NIH Consensus Statement

Volume 12, Number 1
February 7–9, 1994

Helicobacter pylori *in Peptic Ulcer Disease*

NATIONAL INSTITUTES OF HEALTH
Office of the Director

About the NIH Consensus Development Program

NIH Consensus Development Conferences are convened to evaluate available scientific information and to resolve safety and efficacy issues related to a biomedical technology. The resultant NIH consensus statements are intended to advance understanding of the technology or issue in question and to be useful to health professionals and the public.

NIH consensus statements are prepared by a nonadvocate, non-Federal panel of experts, based on (1) presentations by investigators working in areas relevant to the consensus questions during a 2-day public session; (2) questions and statements from conference attendees during open discussion periods that are part of the public session; and (3) closed deliberations by the panel during the remainder of the second day and morning of the third. This statement is an independent report of the panel and is not a policy statement of the NIH or the Federal Government.

Free copies of this statement and bibliographies prepared by the National Library of Medicine are available from the Office of Medical Applications of Research, National Institutes of Health, Federal Building, Room 618, Bethesda, MD 20892, or the NIH Consensus Program Information Service at 1-800-NIH-OMAR (644-6627). A catalog of other free NIH Consensus Statements is also available from these sources.

For making bibliographic reference to the consensus statement from this conference, it is recommended that the following format be used, with or without source abbreviations, but without authorship attribution:

Helicobacter pylori *in Peptic Ulcer Disease. NIH Consens Statement 1994 Feb 7–9; 12(1): 1–22.*

NIH Consensus Statement

Volume 12, Number 1
February 7–9, 1994

Helicobacter pylori *in Peptic Ulcer Disease*

NATIONAL INSTITUTES OF HEALTH
Office of the Director

Abstract

The National Institutes of Health Consensus Development Conference on *Helicobacter pylori* in Peptic Ulcer Disease brought together specialists in gastroenterology, surgery, infectious diseases, epidemiology, and pathology, as well as the public, to address the following questions: (1) What is the causal relationship of *H. pylori* to upper gastrointestinal disease? (2) How does one diagnose and eradicate *H. pylori* infection? (3) Does eradication of *H. pylori* infection benefit the patient with peptic ulcer disease? (4) What is the relationship between *H. pylori* infection and gastric malignancy? (5) Which *H. pylori*–infected patients should be treated? (6) What are the most important questions that must be addressed by future research in *H. pylori* infections? Following 1½ days of presentations by experts and discussion by the audience, a consensus panel weighed the evidence and prepared their consensus statement.

Among their findings, the consensus panel concluded that: (1) ulcer patients with *H. pylori* infection require treatment with antimicrobial agents in addition to antisecretory drugs whether on first presentation with the illness or on recurrence; (2) the value of treating nonulcer dyspepsia patients with *H. pylori* infection remains to be determined; and (3) the interesting relationship between *H. pylori* infection and gastric cancers requires further exploration.

The full text of the consensus panel's statement follows.

Introduction

Peptic ulcer disease is a chronic inflammatory condition of the stomach and duodenum that affects as many as 10 percent of people in the United States at some time in their lives. The disease has relatively low mortality, but it results in substantial human suffering and high economic costs.

In the early 20th century, the pathogenesis of the disorder was believed to be related to stress and dietary factors. Thus, treatment focused on hospitalization with bed rest and prescription of special bland foods. Later the concept arose that peptic ulcer disease was caused by the injurious effects of digestive secretions such as gastric acid; hence, antacids became the standard of therapy. In 1971, Sir James Black identified a subtype of the histamine receptor (H_2 receptor) that appeared to be the principal mediator of gastric acid secretion. Antagonists of this receptor proved to be safe and effective therapy for peptic ulcer disease. More recently, inhibitors of the proton pump (H^+,K^+-ATPase) in gastric parietal cells have proved to be rapidly effective and extremely potent antiulcer drugs. Other drugs that appear to enhance mucosal defense such as bismuth compounds, sucralfate, and prostaglandins have also been applied to the treatment of peptic ulcers. Despite these sophisticated therapeutic agents, the disturbing problem of the high recurrence rate of peptic ulcer, even after complete healing, remains.

