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Year's comments for 2005

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For several years, new sequences of microbial genomes have been the highlights of microbiology and a major topic of our yearly comments. But sequencing has become "routine" and, at the time this editorial is being written, the complete sequences of 284 prokaryotic genomes and 40 eukaryotic genomes have been published. This allows us to focus our comments on those events from 2005 that have attracted the attention of both researchers and the media. These include the Nobel Prize in Physiology or Medicine, which was awarded for the discovery of the role of *Helicobacter pylori* as the causal agent of gastric ulcers; the worldwide effort to fight malaria, a disease that mainly affects developing countries; and the global spread of avian influenza, which is becoming a panzootic.

The 2005 Nobel Prize in Physiology or Medicine was awarded to a discovery in the field of bacteriology that was made in 1982, when J. Robin Warren and Barry J. Marshall first observed the presence of *Helicobacter pylori* (then *Campylobacter pylori*) in the human stomach and related it to subsequent gastritis and peptic ulcers [3]. Warren and Marshall provided evidence that the presence of *H. pylori* in the stomach was always associated with an inflammation of the underlying gastric mucosa. For the medical community, recognizing that *H. pylori* caused ulcer meant a major paradigm shift: such a disease could no longer be considered to be psychosomatic; instead, it would enter the realm of infectious disease [4]. Throughout the century-long history of the Nobel Prize in Physiology or Medicine, about 21 works related to microbiology have received awards (Table 1).

Pathologists noted the presence of spiral bacteria in the human stomach as early as 1906. Although similar observations were repeatedly reported during subsequent decades, they did not receive much attention because the bacteria could not be cultured. Also, it was long believed that the normal human stomach was sterile, as a consequence of the extremely low pH of gastric acid. Cultivation of a novel bacterium from the gastric mucosa, in 1982, marked a turning point in our understanding of gastrointestinal microbial ecology and disease. Marshall and Warren described spiral or curved bacilli in histological sections. Moreover, the bacteria were often seen in malignant or ulcerated gastric tissue. However, the idea that bacteria, and not stress or acid, were the cause of ulcers flew in the face of medical dogma. Conclusive evidence for a pathogenic role of *H. pylori* came from trials showing that elimination of the bacterium dramatically changed the clinical course of ulcer. This finding was confirmed by Marshall, who swallowed a broth of *H. pylori* and soon thereafter developed gastritis, the prelude to ulcers. He recovered from the disease after treatment with antibiotics. (Warren could not join him in the experiment because he already suffered from peptic ulcer.) Subsequently, the two investigators successfully treated other people suffering from ulcers, in the process clearly identifying the bacterium as the culprit. In 1994, *H. pylori* was the first bacterium, and the second infectious organism after hepatitis B virus, to be classified as a class I carcinogen according to the World Health Organization (WHO) criteria. [As a historical curiosity, note that the 1926 Nobel Prize (Table 1) was awarded for the discovery of a nematode (a worm) that "was carcinogenic".]

Like other bacteria specialized to live in a single environment, *H. pylori* has a small genome. *H. pylori* strain 26695, the first to be sequenced (in 1997) has a circular chromosome of 1.66 Mb. A second complete genome sequence (strain j99) of 1.64 Mb was published in 1999. The apparent lack of recombination/repair genes in the *Helicobacter* genome offers a plausible explanation for its high rate of mutation. Nevertheless, the reasons why *H. pylori* integrates very small pieces of foreign DNA into its chromosome are currently unknown. The bacterium was thought originally to be a member of the genus *Campylobacter* and was named *Campylobacter pyloridis*, later corrected to *Campylobacter pylori* and finally *Helicobacter pylori* (the new genus *Helicobacter* was established in 1989). It is classified in the epsilon subdivision of the proteobacteria on the basis of its 16S rRNA. There are more than 20 *Helicobacter* species that colonize both the gastric mucosa and the intestinal tract and/or the liver (enterohepatic) of humans and other mammals, such as the human enteric pathogens *H. fennelliae*, and *H. cinaedi*. Bile-resistant organisms were first isolated from the biliary tract and liver of rodents (*H. hepaticus*, *H. bilis*), while another *Helicobacter* species (*H. felis*) is known to infect cats (Fig. 1).

