

## A MESSAGE FROM RICHARD S. BLUMBERG, M.D. Chairperson, National Scientific Advisory Committee

This year, I began my term of office as the new Chairperson of the National Scientific Advisory Committee (NSAC). I am deeply grateful to my predecessor, Charles O. Elson, M.D., and the dedicated



researchers who served with him on the NSAC, for their outstanding work. I am happy to report that we are entering a golden age for biomedical research in general, and IBD in particular. The efforts of the last decade have resulted in new therapies for Crohn's and colitis patients, as well as a greater understanding of these diseases.

Every day, my colleagues and I work with people who have Crohn's disease or ulcerative colitis. IBD affects almost one million Americans. We fight these diseases with all that is available to us, including medications, nutritional therapies, and surgery. In many cases, patients do quite well on a particular therapy, or on a combination of treatments. But there are those patients who come to us, and we simply don't have the means to help them, despite our best

efforts. It is frustrating for us, and it is debilitating and painful for our patients.

That's why we still have so much work to do. Therapies for IBD have become more targeted to specific mechanisms of the disease, and basic research is being translated into new treatments with great speed. But there are still a great many patients who are waiting for new therapies that only new research will discover.

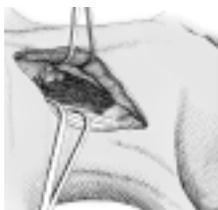
The most important ingredients for our future success are the philanthropy, hard work, and dedication that will achieve CCFA's mission. Through our strategic plan for research, the foundation will continue its outstanding leadership and have an even greater impact on IBD investigation in the 21st century.

I am honored to serve as NSAC Chairperson and I look forward to working with you all to meet the goal of a future without Crohn's and colitis.

**RICHARD S. BLUMBERG, M.D.**

### 1612

First report by Wilhelm Fabry of Germany on autopsy of boy whose symptoms would today be classified as Crohn's disease.



### 1800s

A Dublin physician describes symptoms, later identified as Crohn's disease, among children, and the first description of ulcerative colitis, by Samuel Wilks, appears in the *London Medical Gazette*.

**In 1893**, temporary colostomy is first performed.

### 1883-1908



More than 300 patients with severe inflammation of the colon are admitted to seven London hospitals. Of these, 141 die from complications.

### EARLY-1900s

Case reports in Europe and the U.S. show increases in the incidence of Crohn's. Often mistaken for a malignant tumor, the condition is dismissed as "untreatable."

### 1900-1919

British researchers find the first link to

cancer in ulcerative colitis patients. They recommend the use of a new diagnostic tool, the electrically illuminated proctosigmoidoscope. **In 1909**, the first examples of the high incidence of colitis in families are discussed at a London medical symposium. Physicians dismiss them as "coincidences."

**In 1913**, the first temporary ileostomy is performed.

### 1920s-1930s

Researchers begin investigating the possibility that an infectious agent may play a role in causing ulcerative colitis and Crohn's disease.

# CONQUERING CROHN'S AND COLITIS THROUGH RESEARCH

**F**or more than 35 years, the Crohn's & Colitis Foundation of America (CCFA) has been at the forefront of medical research in inflammatory bowel disease (IBD).

Although Crohn's disease and ulcerative colitis are two separate and distinct inflammatory bowel diseases, they share many of the same symptoms, including inflammation of the intestines, abdominal pain, cramping, and diarrhea. These symptoms range in severity and often are debilitating, greatly altering patients' quality of life. But a new Golden Age of research is beginning: We are about to enter an era in which we will learn more than we've ever known before, and we will use this knowledge to provide life-enhancing therapies more quickly than was thought possible just 20 years ago.

## A FOUNDATION FOR FUTURE RESEARCHERS

Despite these major advances, we still don't know what causes IBD. Leading scientists and physicians in the field have determined that these diseases may be the result of an overactive immune response in the intestines. This abnormal immune response is believed to occur because an environmental factor, such as a bacterium, triggers the

disease—but only in people who have a genetic predisposition to IBD.

There are two main research categories: basic research, which explores the science, such as the underlying cause of the disease; and clinical research, which determines which medical and surgical options work best for patients. The timeline in this section illustrates many of the significant milestones in IBD research, as well as the environment in which they occurred.

The timeline shows how IBD was first identified in 1612, although the diseases did not yet have names. Through the centuries, physicians saw patients with IBD, but were at a loss to help them. It was almost 300 years before a surgical intervention, such as a temporary colostomy, was first performed. But the 20th century was a time of great progress in medicine. Physicians and scientists like Jonas Salk, who conquered polio, Alexander Fleming, who conquered pneumonia, and Selman A. Waxman, who conquered tuberculosis, based their discoveries and innovations on the pioneering work of those who had come before. In the 19th century, the work of scientists like Edward Jenner, Joseph Lister, and Louis Pasteur created a vast compendium of medical knowledge that provided a solid foundation for future researchers.

### 1920s-1960

Researchers use a variety of methods to reproduce human ulcerative colitis in animals. None is successful.

### 1930

In two clinical reports, psychogenic factors are implicated in ulcerative colitis. Psychiatric and psychoanalytical

concepts will continue to dominate the treatment of IBD until the 1950s.

### 1932

Three physicians—Oppenheimer, Ginsburg, and Crohn—at Mt. Sinai Hospital in New York City publish the first description of "regional enteritis" in the *Journal of the American Medical Association*.

The disease later is named after one of these researchers, Dr. Burrill Crohn.



Dr. Burrill B. Crohn

### 1940s

Dr. Nana Svartz, a Swedish rheumatologist, is the first doctor to use sulfasalazine to treat ulcerative colitis. This becomes the standard treatment for the next 50 years.