In 1982, Warren and Marshall provided the first insight into another important pathogenic factor in peptic ulcer disease. They isolated a spiral urease-producing organism (later identified as *Helicobacter pylori*) nestled in the narrow interface between the gastric epithelial cell surface and the overlying mucus gel. In their early studies, the presence of this organism was shown to be highly correlated with antral gastritis as well as with gastric and duodenal ulcers, and eradication of this organism effectively eliminated ulcer recurrences. Furthermore, a disturbing epidemiologic relationship between *H. pylori* infection and gastric malignancies was reported. Such studies have given rise to

the hypothesis that *H. pylori* is a major etiologic factor in peptic ulcer disease and that diagnosis and eradication of the organism are necessary for optimal therapy of the disorder.

To address these issues, the National Institute of Diabetes and Digestive and Kidney Diseases, together with the Office of Medical Applications of Research of the National Institutes of Health, convened a Consensus Development Conference on *Helicobacter pylori* in Peptic Ulcer Disease. The conference was cosponsored by the National Institute of Allergy and Infectious Diseases. Following a day and a half of presentations by experts in the relevant fields and discussion from the audience, an independent consensus panel composed of specialists and generalists from the medical and other related scientific disciplines, as well as representatives from the public, considered the evidence and formulated a consensus statement in response to the following six previously stated questions:

- What is the causal relationship of *H. pylori* to upper gastrointestinal disease?
- How does one diagnose and eradicate *H. pylori* infection?
- Does eradication of *H. pylori* infection benefit the patient with peptic ulcer disease?
- What is the relationship between *H. pylori* infection and gastric malignancy?
- Which *H. pylori*–infected patients should be treated?
- What are the most important questions that must be addressed by future research in *H. pylori* infections?

What Is the Casual Relationship of *H. pylori* to Upper Gastrointestinal Disease?

A strong association between *H. pylori* and upper gastrointestinal disease has been reported. The causal relationship between *H. pylori* and chronic superficial gastritis is well established. The evidence for this statement is as follows:

1) Virtually all *H. pylori*-positive patients demonstrate antral gastritis.

2) Eradication of *H. pylori* infection results in resolution of gastritis.

3) The lesion of chronic superficial gastritis has been reproduced following intragastric administration of the isolated organism in some animal models and oral administration in two humans.

A causal relationship between *H. pylori* and peptic ulcer disease is more difficult to establish from the available data in part because of the lack of an animal model and because only a small proportion of individuals harboring the organism develop ulceration. However, nearly all patients with duodenal ulcer have *H. pylori* gastritis. Thus infection with the organism may be a prerequisite for the occurrence of almost all duodenal ulcers in the absence of other precipitating factors such as nonsteroidal anti-inflammatory drug (NSAID) use or Zollinger-Ellison syndrome. The association between *H. pylori* infection and gastric ulcer is only slightly less strong, in that 80 percent of patients with non-NSAID-induced gastric ulcers are infected. Nevertheless, it is important to note that the majority of *H. pylori*–infected individuals do not develop duodenal or gastric ulcers. These facts imply that host characteristics, strain variability, or other factors play a role in the pathogenesis of peptic ulcer disease.

The strongest evidence for the pathogenic role of H. *pylori* in peptic ulcer disease is the marked decrease in the recurrence rate of ulcers following the eradication of infection. The prevention of recurrence following *H. pylori* eradication is less well documented for gastric ulcer than for duodenal ulcer, but the available data suggest similar efficacy.

In the case of duodenal ulcer, it is curious that in some studies the organism is more often present in the antrum than in the duodenum, where the ulcer is found. Suggested mechanisms by which an antral organism causes a duodenal lesion include bacterial colonization of gastric metaplasia in the duodenum, secondary changes in gastric acid or duodenal bicarbonate secretion, or changes caused by products of the infecting organism and/or the inflammatory response of the host. Further studies are needed to clarify the mechanisms of bacterial pathogenesis and host responses leading to duodenal ulceration.

To date there is no convincing evidence for an association of *H. pylori* infection with nonulcer dyspepsia. The prevalence of *H. pylori* infection is no higher in patients with nonulcer dyspepsia than in the general population. Although some patients with nonulcer dyspepsia may have symptoms that are related to the presence of *H. pylori*, there are no data to demonstrate how to identify such a subject. Studies are needed to determine whether *H. pylori*–infected patients with nonulcer dyspepsia would benefit from treatment of the infection.

How Does One Diagnose and Eradicate *H. pylori* Infection?

A fundamental principle of specific antimicrobial therapy is accurate diagnosis. Numerous validated methods to diagnose patients with *H. pylori* infection are in use. These methods can be divided into invasive and noninvasive diagnostic tests.

