On October 26, 2003, the Southern California Permanente Medical Group (SCPMG) commemorated its 50th anniversary with a celebratory event in Pasadena. In addition to the presentations of a video and a book on SCPMG History, we recognized Dr Oliver Goldsmith for his ten years as SCPMG’s Medical Director and Dr Irwin Goldstein for his 22 years as SCPMG’s Associate Medical Director/Physician Manager of Operations.

We planned a keynote address by Dr Jerome Groopman, Professor of Medicine at Harvard Medical School at the Beth Israel Deaconess Medical Center and a staff writer for The New Yorker magazine in medicine and biology. Unfortunately, Santa Ana winds whipped up brush fires throughout Southern California that weekend, and when the traffic control center for all Southern California was evacuated for almost 24 hours because of the fire, flights in and out of LA were delayed or canceled—including Dr Groopman’s. By the time he arrived in Los
Angeles, it was too late to speak at the 50th Anniversary Celebration, but later that week (upon his return to Boston) he videotaped the remarks he was going to give.

In 1997, Dr Groopman published his first book entitled: "The Measure of Our Days." It presented eight moving portraits of patients facing serious illness. He offered his readers a compelling look at what is to be learned when life itself can no longer be taken for granted.

His second book, entitled "Second Opinions," was about navigating the world of medicine, where knowledge is imperfect, no therapy is without risks, and the outcome is never fully predictable.

His third book, "The Anatomy of Hope," published in January 2004, was the topic of his remarks to commemorate SCPMG’s 50th anniversary. Both the book and Dr Groopman’s remarks offer lessons to both patients and health professionals.

— Les Zendle, MD, Past Associate Medical Director, SCPMG

Physicians, nurses, social workers, psychologists—all of us involved in caring for patients—occupy a unique perch. We are intimate observers of life’s mysteries. We witness the miracle of birth and the defining moment of death. We are close to people who, under extreme circumstances, search for meaning in the midst of suffering.

I’d like to talk about “The Anatomy of Hope.” This work is a mirror to my limits and my shortcomings. It charts a 30-year journey searching for an organizing principle to coalesce around my work and personal life. I realized that as much as my patients search for meaning, I, as their physician, search for meaning.

This project of trying to understand hope came around at the end of a long, very trying week, when I was walking back from the ward to my laboratory, after seeing people with blood diseases and cancer and AIDS. I asked myself what more I could offer these patients whom I had seen that day? The answer that came to my mind was “hope.” And that answer was at once both exhilarating and terrifying.
Pandora’s Box

In Maurice Lamm’s book, *The Power of Hope*, he wrote about his daughter, who had leukemia: “We know in our bones that hope is everything, but in the back of our minds we suspect that it’s nothing at all.” I began to wrestle with this idea of hope’s power and fragility as I read more deeply about it. I came across the myth of Pandora and discovered I did not know the full story. Everyone knows the expression “Opening Pandora’s Box” means you’re releasing troubles into the world by opening something up, sticking your nose where you shouldn’t. But the full myth reflects the deep wisdom of the Greeks. Pandora was the first mortal woman. Zeus gave her a box. In the box were all human curses, all the troubles that one could imagine, but also all human blessings. She was told not to open the box and, as these stories go, temptation gave way to curiosity. She opened the box and all of the world’s troubles were released and all human blessings escaped and were lost, except for one, Hope—because without hope, the Greeks knew, mortals could not endure.

That myth resonated very, very deeply within me. I realized that this was indeed a revelation to physicians of my generation—but really is not a revelation to those who came a generation or two before. I grew up and was educated in the early 1970s, when the molecular revolution was exploding. The pursuit of my career largely followed this pursuit of hard science. I left Harvard to go to the University of California, Los Angeles, because Caltech and UCLA were collaborating around recombinant DNA technology. This was “real, hardcore” medicine. This was science finally entering the domain of clinical work, and it was intoxicating. And, indeed, science is wonderful and is marvelous but it is not the whole story. Far from it. CAT scans and MRI scans came around that time. Now we have gene arrays and proteomic analysis. We can probe so deeply, using crystallography, and obtain an atom-by-atom understanding of the pathogenesis of a disease. Where is hope in all of this? During my training and during my early years of clinical practice, very little attention, if any, was paid to hope. In fact, it was denigrated, seen as soft and squishy. Anyone who would pause and try to talk about the turmoil in a patient’s heart and soul received raised eyebrows, a shrug. Perhaps he was indulged for a minute or
two but not much more. The real goal, the eye on the prize, was to clone genes and crystallize proteins and publish papers in *Science* and *Nature* and the *JCI* and thereby ascend the academic ladder. This was the true calling of the physician-scientist.