Helicobacter pylori has been found in the stomachs of humans in all parts of the world (and is commonly isolated from nonhumans as well). In developing countries, 70 to 90% of the population carries *H. pylori*, while in developed countries the

Table 1. Main Nobel Prizes in Physiology or Medicine related to microbiology

Year	Scientists	Work	Field*
1901	Emil von Behring	For his work on serum therapy, especially its application against diphtheria	I
1902	Ronald Ross	For his work on malaria showing how the parasite enters the host	P
1905	Robert Koch	For his investigations and discoveries in relation to tuberculosis	B
1907	Alphonse Laveran	In recognition of his work on the role played by protozoa in causing diseases	P
1908	Paul Ehrlich, Ilya Mechnikov	In recognition of their work on immunity	I
1919	Jules Bordet	For his discoveries related to immunity	I
1926	Johannes Fibiger	For his discovery of the *Spiroptera carcinoma* [a nematode "causing cancer"]	P
1927	Julius Wagner-Jauregg	For his discovery of the therapeutic value of malaria inoculation in the treatment of dementia paralytica	P
1928	Charles Nicolle	For his work on typhus	B
1939	Gerhard Domagk	For the discovery of the antibacterial effects of prontosil	A
1945	Ernst B. Chain, Alexander Fleming, Howard Florey	For the discovery of penicillin and its curative effect in various infectious diseases	A
1951	Max Theiler	For his discoveries concerning yellow fever and how to combat it	V
1952	Selman A. Waksman	For his discovery of streptomycin, the first antibiotic effective against tuberculosis	A
1954	John F. Enders, Frederick C. Robbins, Thomas H. Weller	For their discovery of the ability of poliomyelitis viruses to grow in cultures of various types of tissue	V
1960	Frank Macfarlane Burnet, Peter Medawar	For their discovery of acquired immunological tolerance	I
1966	Peyton Rous [Charles B. Huggins]	For his discovery of tumor-inducing viruses [For his discoveries concerning hormonal treatment of prostatic cancer]	V
1972	Gerald M. Edelman, Rodney R. Porter	For their discoveries concerning the chemical structure of antibodies	I
1975	David Baltimore, Renato Dulbecco, Howard M. Temin	For their discoveries concerning the interaction between tumor viruses and the genetic material of the cell	V
1976	Baruch S. Blumberg, D. Carleton Gajdusek	For their discoveries concerning new mechanisms for the origin and dissemination of infectious diseases	B-V
1997	Stanley B. Prusiner	For his discovery of prions, a new biological principle of infection	V
2005	Barry J. Marshall, J. Robin Warren	For their discovery of the bacterium *Helicobacter pylori* and its role in gastritis and peptic ulcer disease	B

Adapted from: The Nobel Foundation [nobelprize.org/medicine/laureates/index.html].
*Field (or related to): A, antibiotics; B, bacteriology; I, immunology; P, protistology, or parasitology; V, virology.

prevalence of infection is lower, ranging from 25 to 50%. The ability to colonize and persist in the human stomach for many years indicates that *H. pylori* is specifically adapted to occupy only this niche, and such adaptation should be reflected in a unique complement of physiological capabilities. Although it is difficult to estimate the requirements for life-long colonization of the human stomach, *H. pylori* is clearly confronted with multiple environmental challenges, such as initial colonization, adherence, resistance to gastric clearance, protection against the host immune system, and transmission to another human individual with a different genetic background.

Possible symbiotic relationships have been debated since the discovery of this pathogen, and the debate has been further intensified by recent studies posing the intriguing possibility that *H. pylori* infection may be advantageous in some humans. This suggestion is based on the increased incidence of several diseases, such as gastro-esophageal reflux disease (GERD), Barrett's esophagus, and adenocarcinoma of the esophagus, following *H. pylori* eradication in some patients.

The cover story of the November 7, 2005 issue of *Time* magazine was devoted to the fight against diseases that affect developing countries. The magazine highlighted the work carried out by a group of 18 "solidarity heroes", as *Time* called them, made up of physicians, researchers, and non-governmental organizations. Among these heroes is Pedro Alonso, director of the International Health Center of the *Hospital Clínic* of the University of Barcelona. Alonso leads a research team that has focused its work on the development of a vaccine against malaria, a disease that annually kills 1.5–2.7 million people worldwide. Ninety percent of malaria's victims are African children less than five years old; and in some African regions almost half of all malaria cases occur in infants less than one year old. Expectations regarding the candidate vaccine currently being tested (RTS.S/AS02A) are quite high. A follow-up of 1442 children who were inoculated in 2003 has shown that the vaccine has retained its efficiency over a 1.5-year period. The RTS.S/AS02A vaccine reduced clinical malaria in 35% of vaccinated individuals, and the severe malaria in 49%. These results, published recently in *The Lancet* and presented at the Multilateral Initiative on Malaria's Pan-African Malaria Conference, held in Yaounde, Cameroon, in November 2005, are very promising. The vaccination project is a joint venture of the International Health Center in Barcelona, GlaxoSmithKline