The invasive tests include endoscopy followed by gastric biopsy and histologic demonstration of organisms, biopsy with direct detection of urease activity in the tissue specimen, and biopsy with culture of the *H. pylori* organism. Although culturing the organism is traditionally considered the "gold standard" for diagnosis of many infectious agents, it is the least sensitive diagnostic test (approximately 70–80 percent positivity). Both histologic demonstration of the organism by Giemsa or Warthin-Starry stains and urease testing have sensitivities and specificities above 90 percent.

Excellent diagnostic sensitivities and specificities (>95 percent) are also obtained with noninvasive tests for the initial diagnosis of *H. pylori* infection. These include serology for immunoglobulin G antibodies to *H. pylori* antigens and breath tests of urease activity using orally administered ^{14}C- or ^{13}C-labeled urea. A number of highly accurate serologic kits for diagnosis of *H. pylori* infection are available. Labeled urea breath tests have had restricted availability as research tools in the past, but commercial assays will be available in the near future.

It is important to note that with the exception of the serologic assays all of the tests for diagnosis of *H. pylori* infection may be falsely negative in patients who have taken antibiotics, bismuth compounds, or omeprazole in the recent past.

Presently, there is no readily available, inexpensive, and accurate noninvasive method to monitor eradication of *H. pylori*. Without such an assay, routine monitoring for relapse, reinfection, or treatment failure cannot be recommended. Even if such a test were available, testing all patients treated for *H. pylori* infection probably would

not be necessary in view of the high efficacy of treatment and low reinfection rate. Important exceptions would be patients with complicated, recurrent, or refractory peptic ulcers who should be evaluated for successful eradication of infection before cessation of antiulcer therapy. Antibody levels decrease slowly following successful eradication of *H. pylori* infection. If the same well-standardized assay is used, a dramatic fall in antibody titer 6–12 months following antimicrobial treatment indicates successful eradication. However, variability among serology tests applied in commercial laboratories may limit their usefulness in confirming *H. pylori* eradication. Although breath testing is the best noninvasive assay for evaluating success of eradication, there are unresolved issues of availability, cost, and ease of use in the practical application of this method. Invasive tests can also be used for documenting cure, but these incur the cost and morbidity associated with endoscopy.

Therapy of *H. pylori* poses several unique challenges. The organism resides under a mucus gel layer in the highly acidic milieu of the stomach, where rapid removal of ingested antimicrobials may occur. These and other factors may contribute to the variable correlation between *in vitro* and *in vivo* antimicrobial activity. A problem in selection of a therapeutic regimen has been the lack of a suitable animal model. For these reasons, much of the available information concerning choice of antimicrobial agents is based on small empirical trials in humans. Multiple agents that have been studied in various combinations include metronidazole, tetracycline, amoxicillin, clarithromycin, bismuth compounds, H_2-receptor antagonists, and proton-pump inhibitors. The choice of a particular regimen must be tempered by the rapidly developing data on optimal therapy.

Consideration of the therapeutic options should take into account efficacy, compliance, side effects, and cost. A triple antimicrobial regimen consisting of bismuth subsalicylate, tetracycline, and metronidazole has been studied extensively and can yield eradication rates of approximately 90 percent. Substitution of amoxicillin for tetracycline or

metronidazole lowers efficacy only slightly (greater than 80 percent). One promising study reported efficacy of approximately 90 percent with the combination of ranitidine, metronidazole, and amoxicillin. Although variable, eradication rates of greater than 80 percent have also been reported with the combination of omeprazole (a proton-pump inhibitor) and amoxicillin. Omeprazole should be given at least twice daily, and the two agents begun at the same time because immediate pretreatment with omeprazole lowers efficacy of the omeprazole–amoxicillin combination. Two- or three-drug regimens should last 2 weeks. If therapy is begun at the time of active peptic disease, treatment with antisecretory agents in addition to antimicrobials is recommended. When multiple drugs are administered at various times in the day, patient compliance may become an important factor affecting efficacy. If symptoms persist or recur after initial treatment, diagnostic reevaluation should be undertaken and a second course of therapy considered. Side effects are more frequent with the three-drug regimen than with the two-drug regimen but have been mild in either case and infrequently have prevented completion of therapy. Serious but rare events such as anaphylaxis, Stevens-Johnson syndrome, and pseudomembranous colitis should be expected as antimicrobial regimens are used more widely. Safety and efficacy of antimicrobial therapy in *H. pylori*–infected children and adolescents have not been studied in detail.