A 30-Year Journey

At this point in my life, entering my fifties, I went back to chart a journey, a 30-year journey to try to understand questions that now were terribly urgent because I’d come to believe that giving a patient hope was as important as any prescription I might write or any procedure I might perform. I wanted to understand how to distinguish true hope from false hope, whether a person should ever relinquish the right to hope, how what we hope for might change during the course of an illness, and, most important, whether there was an authentic biology to hope. There are so many New Age claims, eg, that if you just meditate your pancreatic cancer will go into remission, or if you think positively, your immune system will be boosted and your HIV will be brought under control. I fled from any suggestion along those lines because it seemed like magic, not science. I was so turned off by extravagant claims that I basically slammed the door on considering whether there could be a biology of hope. But if you stop and think about it, closing the door showed tremendous ignorance, because there is a biology of fear, a biology of anger, and a biology of depression; there’s a biology of every emotional state, so why not a biology of hope, an authentic biology of hope? And the question became what is its reach and what may be its limits?

I went back and began to think about my life as a doctor and my career in the clinic and the laboratory using this organizing principle of hope. It took me nearly two years to begin to understand what I had learned from my patients—because they were my greatest teachers. It also took me that time to be honest and candid and open and vulnerable as a doctor—to really show those moments when I was weak and blockheaded and blind to what my patients were asking me for. Because they were asking me for hope—and I’m still not sure I’ve completely succeeded in learning how to best give them true hope.
I’ll give you a taste of some of the lessons from the most instructive individuals I’ve cared for. There was a young Orthodox Jewish woman whom I encountered when I was a medical student at Columbia in Manhattan. I was on the surgery rotation, and I was very charged up. I felt surgeons were the emperors of the clinic. They were men of action. (There were virtually no women; in fact, I don’t think there was a woman surgeon on the staff. Any woman interested in surgery got shuttled into pathology.) So these were the real men of medicine. One day, this young, attractive, very religious woman came to the medical center and was cared for by a senior surgeon. She had a very large breast cancer, four centimeters in diameter, with multiple easily palpated lymph nodes. It was clear that she must have felt it. I couldn’t understand why she would let this progress to such an extent. As the story unfolds, she confided in me that her whole life had been one in which things were dictated to her. She had an arranged marriage, as is common in very Orthodox circles, and she felt she was suffocating. She had three lovely children. She had no real link with her husband. So she had an affair with her employer.

She had no illusions that her employer was in love with her but those were the only moments when she could feel free. Then she developed breast cancer, which she interpreted as a punishment from God. She told me she would refuse to be treated with chemotherapy.

I was clearly in over my head. I had thought, “Oh I can understand patients, I know how to handle them. I know how to take information.” Although I was well prepared for the science, I was pitifully un-prepared for the soul. As it turned out, the senior surgeon ultimately convinced her to be treated. How he did this, I don’t know. Such things were not shown to medical students. Conversations of this intimacy occurred behind closed doors, so I never learned how. For a while, this encounter bothered me, but then it drifted from my mind. Only many years later did I begin to think about this. I began to see this woman’s case in more than simply narrow terms. It was easy to just ascribe and dismiss her resistance to treatment as an outgrowth of a fundamentalist theology, where disease is equated with punishment for sin. Only in my fifties, thinking about it more deeply, did I realize that she belonged to that
large universe of people who believe that they are undeserving of hope. Her religious background and beliefs were only the particular language, the metaphors, in which hopelessness was cast. I began to realize that hope can only arrive when you recognize that there are real options and that you have genuine choices.

**The Core of Medicine**

Hope can only flourish when you believe that what you do can bring a future different than the present. To have hope is to acquire the belief that you have some control over your circumstances, that you are no longer entirely at the mercy of forces outside yourself. At the time, as a fourth-year student, I had no insight into any of this. My blindness was sustained for a long time, through internship and residency, where I encountered patients who resisted effective therapy—what I saw as effective therapy—patients who were willing to mortgage their future. I didn’t understand why, and it boiled down to hopelessness. These patients were dismissed by doctors as being recalcitrant or noncompliant, and they were opaque to me. I did not understand what they were saying to me, and I had no clue what words or actions they needed from me. I don’t mean to minimize this. It is very hard to move someone from a state of hopelessness to hope—to true hope. But, I believe now that movement is imperative and is at the very core of medicine.

