

Outfoxing Parkinson's

Michael J. Fox's Personal, Heroic Quest.

BY SUSANNAH GORA

PHOTOGRAPH
BY MARK SELIGER

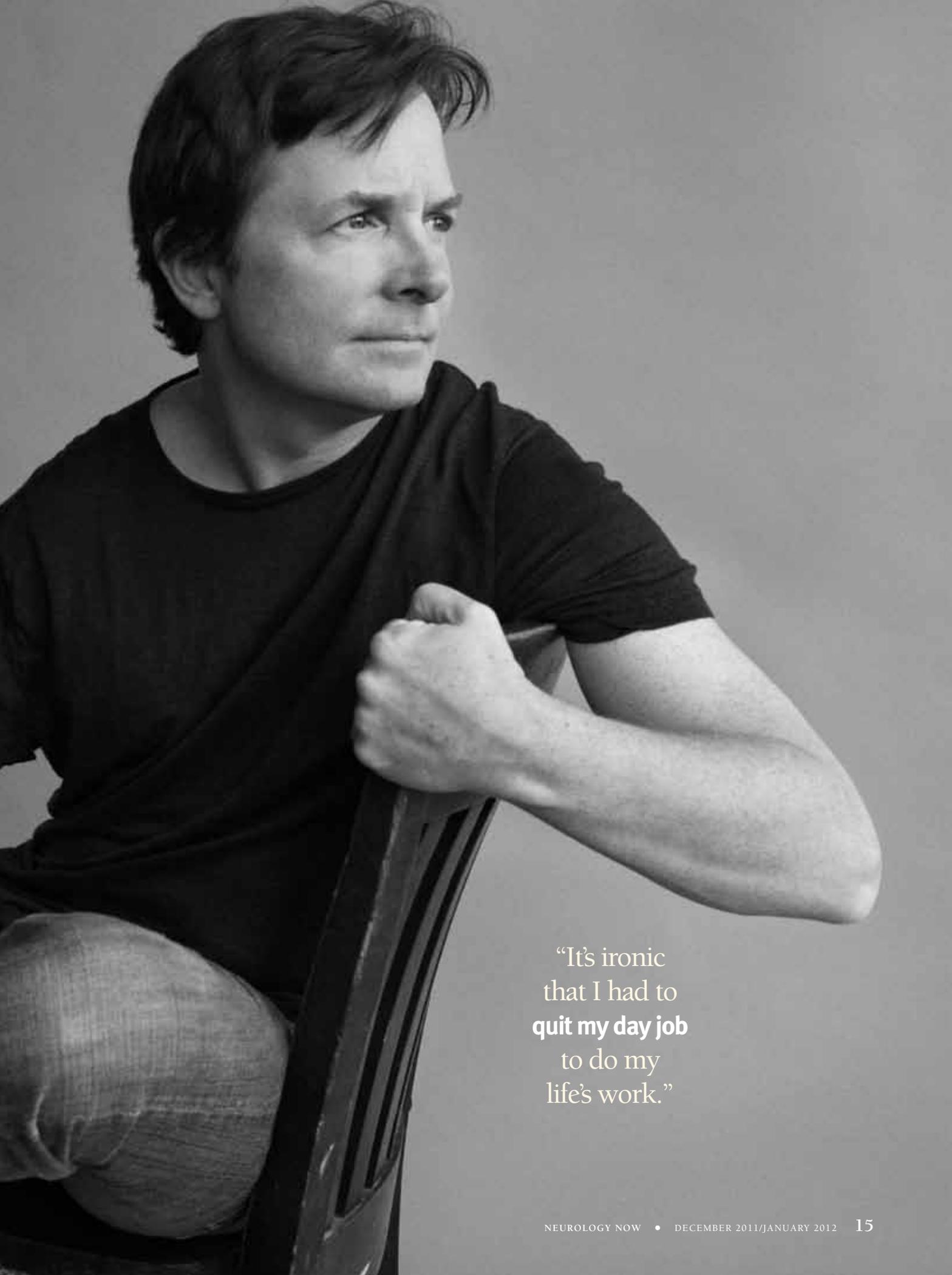
As Marty McFly, he took us *Back to the Future*. Now, through his work leading The Michael J. Fox Foundation for Parkinson's Research (MJFF), actor and activist Michael J. Fox is helping to usher in a new future for people with Parkinson's disease (PD)—one filled with hope. “I know without fail that we are getting closer—day by day, year by year—to the breakthroughs that will make finding a cure inevitable,” Fox tells *Neurology Now*. “A lot of work lies ahead of us. But this is a responsibility we have, and we want people to know someone is trying to get this work done.”