Resistance to antimicrobials, in particular to nitroimidazoles such as metronidazole, is an important problem and a cause for treatment failure in some studies. Resistance to metronidazole varies worldwide, with the highest rates (40–50 percent) in underdeveloped countries. Application of currently available one-drug regimens has led to enhanced antimicrobial resistance and thus is strongly discouraged. The widespread application of antimicrobial regimens to treat *H. pylori* infection may magnify the problem of drug resistance. Thus alternative treatment or prevention strategies such as vaccines or immunotherapy may deserve attention in the future.

Does Eradication of *H. pylori* Infection Benefit the Patient With Peptic Ulcer Disease?

Helicobacter pylori infection is strongly associated with the predominant forms of peptic ulcer disease and appears to play an important contributory role in their pathogenesis; thus, it is reasonable to suggest that eradication of *H. pylori* infection may benefit patients with peptic ulcer disease. Although further studies are needed to delineate fully the role of *H. pylori* eradication in many other patient populations, available studies have demonstrated clearly the principal benefit of eradication in patients with peptic ulcers, a substantial reduction in the risk of ulcer recurrence (to less than 10 percent in 1 year). The evidence is more complete for patients with duodenal ulcers than for those with gastric ulcers, although the benefits to the two sets of patients appear to be comparable. The side effects of current regimens for eradication of *H. pylori* infection are generally minor and are outweighed by the benefit of reduced ulcer recurrence. When combined with standard antisecretory therapy, *H. pylori* eradication may contribute to a modest reduction in time to ulcer healing. Moreover, eradication of *H. pylori* infection may enhance healing of ulcers refractory to conventional therapy.

A separate question is whether *H. pylori* eradication prevents future problems in peptic ulcer patients with a history of bleeding or other complications. Although preliminary data indicate such efficacy, more definitive data are needed.

The benefits of eradicating *H. pylori* infection in patients with peptic ulcer disease may vary depending on a variety of factors including those related to the host, the organism, and the environment. Such factors include patient demographics (age, socioeconomic status, concurrent illness, behavioral factors), frequency of reinfection, mode of transmission, and strain variation.

The potential cost savings associated with treating *H. pylori* infection have not been established but may be substantial. Carefully designed economic analyses are needed to assess more completely the cost-effectiveness of *H. pylori* eradication in peptic ulcer disease patients.

What Is the Relationship Between *H. pylori* Infection and Gastric Malignancy?

Adenocarcinoma of the stomach is one of the most common malignancies in the world, although it is relatively uncommon in the United States (24,000 new cases and 14,000 deaths per year). There is evidence that *H. pylori* infection is associated with adenocarcinoma of the body and antrum of the stomach. However, gastric cancer occurs in some individuals with no evidence of *H. pylori* infection, and in the United States, fewer than 1 percent of *H. pylori*–infected individuals will ever develop gastric cancer. The effect of prevention or treatment of *H. pylori* infection on gastric cancer risk has not been studied adequately.

Descriptive epidemiologic data indicate that gastric cancer occurs more frequently in some populations that have higher rates of *H. pylori* infection. Rates of both *H. pylori* infection and gastric cancer correlate inversely with socioeconomic status, increase as a function of age, have declined in successive birth cohorts in developed countries, and occur less commonly in whites than in African Americans and Hispanics in the United States. A geographic correlation has been found between *H. pylori* infection and gastric cancer death rates. However, some clear examples exist of disparity in the epidemiology of the two diseases. Gastric cancer is more common in men than in women, whereas the rates of *H. pylori* infection are not different between the sexes. Some populations are reported to have a high rate of *H. pylori* infection but low rates of gastric cancer. These disparities indicate that factors other than *H. pylori* infection are also important in gastric cancer risk.

Some but not all of the retrospective serologic studies have shown that patients with gastric cancer more frequently have *H. pylori* infection than do controls. The strongest evidence that *H. pylori* infection is associated with gastric cancer comes from three prospective

cohort serologic studies, which indicate that *H. pylori*–infected individuals have a significantly increased rate of gastric cancer. There is no association in any of these studies between *H. pylori* infection and cancer in the gastric cardia and gastroesophageal junction, which is increasing in incidence in the United States.