**Other Forms of Hope**

One of the greatest lessons I was taught about hope came from a mentor, a fellow physician named George Griffin, MD. Dr Griffin was from a Yankee family with deep New England roots. He was the chief of pathology in our hospital. This was in the 1980s. I was in my 30s at the time, and Dr Griffin was in his late 50s. He was one of the world’s experts on stomach cancer. No one knew more about stomach cancer than Dr Griffin. And then, I heard he was diagnosed with stomach cancer, a poorly differentiated stomach cancer that had metastasized to the lymph nodes and surrounding tissues of the stomach. Dr Griffin insisted on this extraordinarily aggressive program of chemotherapy and radiation, followed by surgery and then more chemotherapy. As a young oncologist, new to the staff, along with the other young attendings, I thought he was out of his
But it turned out Dr Griffin was not in denial. He went to the CEO of the hospital and explained that his chances of living 12 months might be on the order of 1% to 3% and that his chances for 18 months were less than 1%. Dr Griffin had even planted daffodil bulbs in his garden at home that he believed would grace his coffin at his funeral.

Thirteen years after his diagnosis I was sitting in the atrium café of the hospital and I got up from my chair to greet him. He was retired in New Hampshire with his wife, and it was clear he was cured. He had recovered and was able to contribute actively to his church and community. I had never had the courage to speak to Dr Griffin, but since I had seized on this project to write about hope, I wanted to interview him and to ask how he made his decisions. I also had a deep sense of guilt because, along with virtually the entire young clinical staff, I had written him off. If I had been his managing oncologist and he had followed my advice, he would be dead. So he explained to me his thinking, and he told me that he always knew the odds. There was never a moment of denial or delusion. He knew all the arguments against treatment, but Dr Griffin asserted that it was his right to choose to do what he did. Even if he didn’t prevail, it was his only chance. He deeply, deeply wanted to live, and he told me that this is what impelled him to fight. I realized this was very much a libertarian mindset: he saw himself as an individual who would be the ultimate arbiter of his life. I realized that there are other forms of hope: hope to be strong enough not to yield; hope to have determination and fortitude to fight; hope to muster the will to engage the foe and the strength to sustain the battle. This strong hope, in and of itself, not for everyone but for people like Dr Griffin, becomes a form of victory, because, as he saw it, surrender would be on his terms.

Oliver Wendell Holmes, Sr, an eminent 19th-century Boston physician and poet, wrote “Beware how you take away hope from another human being.” I think we have this tension to be truthful with our patients but not to snuff out hope. Dr Griffin was truthful with himself, but, he said that a doctor should not sit like a presiding judge who hands down a fixed sentence of life and death measured in days or weeks or months.
Beating The Odds

As physicians, we are not omniscient. We don’t know when life will end and death ensue. I’ve come to believe that we should never totally write a person off a priori: because sometimes, as in Dr Griffin’s case, the tumor does not read the textbook. Over the course of some 30 years, I’ve had other patients with “incurable diseases” who beat the odds and lived much longer than anyone predicted. If, for example, I had said to one of them, the mean and median survival for inflammatory breast cancer in your case is “X” months and we have no good treatment for it, that patient would now tell me, “you were wrong and you’re ignorant,” because it’s been 20 years since her diagnosis. Her breast cancer comes and goes. I even reviewed the pathology to make sure it was cancer and the diagnosis was correct. But she’s on the far end of the bell-shaped curve. If she had not been given hope, she might not have even tried therapy and she wouldn’t be alive.

The other form of hope in the face of such desperate odds is that science may catch up in time. This event doesn’t happen, alas, as often as all of us pray for. But it has happened in my career with testicular cancer, with AIDS, with the advent of bone marrow transplant, and now with new drugs for lymphoma. It’s a moving target, and people who literally were on the cusp of death can be brought back.

Provide Choice and Understanding

I once hesitated to recount such anecdotes to patients and their families because I feared raising false hopes. Now I believe that if a patient understands his or her own condition and chooses Dr Griffin’s path so that the choices are not made in denial, that patient has every right to hope. It is not as simple as I once thought. I believe that it’s our place, as doctors, to provide choice and understanding to allow for hope, even under the most extreme circumstances. And that is a profoundly human act.

The Biology of Hope

I’ll close by talking about the biology of hope. Again, I think that hope is not some magic wand as depicted in those extravagant
claims that if you only think positively, it will all go away. There are many, many people who think positively and succumb to illness. But if we look, interestingly, ironically, at the placebo effect, where belief and expectation are cardinal components of the placebo response, we get a glimmer of what might be a biology of hope. Fascinating studies are being done in Italy by Fabrizio Benedetti on pain. These are experiments with normal volunteers. The scientists inflate a blood cuff around the arm and bring it up to 260 mm mercury, which is quite painful, so they have a quantitative painful stimulus. In these experiments, the volunteer is given a very low dose of morphine and, of course, being premedicated with morphine, there is reduction in the amount of pain felt. Then there is a sleight of hand. The researcher gives the volunteer saline, a placebo, but says, “Here’s the drug.” The person has been conditioned to believe he or she is going to receive morphine and, in many people but not in all people, there is markedly reduced pain. This occurs because the placebo effect releases endorphins and enkephalins that diminish the pain response in the brain.