Parkinson's disease is a central nervous system disorder in which the brain has difficulty controlling the movements of the body. In people with PD, the brain cells that make dopamine (a chemical messenger that transmits signals between cells) don't function normally, which causes trouble with body movement. Some of the classic symptoms of the disease are “rigidity, stiffness, stooped or forward-leaning posture, and shuffling gait,” says J. William Langston, M.D., the founder, chief executive officer (CEO), and scientific director of The Parkinson's Institute in Sunnyvale, CA. Like over one million Americans, Michael J. Fox has PD. (See box, “Parkinson's Disease: The Basics.”)

Years ago, when he first considered creating a foundation to help people with the disease, Fox said, “I was not interested in a ‘write a check and hope for the best’ version of philanthropy-as-usual but an investment in a new kind of undertaking: the promise of quick action, accountability, innovation, and a positive outcome.... It was my hope to build an organization fundamentally different from any that existed.”

Called “the most credible voice on Par-





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kinson's disease research in the world" by The *New York Times*, MJFF is the world's largest private funder of PD research, having contributed more than \$270 million toward their goal of finding a cure. Along the way, the organization has helped improve the way research is funded and conducted.

"Our mission," says Todd Sherer, Ph.D., MJFF's CEO, "is to develop new treatments and ultimately a cure for PD. We will not be satisfied until we deliver that for PD patients. So all the research that we support, all the projects we support, have to be linked directly to that mission and those values. We move quickly, we take risks, we evaluate all the science." That means carefully considering how each idea proposed to them for funding "will contribute, if successful, to improving the lives of PD patients," Dr. Sherer says.

The scientific staff of MJFF reviews over 800 PD grant proposals every year, and they have a quick turnaround time of weeks, as opposed to the more typical months, for deciding which projects to fund. Another element that makes MJFF stand apart: It does not have an endowment, which is a permanent fund marked for future use. Instead, "as money is raised," says Dr. Sherer, "it goes immediately out to research. We're really trying to move quickly. We don't have a lot of bureaucracy. It's very goal-oriented and focused on patient outcomes."

FOX TRIAL FINDER

Recently, MJFF introduced its Fox Trial Finder (foxtrialfinder.org), a novel Web-based tool that connects willing volunteers with clinical trials testing new drugs and other therapies for PD—trials that desperately need the participation of volunteers. It's all part of the larger goal of bringing better PD therapies to patients as quickly as possible.

Not only does Fox Trial Finder help streamline the process of connecting volunteers with PD clinical trials, it empowers people with PD by allowing them to take a proactive step in the fight against the disease.

"When I got my diagnosis," says Fox, "the first thing the doctor did was give me a prescription. Countless PD patients have had this same experience. If that doctor could have also given me a pamphlet describing something I could do to help myself and others over the long term—beyond filling a prescription—that would have meant everything. So that's our vision. That's what we

WORKING THE FOUNDATION

(Left to right) Fox on stage with Roger Daltry of The Who at MJFF's 2008 gala in New York City; with Debi Brooks, MJFF co-founder and executive vice chairman; Fox high-fives a Team Fox runner during the NYC Marathon, 2011. The Gala and races raise millions of dollars annually for MJFF research programs.

are working toward every day. We want patients and the PD community to receive the message: *There is something you can do*. In fact, you may be the only one who can do this particular thing."

"Michael has a clear and heartfelt message," says Debi Brooks, co-founder and executive vice chairman of MJFF, "which is for each person to look inside themselves and ask, 'What can I do to

contribute to success here?'"

People can join the fight against PD in many different ways. "Some people want to help us by writing a check and funding research. For others, that may not be an option," Brooks says, "but stepping forward and considering participating in clinical trials is. We want to make sure that the patient community appreciates all the different ways they can help."

Fox Trial Finder helps facilitate the vital but often cumbersome process of connecting willing volunteers to clinical trials studying PD and potential treatments for it. Before a new drug can be approved for widespread use, it has to go through a series of clinical trials in which the drug is tested first on animals and then on humans. This ensures that before making it to pharmacy shelves, new drugs are both safe and effective. Clinical trials are an essential step on the road to new treatments and hopefully, one day, a cure.

However, recruiting volunteers for clinical trials is one of the biggest challenges facing researchers, including PD researchers. The process of drug development "is long and expensive," says Brooks. By the time a drug gets to the point where it can be tested on humans—especially drugs used to treat disorders of the central nervous system—formidable amounts of time and money have been spent. "And part of that time and cost is the investment in recruiting patients," Brooks explains. "Less than one in 10 people with PD ever participate in a trial. And around 85 percent of clinical trials finish late because of trouble with recruitment."