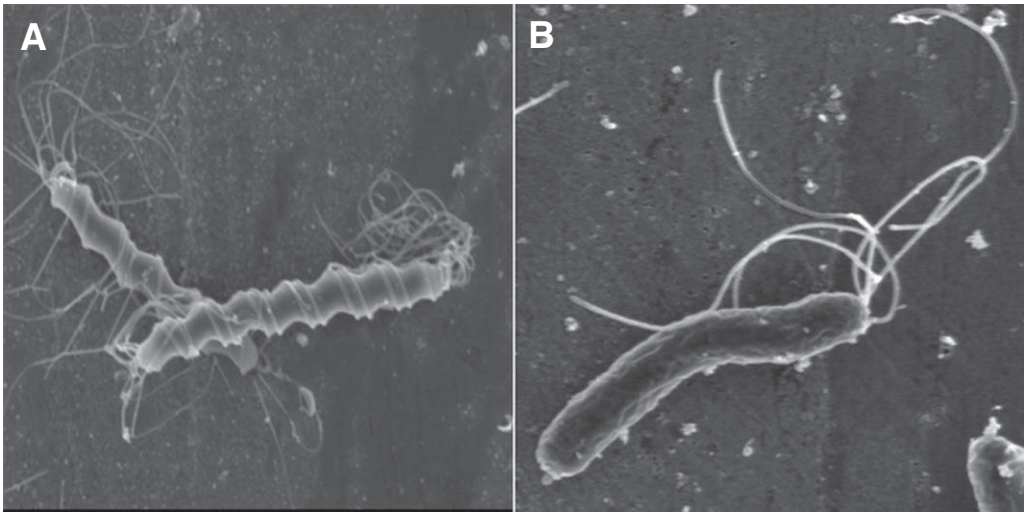

Fig. 1. (**A**) Scanning electron micrograph of *Helicobacter felis* isolated from the gastric mucosa of a cat. The characteristic spiral morphology and periplasmic fibers are shown. (**B**) Scanning electron micrograph of *H. pylori* from human gastric epithelium. The gently curved morphology, multiple polar flagella, and absence of periplasmic fibers are shown. Micrographs courtesy of Lucinda Thompson, presently at Stanford University, USA.

(GSK) Biologicals, and the Center for Health Research in Manhiça, Mozambique, and has received funds from the Bill & Melinda Gates Foundation.

Another initiative is The International Preventive Treatment in Infants (IPTi) Consortium [http://ipti-malaria.org], which evaluates new studies on malaria control in infants and coordinates research on malaria carried out by centers in Africa, Europe, and the United States, as well as by WHO and the United Nations Children's Fund (UNICEF). The IPTi Consortium, also sponsored by the Bill & Melinda Gates Foundation, has set up its Secretariat at the International Health Center in Barcelona, and Andrea Egan has been appointed as Coordinator. Egan is a British scientist with extensive experience in malaria research, carried out in the UK, Gambia, the USA and Mali. On the way towards the development of an effective malaria vaccine, intermittent preventive treatment is a novel promising strategy to control malaria. Children receiving antimalarial drugs intermittently during their first year of life have half the risk of contracting the disease and of developing infantile anemia. As children are usually the group at highest risk of disease and death, targeting them is an effective way to control the disease. By coordinating research and treatment strategies, the Consortium is also able to standardize approaches to the measurement of outcome. It can also conduct trials designed with the same objective and at many sites, which is essential because the pattern of malaria can vary greatly between geographic regions.

A recurring microbiological topic during 2005 has been the widespread outbreaks of avian influenza, or "bird flu", throughout southeastern Asia. Like other influenza viruses, avian influenza viruses are segmented genome RNA viruses belonging to the family Orthomyxoviridae. The current epizootic, which began in 2004, is caused by a H5N1 virus (H and N stand for the hemagglutinin and neuraminidase surface antigens), and there is tremendous concern that, although such viruses tend to be highly species-specific, H5N1 will eventually cross the species barrier to infect humans. More than 100 human cases of avian influenza have been reported during the current outbreaks. Nevertheless, this is a small number compared with the millions of birds that have been affected and the many occasions of human exposure. However, simultaneous infection of humans (or swine) by avian influenza and human influenza virus could occur, and the inevitable reassortment of genome subunits between the two viruses could result in a highly virulent, novel influenza virus with pandemic potential [2].

On April 28, 2005, the European Commission adopted a proposal for a Directive establishing updated EU-level measures on the control of avian influenza. Widely updated information on both the outbreak of avian influenza in Europe and the measures adopted by the EU can be found at the "Animal Health Welfare" website of the European Commission: [http://europa.eu.int/comm/food/animal/diseases/controlmeasures/avian/index_en.htm]. WHO also has a website providing information about avian influenza, including a description of the disease; its diagnosis and treatment; surveillance; infection control; food safety; and WHO guidance on public health measures in countries experiencing initial outbreaks of H5N1 avian influenza: [http://www.who.int/csr/disease/avian_influenza/ en/].