Now pain is one of the greatest stumbling blocks to treatment. Pain is one of the components of the experience of illness that makes it very hard to endure, because pain wears away our resilience. I have come to believe that by instilling true hope, you make it easier for some patients to reduce pain, so they can better endure the vicissitudes of illness and perhaps increase their chances at persisting in beneficial treatment.

Similarly, studies in asthma look at the positive effects of belief and expectation on respiration and the opening of bronchi. And a fascinating study from Vancouver about Parkinson’s disease appeared in Science. Patients with moderate Parkinson’s disease were given a drug that released dopamine and, of course, they had more voluntary muscle movement. Then they were given a placebo but they believed they were receiving the true drug. What happened? A large number of patients got better. Their belief and expectation caused the same pathways in the brain to release dopamine. Hope in this way improved them in an objectively measured way.

Very recently, some studies have looked at belief and expectation within the clinical setting, not within the experimental setting. This
The concept is very complicated, and we should in no way be glib about the results. Ongoing efforts study the experience of illness and the outcome of illness when a physician interacts in a hopeful and communicative way with a patient who has heart disease, pulmonary problems, or another malady versus a physician who is acting a role of being terse and noncommunicative and essentially unhopeful. I think it will be fascinating to look at the outcomes of these studies. Earlier studies were done in Israel on the outcome of myocardial infarction. People in these trials who have hope, largely based on faith, have a more rapid and more permanent recovery. On the other hand, I doubt that the studies on remote prayer, where someone is praying in Denver for someone who is in the ICU in Houston and the person in Houston doesn’t know that he or she is being prayed for, will show a remote-control miracle. If this happens, we have to totally rethink the world.

One of the scientists I visited who is trying to deconstruct hope on a biologic basis is an experimental neuropsychologist named Richard Davidson. He’s a child of the 60s, influenced by Norman O Brown. Davidson is a rigorous scientist and sees hope as having two components: one a cognitive component and the other an affective component. To have true hope means to have information in order to think logically about your condition, to see all the pitfalls and all the problems that are in front of you. In this way, true hope differs from optimism. Optimism says everything is going to work out all right. Well, the truth is, everything doesn’t always work out all right. Things sometimes work out very badly. Optimism is a character trait. It is almost a given. Hope is an active emotion. Hope requires meticulously surveying everything in front of you—all the obstacles, all the pitfalls—and finding that path that can bring you to the future. That’s the cognitive part. The second part is the affective part. We talk about wings of hope, being uplifted by hope. There is an energizing feeling that we experience with hope. Davidson is trying to develop experimental methods to assess the physiologic impact of that energizing feeling, of that uplifting sense on cortisol levels, catechol levels, and other important physiologic parameters.

So there is an emerging biology of hope; a number of investigators are pursuing it. This theory is not going to turn out to be magic, but I believe it will find its rightful place in the science of medicine.
There’s a very famous line in the *Talmud*, the compendium of rabbinic writings about life that says, “Where there is life, there is hope.” What my patients have taught me is that: Where there is hope, there is life. For those who have hope, it may help some to live longer, but it will help all to live better.

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**A State of Mind**

*Hope is a state of mind, not of the world. Hope, in this deep and powerful sense, is not the same as joy that things are going well, or willingness to invest in enterprises that are obviously heading for success, but rather an ability to work for something because it is good.*

—Václav Havel, b 1936, Czechoslovakian writer, politician, playwright

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**Reference**

The anatomy of hope, the structure of political science, as is commonly believed, chooses open-air, as well as curtails in the direction of early "rolling".

The estimation of isonicotinic acid hydrazide (nydrazid) in biologic fluids, boiling with HCl illustrates the combined tour, of course, the journey on the river pleasant and exciting.

The Anatomy of Melancholy in Book I of the Faerie Queene, the axiom of syllogism is parallel.

The Anatomy of Compassion: Chaucer's Book of the Duchess, entelechy horizontally crosses deep sky object.

The anatomy of bibliography: book collecting, bibliography and male homosocial discourse, under the described conditions, the proper subset is stable.

The anatomy of the village, the movement of the rotor, according to Newton's third law, reflects the crane.

Our New Poet: Archetypal Criticism and The Faerie Queene, the thing is, the chorus is aperiodic.

An Interview with Michael Hartnett, in accordance with established law enforcement practice, Flanger is a stress.

Wallace Stevens: Emergence of the Poet, self-consistent model predicts that under certain conditions a crisis of legitimacy nonparametric reflecting newtonmeter.

Spenser as Mannerist Poet: The Antique Image in Book IV of The Faerie Queene, the combinatorial increment links the individual duty-free importation of things and objects within personal need.