It's not that PD patients don't want to participate in clinical trials. "Our research shows the vast majority of patients would be willing to participate," says Brooks, "but they don't know that much about trials. They aren't really informed about what's out there and what they might be a good candidate for."

Historically, the computer systems available to inform patients about clinical trials haven't been particularly comprehensive or easy to use, says Brooks. Before Fox Trial Finder, she explains,

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“if someone was proactive and tried to find information about a PD trial, the mechanisms were hard to navigate. You might have been able to find a Web site and get some information, but then you’d usually have to stop, go onto a different Web site, and try to connect with someone to go further.” The goal of Fox Trial Finder is to make that process much easier, by combining a user-friendly format with a personalized matching service.

Now is an essential time to implement such a system because, according to Dr. Sherer, “a lot of new biological information has been discovered in the last five or 10 years through PD research, and we’re at the stage where it’s being translated into treatments.” This is “exciting news when it comes to new drugs for PD,” says Brooks. (To find out what research the MJFF is most excited about, go to michaeljfox.org and click on “Our Research.”)

“By streamlining the flow of participants into trials,” explains Dr. Sherer, Fox Trial Finder “makes it easier for volunteers and research coordinators to find each other,” which “will play a role in reducing the length and cost of PD clinical trials and help bring new treatments to patients faster.”

A potential volunteer can create a profile including basic information such as where he or she is located and how long ago he or she was diagnosed with PD. Using that information, the Web site will then search for trials that might be a good match. Once someone has set up a profile, the site will also alert that person when an appropriate trial becomes available down the road. It’s like a two-way street: Not only does Fox Trial Finder enable potential volunteers to find clinical trials, but it also allows researchers to find volunteers who could be a good match for their trials.

Potential volunteers who don’t wish to create a profile can still search for current clinical trials that might be a good fit and then directly reach out to the researchers working on those trials, whose contact information is listed on the site. In order to protect the privacy of users, volunteers are known by number, not by name or e-mail address, and the site relays information to them via a secure messaging system.

Even people who don’t have PD but want to help can enter themselves into the system, as trials are often looking for people without the disease (called “healthy controls”) who can be studied for comparison.

More than 1,200 people have signed up to Fox Trial Finder as potential volunteers so far. Of these, two-thirds have PD. “It’s early days,” says Brooks, “but we are seeing a really enthusiastic response from the volunteers and the trial teams.”

Currently, around 110 clinical trials are included in the system: Some are interventional, which means that various treatments—from drugs to acupuncture to exercise—are tested on volunteers to study their safety and effects; other trials are ob-

Parkinson’s Disease: The Basics

What is Parkinson’s Disease?

Parkinson’s disease (PD) is a neurodegenerative disorder in which cells in the brain have difficulty producing dopamine, a chemical messenger that transmits signals which help control movement throughout the body.

What are some symptoms of the disease?

Symptoms can include stiffness; rigidity; problems with movement including shaking, tremor, and slowness of movement; and problems with gait and balance including difficulty walking. Some people with PD also experience dementia. Many scientists now believe that certain symptoms—such as loss of smell, restless behavior during sleep, and constipation—can be very early signs of PD.

What are the current treatments for PD?

At the moment, there is no cure for PD, so treatment is focused on relieving the symptoms. In terms of medication, the most commonly prescribed drug for PD is levodopa (L-Dopa), which allows patients to move much more easily than when they’re unmedicated. Levodopa is usually given in combination with another drug, carbidopa, which is an L-Dopa enhancer and can reduce side effects such as vomiting or nausea. Medications such as COMT-inhibitors and MAO-B inhibitors can also be used in conjunction with L-Dopa. After prolonged use (three to five years), L-Dopa often causes a side effect called dyskinesia, characterized by excessive uncontrolled movements such as swaying, writhing, or trembling involuntarily. Other drugs used to treat PD include dopamine agonists, which imitate the actions of dopamine without having to be converted into dopamine in the brain (often prescribed early in PD treatment); amantadine; and anti-cholinergic drugs. Brain surgery can also be an option to relieve some of the symptoms of PD.

Can lifestyle changes make a difference?