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The relationship between the Spanish Society for Microbiology (SEM) and the American Society for Microbiology (ASM) continues to grow. The SEM has mediated agreements between the ASM International Committee and Spanish universities and research centers to launch a program of scholarships for young Latin American researchers to train in Spanish laboratories. The ASM has supported microbiology education and research internationally since the 1970s, promoting partnerships between North American microbiologists and foreign scientists and students. It also provides training in several related fields, collabo-

rating with international organizations, including the Pan American Health Organization (PAHO), the United Nations Educational, Scientific and Cultural Organization (UNESCO), the International Union of Microbiological Societies (IUMS), and microbiological societies from all over the world. In Spain, the ASM has already signed two agreements, one with the University of Salamanca and the other with the University of the Balearic Islands. To discuss these developments as well as other aspects of the relationship between the ASM and the SEM, Stanley Maloy, current ASM President, and Lily Schuermann, ASM Director of International Affairs, came to Spain on the occasion of the 20th Conference of the SEM (Cáceres, Sept. 19–23, 2005). Maloy talked about "The future of microbiology: An international partnership." Back in the United States, he wrote to us about their (his and Schuermann's) visit to Spain: "We thoroughly enjoyed hearing the excellent microbiology presented at the meeting, making many new scientific friends, and learning more about how the ASM might enhance collaborations with Spanish microbiologists, […] I was particularly impressed with the outstanding quality of the young microbiologists participating in the meeting, and I thoroughly enjoyed learning about your science."

INTERNATIONAL MICROBIOLOGY readers are aware of the journal's commitment to open access publication [1]. This has been our policy even before the term "open access" was coined. For a non-first-rank journal, however, open access is a double-edged sword: whereas it makes it possible to increase the journal's readership, open access encourages many would-be scientific authors to submit their articles to the journal. An analysis by country of both the visits to our website and the origin of articles submitted to INTERNATIONAL MICROBIOLOGY shows that the number of articles, especially from scientists in several non-English-speaking countries, has greatly increased. These figures also tell much about the increasing visibility of the journal. Most identified visits over the period January–November 2005 were from Spain (25.7%), followed by the United States (15%), India (5.7%), Mexico (4.9%), the United Kingdom (3.6%), and Germany (3.4%). Google has been the search engine most widely used to reach the INTERNATIONAL MICROBIOLOGY website.

From November 2004 to November 2005, 112 'articles' (research articles, reviews and research notes) were submitted for publication to INTERNATIONAL MICROBIOLOGY, of which 29 (25.9%) were published. While this implies a rejection rate higher than in 2004, it is a result of the considerable increase in the number of articles received rather than a decrease in the quality of the articles submitted. The total number of articles published, including 'complements' (editorials, perspectives, and obituaries), was 44. On the occasion of the 13th International Biodeterioration and Biodegradation Symposium, held in Madrid in Sept. 4–9, 2005, the September issue was published as a monograph that included outstanding contributions to the meeting.

The Directory of Open Access Journals (DOAJ), which includes in its databases only journals that are completely open access (those that have an embargo period are excluded), comprises 22 journals whose subject is microbiology. None of these is among the journals with the highest impact factors, although this is, at least in part, due to the fact that several of them are rather specialized (immunology, filaria, antimicrobials, halophiles, mycology, pathogens, etc.). However, the impact of many open-access journals will surely increase in the future, for two reasons: (i) A growing number of funding agencies are requiring that articles describing agency-funded research be published in open-access journals, and (ii) that the journals where those articles are published must fulfill several requirements regarding quality. A recent order of the Spanish Ministry of Education and Science [BOE, 7 Nov. 2005, pp. 36470–6] on the evaluation of research included the criteria for a means of diffusion (journal, book, conference) to be recognized as being of minimum impact for what is published in it. Those criteria were based on: (i) the informative quality of the journal as a means of scientific dissemination; (ii) the quality of the editorial process; and (iii) the scientific quality of the journals themselves. Our journal satisfy all these criteria.

The number of journals covered in the ISI citation databases that have switched to an open-access distribution model is increasing, and new open-access journals have been added to the ISI databases. In October 2004, the largest numbers of open-access journals indexed by ISI were in medicine and life sciences. However, it was in the fields of physics, engineering, and mathematics that open-access journals were more frequent among the highest ranking journals in their categories [5].

Joining the open access initiative comes at a cost that not all journals can afford. If readers no longer pay the cost of publishing, other ways to cover expenses must be sought. The generosity of institutions and centers that pay for subscriptions to the journal—despite the on-line availability, at no charge, of the entire contents of the journal—and the participation of an editorial team devoted to the journal as if it were an all-volunteer, 'non-governmental organization', make possible the publication of INTERNATIONAL MICROBIOLOGY and its contribution to promoting microbiology in Spain, Portugal and Latin America, and expanding microbiological knowledge worldwide.

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