Non-Hodgkin's lymphoma of the stomach is a rare disorder that accounts for only 3 percent of gastric malignancies. Mucosa-associated lymphoid tissue (MALT) lymphomas, which constitute a subset of non-Hodgkin's lymphoma, are low-grade clonal neoplasms that are thought to arise from lymphoid aggregates in the lamina propria. Preliminary epidemiologic data suggest that *H. pylori* infection is associated with both non-Hodgkin's lymphoma and MALT lymphomas of the stomach. Further study of the relationship between *H. pylori* infection and gastric lymphomas is warranted.

In summary, if there is any causal relationship between *H. pylori* infection and gastric cancer, clearly other factors are also important in gastric carcinogenesis. *H. pylori* eradication for the purpose of preventing gastric cancer cannot be recommended at this time.

Which *H. pylori*–Infected Patients Should Be Treated?

There are ample data to support the antimicrobial eradication of *H. pylori* infection in patients with peptic ulcer disease. All patients with gastric or duodenal ulcers who are infected with *H. pylori* should be treated with antimicrobials regardless of whether they are suffering from the initial presentation of the disease or from a recurrence. *H. pylori*–infected peptic ulcer patients who are receiving maintenance treatment with antisecretory agents or who have a history of complicated or refractory disease should also be treated for the infection. The presence of NSAID's, including aspirin, as a contributing factor should not alter the antimicrobial regimen, but whenever possible, these drugs should be discontinued. However, in asymptomatic *H. pylori*–infected patients without ulcers, the data are not sufficient to support prophylactic antimicrobial therapy to prevent ulcer disease in the future or to reduce the likelihood of developing gastric neoplasia. Also, no convincing data exist to support routine treatment of patients with nonulcer dyspepsia who are infected with *H. pylori*. Thus, at the present time there is no reason to consider routine detection or treatment of *H. pylori* infection in the absence of ulcers. Carefully controlled prospective studies are needed to assess the benefits of treating nonulcer dyspepsia patients with *H. pylori* infection. It is self-evident that no patient should be treated for *H. pylori* unless one of the sensitive and specific tests previously discussed demonstrates infection.

Bleeding is the complication of peptic ulcer disease associated with the highest mortality rate and, therefore, demands aggressive therapy. The available data suggest that after these ulcers heal, the likelihood of recurrence with bleeding is significantly reduced by maintenance antisecretory therapy. Preliminary studies indicate that eradication of *H. pylori* infection may be equally efficient in preventing the recurrence of ulcer bleeding. Until these studies can

be confirmed, maintenance antisecretory therapy may be prudent in such patients even after *H. pylori* eradication in view of the high risks associated with rebleeding.

Guidelines for the routine antimicrobial treatment of *H. pylori* infection

Patient status	*H. pylori* negative	*H. pylori* positive
Asymptomatic (no ulcer)	No	No
Nonulcer dyspepsia	No	No
Gastric ulcer	No	Yes
Duodenal ulcer	No	Yes

What Are the Most Important Questions That Must Be Addressed by Future Research in *H. pylori* Infections?

Although much is known about the role of H. *pylori* in gastrointestinal disease, many issues are still unresolved.

Further well-designed studies on the role of *H. pylori* eradication in the management of peptic ulcer disease are needed, particularly in populations not well studied to date, including children, patients with gastric ulcers, and patients with duodenal or gastric ulcers with complications. These studies should utilize standard definitions, be randomized, be analyzed on an intent-to-treat basis, have sample size adequate to detect clinically meaningful differences between treatment arms, and be double-blind whenever possible.

Fundamental questions remain concerning the initial evaluation of a patient who presents with dyspepsia. Should that patient be tested for *H. pylori* infection? Should that patient be treated empirically for *H. pylori* infection if it is present? The answers to these questions depend in part on whether antimicrobial therapy relieves symptoms in some or all symptomatic patients with *H. pylori* infection and gastritis but without ulcers. If the answer is yes, patients presenting to the physician with dyspepsia should be tested for *H. pylori* infection and, if the results are positive, be treated with antimicrobial therapy. However, if symptomatic *H. pylori*–infected patients without ulcers do not respond to antimicrobial therapy, it will continue to be imperative to confirm the diagnosis of peptic ulcer disease in order to identify the patients who will benefit from treatment of their infection. Under these circumstances, the question arises as to whether it is necessary, appropriate, and cost-effective to perform endoscopy in dyspeptic patients at initial presentation.

Another major question that remains to be answered is whether eradication of *H. pylori* infection prevents gastric cancer. Such a question cannot be answered directly without a long and costly study. Thus, an alternative approach might be to conduct studies looking at intermediate endpoints that are thought to predict the evolution of malignancy and their response to *H. pylori* eradication. Epidemiologic studies are also needed to define more precisely the subset of *H. pylori*–infected individuals who will develop gastric cancer.

