we take the placebo effect and just throw it in the waste paper basket. Let's look at these placebo effects as a major question, a major component of medicine, a major consequence in health care. To what extent does the ritual, one particular ritual, in this case the ritual of acupuncture versus the ritual of taking a pill. Those rituals are different. What's the consequences of those rituals in terms of people feeling better, in terms of people feeling more intact, being able to work better. How do those rituals--? Do those rituals elicit different healing?

ALAN ALDA In this study, you replicate the experience of acupuncture without actually giving acupuncture. How do you do that?

TED KAPTCHUK The basic idea is that the needle...It's a magic sword principle. When you have a magic sword you stick it in. But instead of the shaft of the sword going into a person, it goes up the handle, so it retracts. So basically this is a needle that looks like it goes in, it feels like it goes in, you see it go in, but in fact it goes up the shaft. And in fact, the first time it was done to me I was sure that they had made a mistake and had given me the real needle.

ALAN ALDA Okay, don't make any mistake and try it on me. Let me see here. I actually have a little inflammation in this finger, so, would you stick me someplace where it would help that finger?

TED KAPTCHUK Sure. I'll cure it for you.

ALAN ALDA Thank you. Because... By the way, even when I know it's a placebo it cures me, so, this'll be fine.

TED KAPTCHUK So basically, this is just.... We do this to both the real needle and the fake needle. The needle is indistinguishable. It's a real needle. There's no way you could tell this is not a regular needle.

ALAN ALDA I feel it. Yeah. I felt it.

TED KAPTCHUK That's the way a real needle would work, and that's the way our placebo works.

ALAN ALDA It's also the way it would happen if the producer was tricking me into getting a real needle because I don't want any real needles in my hand. And this is exactly the way it would happen.

TED KAPTCHUK Well, actually we'll have to see. Make sure it's the placebo needle. We'll pull it out. Should I pull it out? And that's it. And then we take this away and that's it. Now, does it cure your hand?

ALAN ALDA It's only a little worse.

TED KAPTCHUK It's gonna get much better in five minutes.

ALAN ALDA Okay, five minutes.

TED KAPTCHUK Let me assure you.

JOE KAY Kathleen, how much pain would you say you're in in terms of your right arm? Would you say mild, moderate, or severe?

KATHLEEN Um, moderate.

JOE KAY Moderate. How bothersome is the pain?

ALAN ALDA (NARRATION) Joe Kay is one of several licensed acupuncturists who are lending their services for the trial.

JOE KAY And how much does the pain interfere with your life? Would you say mildly, moderately, or severely?

KATHLEEN Moderately.

ALAN ALDA (NARRATION) He'll be using the discs and tape - so that the sham needles won't simply fall out - on all the subjects in the trial.

ALAN ALDA People who come to you as part the study who have had acupuncture before, are there people like that?

JOE KAY Yes. Yes, certainly.

ALAN ALDA So when you suddenly put the disk and the tape on them, do they say, what's this? I've never had acupuncture like this before.

JOE KAY Many times. But again, with acupuncture, there's many different styles of acupuncture. It's been around for a couple thousand years so there's many techniques that are used. And I just explained to people that this is one technique that's used to make sure that we get the exact point.

JOE KAY Okay. That feel okay?

ALAN ALDA Now the patient doesn't know if these are an actual application of acupuncture needles or a sham procedure?

JOE KAY Right. Even if the patient has had an acupuncture some place else. They really don't have any idea.

ALAN ALDA And neither do I know, if it's real or not.

JOE KAY Right.

ALAN ALDA Now keep going. I want to see if I can guess.

JOE KAY Okay.

ALAN ALDA Would it spoil things for me to say what I think it is?

JOE KAY No.

ALAN ALDA I think it's the real thing.

JOE KAY Okay.

ALAN ALDA There's something about the way you had to get it in there. It didn't seem like the fake needle.

JOE KAY You could be right.

ALAN ALDA So let me just get this part of it straight. This is sort of a placebo effect we're doing here. Kathleen, you're not really a patient.

KATHLEEN No, I'm not.

ALAN ALDA This is just demonstrating how the study works. KATHLEEN Right.

ALAN ALDA So--. Do you know what kind of a needle was going into you?

KATHLEEN Honestly, I thought I'd be able to tell, I really did. I'm gonna have to ask Joe. I really don't know what I had. I really don't.

ALAN ALDA What was it, actually? What were you putting in her?

JOE KAY I actually used the placebo needles.

ALAN ALDA The placebo needles.

KATHLEEN Wow.

ALAN ALDA And you couldn't tell--.

KATHLEEN I couldn't. I thought I was getting the real treatment. I thought Joe was going to tell me later he really used the needles. I'm surprised. I really am.

ALAN ALDA (NARRATION) Kathleen wasn't the only subject to be fooled by the fake procedure.

JOE KAY I had one participant in this study who I was using the sham needles on, and it was someone who had RSI for many years. And after about four treatments, it was completely gone.

ALAN ALDA After four treatments, the person was okay?

JOE KAY After four treatments...they were okay.

ALAN ALDA And had they had any kind of acupuncture treatment before?

JOE KAY No, they never had acupuncture before.

ALAN ALDA And so they got better from the sham needles.

JOE AKY Right.

ALAN ALDA Wow. How did that make you feel?