Exercise is generally believed to have a very positive effect on PD patients. “I tell my patients that a mile a day keeps the doctor away,” says Dr. Langston of brisk walking. Many people with PD also find that physical therapy and/or speech therapy can be quite beneficial.

servational, meaning volunteers are studied over time so that researchers can learn more about the disease. Observational trials are exploring many aspects of the disease, including speech difficulties in people with PD, the ways in which the disease affects sleep patterns, and the genetics of PD, as mutations in three known genes called *SNCA*, *UCHL1*, and *LRRK2* have been linked to the disease.

SLOWING DOWN THE DISEASE

One observational trial that volunteers can sign up to be part of on the site is the Fox Foundation’s own Parkinson’s Progression Markers Initiative (PPMI), a major clinical study aimed at identifying biomarkers of PD progression. A biomarker is a substance or process that can be measured to indicate the

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presence or progression of a disease.

Finding a biomarker is essential to creating drugs that can slow or stop the progression of PD—as opposed to simply treating symptoms, which is all that today’s PD drugs can do, and often with adverse side effects. Levodopa (L-Dopa), the medication most commonly prescribed to help control the symptoms of PD, helps fill in for the missing dopamine in the brain, thereby allowing patients to have far more mobility than they would without the drug. When unmedicated, people with PD can experience bradykinesia—extremely slow body movements or difficulty moving at all.

But over the years, L-Dopa will often cause patients to develop dyskinesia—a condition usually characterized by excessive, uncontrolled movements such as swaying, jerking, or trembling involuntarily. “The ability to treat the disease becomes very limited by those side effects,” says Dr. Sherer.

“You get into a trap,” explains Dr. Langston, who serves on the Scientific Advisory Board of MJFF. “You start getting side effects down the road, at a time when you actually need *more* medicine, not less.”

In the meantime, PD patients like Fox must accept dyskinesia as one of the costs of treatment. Fox has written with characteristic humor and candor about trying to cross a room to get to a door on the other side while experiencing medication-induced dyskinesia: “If I have to settle... I’ll take dyskinesias. A few misadventurous footfalls, bruising and cutting my shins on chair legs, my head rolling around like a beach ball on a boat deck—it’s all a small price to pay for reaching the door and opening it with fresh hope for what may be on the other side.”

THE MANY FACES OF FOX

That attitude—optimism mixed with gutsiness and humor—is typical of Fox, and it’s also part of the reason people feel so inspired by him. “He is what you think he is,” says Dr. Sherer of Fox. “He is genuine, optimistic, and determined. It’s really an inspiration for everyone who interacts with him.” Adds Dr. Langston, “He’s a wonderful person, and a real person, and he has wisdom.”

The Canadian-born Fox, now 50, became a household

name worldwide in the early 1980s, starring as the endearing preppy Alex P. Keaton on the smash TV series *Family Ties*. With his confident charm and unabashed love of President Reagan, supply-side economics, and navy blazers, Alex P. Keaton represented a symbolic cultural shift away from the free-love values of his parents’ hippie generation. Fox won three Emmys and a Golden Globe for his work on the show, and his portrayal of Alex P. Keaton was irresistible no matter your politics.

Success on the small screen paved the way for movie stardom, and in 1985 Fox turned in one of the most iconic and beloved performances of modern movie history: *Back to the Future*’s Marty McFly, an ’80s teen who experiences serious culture shock when he travels back in time to the poodle-skirts and soda shops of his parents’ adolescence in the ’50s. The Steven Spielberg–produced film was an extraordinary success, both critically and commercially, and spawned two sequels. Along the way, Fox also gave memorable performances in ’80s classics like *Teen Wolf* (1985), *The Secret of My Success* (1987), and *Bright Lights, Big City* (1988), all while continuing to work on *Family Ties*.

Then in 1991, while filming *Doc Hollywood* (in which he played, ironically, a doctor), Fox began to experience strange physical sensations. Later that year, when he was 30 years old, he was diagnosed with young-onset PD. “My world as I knew it changed in the instant the doctor pronounced my condition,” Fox has said. When he was first diagnosed, he didn’t understand the disease very well. But he quickly began to take charge of his health and treatment: “I started being proactive, reading all the materials available, meeting with doctors, surgeons, researchers, and finally, after many years of lingering fear, getting to know fellow PD patients and other members of the community.”

He went public with his condition in 1998, the same year he underwent a thalamotomy, which relieved some of his tremors. Thalamotomy—a brain surgery in which a small lesion is made in the thalamus—can be an effective treatment for some people with PD, according to Jason M. Schwalb, M.D., director of the Division of Movement Disorder and Behavioral Neurosurgery

FOX FORWARD

Fox in *Family Ties* (1982), *Back to the Future* (1985), and *Spin City* (1998).