### 1950s

Adrenocorticotrophic hormone (ACTH) and cortisone are developed and become standard treatments for IBD. As doctors note the impact of these drugs on their patients' condition, emphasis on the role of psychogenic factors begins to diminish. Also, the discovery of the

double helix by Watson and Crick ushers in the era of genetic research.

### 1950

The federal government's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), a division of the National Institutes of Health (NIH), is established.



**CCFA RESEARCH ACHIEVEMENTS:**

- Contributed to the identification of two regions on chromosomes that contain genes for IBD.
- Contributed to the discovery of NOD2, the first gene for Crohn's disease.
- Identified and developed appropriate animal models as an essential research tool.
- Funded research about TNF-alpha that contributed to understanding the importance of its role in IBD. Antibodies to this immune system chemical are the basis for a number of biologic therapies, including infliximab (Remicade®).

**“CHALLENGES IN IBD”: CCFA’S STRATEGIC PLAN FOR RESEARCH**

More than just providing funding, CCFA has also developed a highly successful strategic plan for research, as well as leading-edge research initiatives. Twelve years ago, CCFA launched “Challenges in IBD Research: Agenda for the

1990s.” This ground-breaking plan sought to define the priorities of IBD research for the future, and, even more important, to identify the resources necessary to move those priorities forward.

The plan was established in three phases. During Phase I, CCFA invited IBD researchers from a variety of scientific disciplines, such as microbiology, immunology, and genetics, to participate in a task force. These researchers then convened subcommittees that drafted papers detailing the ideal course of research within their discipline. In Phase II, the researchers were invited to a three-day-meeting. Here, the initial papers were discussed, then elements within those fields were ranked in order of priority. Phase III was a white paper, which presented these priorities to the scientific community.

Based on the goals set forth in “Challenges,” CCFA created several resources that have since revolutionized the field of IBD research. These include the development of animal models to study the course of the disease in a laboratory setting, and the establishment of a DNA and tissue cell line bank, a vital resource for scientists who are searching for the genes linked to these diseases.



**1970s**

The NIH conducts the National Cooperative Crohn's Disease Study (NCCDS), the first large-scale study of Crohn's in the U.S. The study finds no difference in effect between placebo and azathioprine. A clinical researcher observed that azathioprine and 6-MP take a long time to work, and

the NCCDS study design did not reflect this. CCFA awards its first grant for a clinical trial to demonstrate that 6-MP is effective in Crohn's disease.

**1971**

A Chicago study, which documents a positive family history for IBD in 113 (17%) of 646 patients, supports

the case that IBD has a genetic component. Several other studies around this time reach similar conclusions.

**1980s**

After surgeons improve the ileoanal anastomosis, or "pullthrough," by constructing an internal pouch, this

operation becomes the most popular ostomy alternative.

**1981**

Researchers identify the first animal that naturally develops a form of colitis resembling the human disease: the cotton-top tamarin, a monkey native to Colombia.

**1988**

The first 5-ASA drug, mesalamine, gains

FDA approval for the treatment of ulcerative colitis.





Alliance. Again, these initiatives demonstrate CCFA's forward thinking in identifying a research need and providing the resource to meet that need. They also demonstrate CCFA's ability to partner with other institutions, to make sure the best and the brightest minds in IBD and related fields are taking part in these endeavors.

As the leader in IBD research, CCFA fully understands the importance of partnerships. We have successfully partnered with the NIH to accelerate progress in IBD research, as well as with other institutions involved in CCFA-sponsored research initiatives, such as the Centers for Disease Control and Prevention (CDC). CCFA and the CDC are working together on an IBD epidemiology study to determine the true prevalence of the diseases, and examine disease trends across regions, different groups and time. This large-scale population study is expected to provide a more accurate assessment of IBD in America than the information currently available. We are also encouraging the spirit of partnership throughout the U.S. by requiring each of our chapters to establish a Research Alliance. A Research Alliance provides opportunities for people who want to contribute to research, but who are unable to fund a project on their own, to join forces with others who also want to support research. Through this partnership, donors can build one-on-one relationships with gifted scientists and share in the

excitement of discovery as the project progresses. For more information on Research Alliances in your area, contact your local chapter.

CCFA's investment in research cultivates and nurtures IBD investigators, who then remain in the field to mentor others. This data has been the foundation for a greater understanding of Crohn's and colitis, and for new therapies.

But there are still so many questions to be answered, and so many patients for whom available therapies are not effective. CCFA-sponsored research could make all the difference for patients and their families who are living with IBD every day. Our research will lead to the discovery of additional genes for Crohn's disease and to the identification of the first gene for ulcerative colitis. It will continue to generate developments that result in new treatments, and one day, to a means to cure and prevent IBD.

The 21st century will see greater strides in IBD research than ever before. Through the support of dedicated scientists, donors, and volunteers, CCFA will be there to lead the way.



**1999**

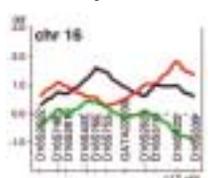
CCFA establishes the DNA and Cell Line Bank and the Clinical Research Alliance.

**2000**

The entire human genome is mapped, revolutionizing genetics research.

**2001**

The first gene to confer susceptibility to Crohn's disease, NOD2 on chromosome 16, is discovered jointly by researchers in Chicago and France, through research partially funded by CCFA.



**2002**

CCFA convenes "Challenges in IBD: Updating the Scientific Agendas," creating the strategic plan for IBD



research over the next five years. The top priorities are identifying major susceptibility genes for IBD, developing surrogate markers of disease activity, and developing a detailed understanding of the regulatory cells in the intestine.

**2003**

Entering the Golden Age of IBD Research: CCFA will be there!