A major opportunity for additional studies is in the area of mechanisms by which *H. pylori* infection leads to gastrointestinal disease. Virulence factors, bacterial genetics, mechanisms of immunity, animal models, antibiotic resistance, and modes of transmission are all issues that should be examined in future studies. Furthermore, the natural history of *H. pylori* infections and the nature of the host-organism interaction require further study. The pathogenic consequences of *H. pylori* infection in childhood and adolescence and the optimal management of infection are additional important questions. More information is needed on the value of testing to confirm eradication after antimicrobial therapy, and antimicrobial regimens need to be optimized to improve treatment efficacy. A comprehensive economic analysis should be conducted to examine the cost-effectiveness of treating *H. pylori* infection.

Conclusion

The discovery of *H. pylori* as a gastrointestinal pathogen has had a profound effect on current concepts of peptic ulcer disease pathogenesis. Evidence presented at this Consensus Development Conference has led to the following conclusions:

- Ulcer patients with *H. pylori* infection require treatment with antimicrobial agents in addition to antisecretory drugs whether on first presentation with the illness or on recurrence.
- The value of treatment of nonulcer dyspepsia patients with *H. pylori* infection remains to be determined.
- The interesting relationship between *H. pylori* infection and gastric cancers requires further exploration.

Consensus Development Panel

Tadataka Yamada, M.D.
Panel and Conference Chairperson
John G. Searle Professor and Chair
Department of Internal Medicine
University of Michigan Medical Center
Ann Arbor, Michigan

Dennis Ahnen, M.D.
Denver Medical Center
Denver, Colorado

David H. Alpers, M.D.
Professor of Medicine
Chief, Gastrointestinal Division
Department of Medicine
Washington University School of Medicine
St. Louis, Missouri

Harry B. Greenberg, M.D.
Professor of Medicine, Microbiology, and Immunology
Division of Gastroenterology
Department of Medicine
Stanford University School of Medicine
Stanford, California

Martha Gray, M.D.
Ann Arbor, Michigan

Kent B. Joscelyn, J.D.
Joscelyn, McNair and Jeffrey, P.C.
Ann Arbor, Michigan

Gordon Kauffman, M.D.
Chief, Division of General Surgery
Department of Surgery
Milton S. Hershey Medical Center
Hershey, Pennsylvania

Daniel K. Podolsky, M.D.
Chief, Gastrointestinal Unit
Department of Medicine
Massachusetts General Hospital
Boston, Massachusetts

Wayne A. Ray, Ph.D.
Department of Preventive Medicine
Vanderbilt University School of Medicine
Nashville, Tennessee

Dennis Schaberg, M.D.
Professor and Chairman
Department of Medicine
University of Tennessee Memphis, College of Medicine
Memphis, Tennessee

Fred E. Silverstein, M.D.
Professor of Medicine
Division of Gastroenterology
University of Washington School of Medicine
Seattle, Washington

Michael V. Sivak, Jr., M.D.
Professor of Medicine
Case Western Reserve University
Chief, Division of Gastroenterology
University Hospitals of Cleveland
Cleveland, Ohio

Ann L.B. Williams, M.B.B.S.
Assistant Clinical Professor
Division of Gastroenterology
George Washington University Medical Center
Washington, D.C.

Robert Yolken, M.D.
Professor of Pediatrics
Director of Pediatrics and Infectious Diseases
Johns Hopkins University School of Medicine
Baltimore, Maryland

Speakers

Martin J. Blaser, M.D.
"Helicobacter pylori—A Human Pathogen"
Addison B. Scoville Professor of Medicine
Director, Division of Infectious Diseases
Professor of Microbiology and Immunology
Department of Medicine
Vanderbilt University School of Medicine
Nashville, Tennessee

Geron Borsch, M.D.
"Beneficial Effects of Eradication of *Helicobacter pylori* in Relationship to Ulcer Complications"
Elizabeth Hospital
Essen, Germany

Pelayo Correa, M.D.
"Biological Plausibility of the Relationship Between *Helicobacter pylori* and Malignancy"
Professor of Pathology
Department of Pathology
Louisiana State University Medical Center
New Orleans, Louisiana