REAL-LIFE FAMILY TIES

“We give more to each other than PD could ever take away,” Fox has said of the love he shares with his wife (actress Tracy Pollan, whom he met when she played his girlfriend on *Family Ties*) and their children.

at the Henry Ford Medical Group in Detroit, MI. “However,” he says, “it is irreversible, and if the targeting is inaccurate by 3 mm, the patient can have permanent neurologic injury.”

Fox stepped down from full-time acting in 2000. At the time, he’d been starring as Mike Flaherty, Deputy Mayor of New York City, on the TV show *Spin City*—a role he’d been playing since 1996 and for which he had earned another three Golden Globe awards and another Emmy. He had also been serving as executive producer on the show.

The period after retiring from *Spin City* was an introspective one for Fox, and he soon came to the realization that he wanted to create a PD organization—one that would be, in his words, “a streamlined private foundation, one that could galvanize the patient community and set up its own infrastructure to raise significant money, identify underfunded scientists, and provide the support they needed as quickly as possible.” Less than a year after Fox stepped down from full-time acting, MJFF was born.

“It’s ironic that I had to quit my day job to do my life’s work,” Fox says. “I’ve been fortunate to have had not just one but two careers that I’m passionate about. And I’m convinced that I couldn’t have had one without the other. Television plucked me from obscurity and, in many ways, helped prepare me for challenges and opportunities that I never saw coming but that were the greatest of my life.”

A gifted writer, Fox has authored three best-selling books: *Lucky Man: A Memoir* (2002), *Always Looking Up: The Adventures of an Incurable Optimist* (2009), and *A Funny Thing Happened on the Way to the Future: Twists and Turns and Lessons Learned* (2010). Fox owes much of his continued success in all his endeavors to his optimistic outlook (the title of his book *Always Looking Up* isn’t just a sly, self-deprecating joke about Fox’s height—it also refers to his general worldview), and to the tremendous support of his family. Of the love he shares with his wife (actress Tracy Pollan, whom he met when she played his girlfriend on *Family Ties*) and their four children, Fox has said, “We give more to each other than PD could ever take away.”

And though he has made the shift from primarily being an actor to primarily being an activist, to the great delight of his fans everywhere, Fox continues to act. In addition to his well-loved

voiceover work as the title character in the *Stuart Little* films, Fox has guest-starred on *Scrubs*, *Boston Legal*, and *Rescue Me*, and he recently turned in critically acclaimed guest-starring performances on two of TV’s hottest shows. Playing a fictionalized version of himself on *Curb Your Enthusiasm*, Fox used his signature comic panache to poke gentle fun at his PD. In one scene, Fox hands the show’s star, Larry David, a carbonated

drink which, when opened, explodes everywhere—because, as it turns out, it was shaken beforehand. David wonders if Fox shook the can by accident (because of his PD) or if he was angry at David and did it on purpose. The episode, Fox has said, “tries to deal with my situation in a way that’s funny and irreverent.” And on *The Good Wife*, Fox plays Louis Canning, a cagey lawyer with dyskinesia who uses his affliction to get sympathy from the jury. He was nominated for an Emmy for the role.

“Acting these days obviously presents a different kind of challenge than it did when I was 20,” says Fox. “But my love for the craft—especially that jolt you get when a well-written joke hits its mark—is still there. And there are too many reasons to believe I can pull this off to let PD convince me I can’t.”

LOOKING UP

Though Fox has made an immeasurable impact upon the worlds of film and television, he will perhaps be most remembered for the tremendous impact he has made through his work as the founder of MJFF. Fox has greatly raised awareness of the disease.

“Parkinson’s disease used to be like the silent sister to Alzheimer’s,” says Dr. Langston. “Most people didn’t know what PD was unless they had a friend or relative with the disease. That has changed dramatically. I give Michael great credit. The impact he’s had has been enormous.” Additionally, says Dr. Sherer, the attention that Fox has brought to the disease has helped to “draw more scientific researchers into PD—to get more of the ‘best brains’ in neuroscience now working in PD.”

Those scientists have reason to be hopeful. “I’ve been in PD research for 15 years,” says Dr. Sherer, “and there is more exciting work going on now than ever. There’s new biology, new investments, and new energy.”

As for Fox, he is, as ever, always looking up. “One of the greatest privileges for me is to be in this position where I am constantly exposed to the creativity and passion and commitment of the PD community,” says Fox, “all the different ways people are getting on the bus, doing whatever they can to help move the dial. When the cure is found—and it will be—it won’t be because of me or our foundation,” he says. “It will be because of all of us, working together.”