JOE KAY Ah, well, from the standpoint of an acupuncturist it made me feel great because the person was better. But, on the other end, though, it was like, gee, what happened there?

ALAN ALDA I wonder if those twenty years of treating people has given you a sense of authority in relation to the patient that's curative in and of itself. You know, they come in, they get a treatment from you, they think, "this person clearly knows what he's doing. I'm gonna get better here." That's not to say that-- That must be part of doctoring.

JOE KAY Yeah. Ultimately, if that's the case, then that's fine. If a person gets better then that's what my goal is.

ALAN ALDA Now, this raises.... I really am interested to know -- why are you taking part in this project? Because, what if it's found out, in the course of this study, it's really not the insertion of a needle in the right place that does it, that has the positive effect. It's just the ritual surrounding it, that the sham needles are just as good as the real needles. What would that do to your practice?

JOE KAY I don't think it would do much to my practice. There's a placebo aspect to any sort of medicine. I mean, even in conventional western medicine as we know it, there's a placebo effect that's in there. And I really feel pretty strongly that, you know, once the data has actually all been crunched, that we'll find out that the real acupuncture is the real thing. If it doesn't and I'm proved wrong, I don't think it's going to necessarily disappoint me or make me change my profession or whatever.

ALAN ALDA But it might make you change your needles. I mean, you--.

JOE KAY I won't change my needles.

ALAN ALDA (NARRATION) But remember, the real focus of this study - which Ted Kaptchuk is still running -- isn't to find out whether placebo acupuncture is as good as the real thing. It's to see if the placebo effect is greater when there's more ritual surrounding a treatment, as in acupuncture, than when the treatment is nothing more elaborate than swallowing a pill.

TED KAPTCHUK Unless we begin to address those questions, a big part, a big big part of what medicine's about, gets left behind, gets put in a trash basket. And one of the things that it's exciting about the new development in placebo research is, some things that are in that trash basket is precious, it's an important

ingredient of what makes people healthy. It's an important ingredient for what makes people feel better. And we have to bring it on to the table.

ALAN ALDA (NARRATION) In the shadow of the Alps, the city of Turin has become well known among researchers exploring the placebo effect. Fabrizio Benedetti and his colleagues - including Antonella Pollo - have in the last several years conducted a series of startling experiments here in the pain clinics of some of the city's largest hospitals. Today, Luama Collosa is the volunteer subject for one of these experiments. The Turin group is studying placebo analgesia - the relief from pain that many people experience when they believe they're getting a painkiller, but in fact are not. In this series of experiments, the Italian researchers will rely not just on Luama's reports of the pain she experiences, but will also be measuring her body's reactions.

FABRIZIO BENEDETTI This is for EKG, electrocardiogram. Electrocardiogram because we want to see whether or not there is an increase or decrease in heart rate during the induction of pain, the experimental pain.

ANTONELLA POLLO These two leads are to measure skin conductance and this is to measure respiratory rate, it goes up and down with the respiration and it comes up as a signal on the screen.

ALAN ALDA (NARRATION) Luama's blood pressure is also being monitored, along with heart rate, breathing rate and skin conductance - a measure of how much she's sweating. The pain she'll experience is induced by inflating a blood pressure cuff, cutting off the blood supply to her arm and hand.

FABRIZIO BENEDETTI In a scale from zero, which means no pain to ten, which means unbearable pain, she will experience around usually after ten minutes, usually about six, seven.

ALAN ALDA (NARRATION) On this day, Luama is getting no treatment, either real or placebo. The goal is to see how her body reacts - to get baseline measures of its response to the pain in her arm.

ANTONELLA POLLO She said that she experienced on a scale of one to ten a pain of six.

ALAN ALDA (NARRATION) The next day, the set-up is the same, except that now she is receiving an injection for the pain. No one in the room knows what she's getting.

FABRIZIO BENEDETTI She knows that she can receive either a placebo or a painkiller.

ALAN ALDA (NARRATION) In previous experiments, the Turin team has shown that when a placebo injection lowers the subject's experience of pain, there's an increase in the brain of natural painkillers, morphine-like chemicals called endogenous opioids. What's more, giving a drug that blocks these opioids cancels out the pain relief caused by placebos.

FABRIZIO BENEDETTI So this means that there is a close correlation, a tight correlation, between activation of endogenous opioids and analgesia, placebo analgesia.

ALAN ALDA (NARRATION) These new experiments are revealing that the body's response to pain also changes during placebo analgesia - so the placebo effect is much more than in the mind. Although the mind must be where it begins - in the expectations of the patient, triggered - as all the new research we seen in this show confirms - by the still mysterious chemistry between a hopeful patient and a caring doctor.

FABRIZIO BENEDETTI They should smile, they should talk to their patients, they should interact a lot with their patients, because there is a very strong indication that all these mechanisms - for example the endogenous opioids, the endogenous painkillers - are released when the patient feels safe, feels comfortable with the doctor.

TED KAPTCHUK Ultimately the way a single human being reacts to a single human being is going to be part of the art of medicine. And I think we can learn a lot about it from research. Do I think science will take all the mystery out of healing? I don't believe so. I think that there's going to be an element of the shaman residing at the core. My effort to do research in placebo is to acknowledge that core, not to destroy that core. 'Cause I don't think it can be destroyed.

[return to show page](#)

© 1990-2002 The Chedd-Angier Production Company, Inc. All rights reserved.