Steven J. Czinn, M.D.
"Complications of Treatment for Eradication of *Helicobacter pylori* Infection"
Associate Professor
Division of Pediatric Gastroenterology
Case Western Reserve University School of Medicine
Division of Pediatric Gastroenterology and Nutrition
Rainbow Babies and Children's Hospital
Cleveland, Ohio

David Forman, Ph.D.
"Evidence for *Helicobacter pylori's* Role as a Risk Factor for Malignancy"
Staff Scientist
Imperial Cancer Research Fund
Cancer Epidemiology Unit
The Radcliffe Infirmary
Oxford, United Kingdom

David Y. Graham, M.D.
"Antimicrobial Regimen Results of Clinical Trials"
Professor of Medicine and Molecular Virology
Baylor College of Medicine
Houston, Texas

Richard H. Hunt, F.R.C.P., F.R.C.P.(Edin.), F.R.C.P.(C), F.A.C.G.
"Does Treatment With Antimicrobials Alter the Natural History of Peptic Ulcer Disease?"
Professor
Division of Gastroenterology
McMaster University Medical Centre
Hamilton, Ontario, Canada

Jon I. Isenberg, M.D.
"Limitations of the *Helicobacter pylori* Hypothesis"
Professor of Medicine
Division of Gastroenterology
Department of Medicine
University of California at San Diego Medical Center
San Diego, California

Dennis M. Jensen, M.D.
"Current Uncertainties About the Impact of *Helicobacter pylori* on the Complications of Peptic Ulcer Disease"

Professor of Medicine
Division of Digestive Diseases
UCLA School of Medicine
Los Angeles, California

Barry J. Marshall, M.D.
"*Helicobacter pylori*—A Historical Perspective"
"Why, How, and When To Use Antimicrobials as Part of the Standard Management of Ulcer Disease in Order To Prevent Recurrences"
Research Foundation for *Helicobacter* and Intestinal Immunology
Charlottesville, Virginia

Julie Parsonnet, M.D.
"Gastric Lymphoma: A Complication of *Helicobacter pylori* Infection"
Assistant Professor of Medicine and Health Research and Policy
Division of Infectious Diseases
Department of Medicine
Stanford University School of Medicine
Stanford, California

Walter L. Peterson, M.D.
"Evaluation of *Helicobacter pylori* in Relation to Other Causes of Peptic Ulcer Disease"
Professor
Department of Internal Medicine
University of Texas Southwestern Medical Center at Dallas
Dallas, Texas

Pentti Sipponen, M.D.
"Limitations of *Helicobacter pylori* Hypothesis in Gastric Cancer"
Department of Pathology
Jorvi Hospital
Espoo, Finland

Duane T. Smoot, M.D.
"*Helicobacter pylori* Diagnostic Tests: Benefits, Sensitivity, and Specificity"
Assistant Professor
Division of Gastroenterology
Department of Medicine
Howard University Hospital
Washington, D.C.

Andrew H. Soll, M.D.
"The Role of Acid Secretion in Peptic Ulcer Pathogenesis"
Professor of Medicine
UCLA School of Medicine
Center for Ulcer Research and Education (CURE)
Los Angeles, California

Amnon Sonnenberg, M.D., M.S.
"Economics of Ulcer Treatment: The Impact of Ulcer Treatment With Antibiotics"
Associate Professor
Division of Gastroenterology
Department of Medicine
The Medical College of Wisconsin
Milwaukee, Wisconsin

Nicholas Joseph Talley, M.D., Ph.D.
"Epidemiology of *Helicobacter pylori* Infections"
Professor
Gastrointestinal Division
Mayo Clinic
Division of Medicine
Nepean Hospital
Penrith, N.S.W., Australia

W. Grant Thompson, M.D., F.A.C.P., F.R.C.P.(C)
"Characterization of Dyspepsia"
Professor of Medicine
University of Ottawa
Chief, Division of Gastroenterology
Ottawa Civic Hospital
Ottawa, Ontario, Canada

G.N.J. Tytgat, M.D.
"Which Treatment Regimens Have Been Shown To Be Effective in the Eradication of *Helicobacter pylori* and Thus Prevented Ulcer Recurrence?"

Professor of Medicine
Division of Gastroenterology and Hepatology
Academic Medical Center
Amsterdam-Zuidoost, The Netherlands

John H. Walsh, M.D.
"The Role of *Helicobacter pylori* in Pathogenesis of Peptic Ulcer Disease"
Professor of Medicine
Gastroenteric Biology Center
Department of Medicine
UCLA School of Medicine Center for the Health Sciences
Center for Ulcer Research and Education (CURE)
Los Angeles, California

T. Ulf Westblom, M.D.
"Susceptibility and Resistance of Antimicrobials in the Treatment of *Helicobacter pylori*"
Division of Infectious Diseases and Immunology
St. Louis University School of Medicine
St. Louis, Missouri

Kenneth G. Wormsley, M.D., D.Sc.
"*Helicobacter pylori* and the Cause of Ulcer Disease"
Department of Medicine
University of Dundee
High Salvington
Worthing
West Sussex, United Kingdom

Planning Committee

Frank A. Hamilton, M.D., M.P.H.
Director
Digestive Diseases Programs
Division of Digestive Diseases and Nutrition
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
Bethesda, Maryland

Martin J. Blaser, M.D.
Addison B. Scoville Professor of Medicine
Director, Division of Infectious Diseases
Professor of Microbiology and Immunology
Department of Medicine
Vanderbilt University School of Medicine
Nashville, Tennessee

Benjamin T. Burton, Ph.D.
Associate Director for Disease Prevention and Technology Transfer
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
Bethesda, Maryland

Leslie Curtis
Writer
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
Bethesda, Maryland

Jerry M. Elliott
Program Analyst
Office of Medical Applications of Research
National Institutes of Health
Bethesda, Maryland

James Everhart, M.D., M.P.H.
Director
Epidemiology and Data Systems Program
Division of Digestive Diseases and Nutrition
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
Bethesda, Maryland

John H. Ferguson, M.D.
Director
Office of Medical Applications of Research
National Institutes of Health
Bethesda, Maryland

Willis R. Foster, M.D.
Senior Staff Physician
Office of Disease Prevention and Technology Transfer
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
Bethesda, Maryland

David Y. Graham, M.D.
Professor of Medicine and Molecular Virology
Baylor College of Medicine
Houston, Texas

William H. Hall
Director of Communications
Office of Medical Applications of Research
National Institutes of Health
Bethesda, Maryland

Jay H. Hoofnagle, M.D.
Director
Division of Digestive Diseases and Nutrition
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
Bethesda, Maryland

Leslye D. Johnson, Ph.D.
Chief, Enteric Diseases Branch
Division of Microbiology and Infectious Diseases
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Bethesda, Maryland

Barry J. Marshall, M.D.
Research Foundation for *Helicobacter* and Intestinal Immunology
Charlottesville, Virginia

Duane T. Smoot, M.D.
Assistant Professor
Division of Gastroenterology
Department of Medicine
Howard University Hospital
Washington, D.C.

John Walsh, M.D.
Professor of Medicine
Gastroenteric Biology Center
Department of Medicine
UCLA School of Medicine
Center for the Health Sciences
Center for Ulcer Research and Education (CURE)
Los Angeles, California

Tadataka Yamada, M.D.
Conference and Panel Chairperson
John G. Searle Professor and Chair
Department of Internal Medicine
University of Michigan Medical Center
Ann Arbor, Michigan

Conference Sponsors

National Institute of Diabetes and Digestive and Kidney Disease
Phillip Gorden, M.D.
Director

Office of Medical Applications of Research
John H. Ferguson, M.D.
Director

National Institute of Allergy and Infectious Diseases
Anthony S. Fauci, M.D.
Director

Statement Availability

Preparation and distribution of this statement is the responsibility of the Office of Medical Applications of Research of the National Institutes of Health. Free copies of this statement as well as all other available NIH Consensus Statements and NIH Technology Assessment Statements may be obtained from the following resources:

NIH Consensus Program Information Service
P.O. Box 2577
Kensington, MD 20891
Telephone 1-800-NIH-OMAR (644-6627)
Fax (301) 816-2494
BBS (301) 816-9840

NIH Office of Medical Applications of Research
Federal Building, Room 618
7550 Wisconsin Avenue MSC 9120
Bethesda, MD 20892-9120

Full text versions of all these statements are also available online to users of the Internet through the following services:

Gopher
gopher://gopher.nih.gov/Health and Clinical Information

World Wide Web
http://text.nlm.nih.gov

ftp
ftp://public.nlm.nih.gov/hstat/nihcdcs

U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES
Public Health Service
National Institutes of Health
Office of Medical Applications of Research
Federal Building, Room 618
Bethesda, MD 20892

Official Business
Penalty for private use $300

BULK RATE
Postage & Fees
PAID
DHHS/NIH
Permit No. G763