Specific etiology was one of the most powerful and productive ideas in the entire history of medicine. Replacing a shadowy intellectual landscape of humors and miasmata with the notion that particular diseases had particular causes, it marked the beginning of the end for both diagnostic imprecision and clinical impotence.

Within the domain we now recognize as microbiology, the prime mover was, of course, Louis Pasteur. He had the genius to discern that the characteristic presence of distinctive types of microbe in different “diseases” of beer, and other natural processes, might be paralleled in human maladies. But it was Robert Koch who outlined the postulates according to which an organism could be conclusively implicated as the agent of a specific disease.

The now-familiar form of the four postulates closely followed Koch’s own work on anthrax. An organism under suspicion as a disease agent should be present in all cases of the disease. It should be cultured in pure form in the laboratory, cause the same disease when inoculated into a healthy animal, and be isolated again from the lesions of the disease. There have in fact been significantly different versions of these tenets over the years, as observed by K. Codell Carter (Medical History, 29:353, 1985). He also claimed that Edwin Klebs, rather than Jacob Henle, should be credited alongside Koch as their creator.

Whatever the historical truth, and however useful they have undoubtedly been, the postulates have also spawned many problems. Rene Dubos highlighted one such in Mirage of Health (Allen & Unwin, 1960) while discussing Koch’s work on tuberculosis. “Most of the persons present in the very room where he read his epoch-making paper in 1882 had been at some time infected with tubercle bacilli and probably still carried virulent infection in their bodies,” he wrote. “At that time, in Europe, practically all city dwellers were infected, even though only a relatively small percentage of them developed tuberculosis.” In a population where Mycobacterium tuberculosis infection is universal, Dubos suggested, the real cause of the disease is not the bacterium but the malnutrition and exhausting work which, for some unfortunate persons, convert infection into pathology.

Half a century later, there are additional grounds for asking whether the tenets of specific etiology can be considered as realistic any more. As well as more sophisticated comprehension of the ecological context explored by Rene Dubos, our understanding of pathogenesis is being continually modified by insights from disciplines such as microbial population genetics and molecular ecology.

We now recognize conditions triggered not by single, defined microorganisms but by consortia coexisting in biofilms. Another type of difficulty is posed by organisms that cannot be cultivated in the laboratory. A third stems from our considerably wider perspective on a disease such as cholera, whose epidemics cannot be fathomed on the traditional, simplistic model of pathogen and host but only through analysis ranging over fields as diverse as climatic change and human social behavior.

Among several attempts over the years to brush up Koch’s postulates to take account of new knowledge, Stanley Falkow’s paper (Rev. Infect. Dis. 10(Suppl 2):S274, 1988) was an elegant restatement in light of modern molecular genetics. Though conceptually updated, his
analysis was notable in continuing to offer the postulates as practical tools.

Less successful have been efforts to redraft the rules in the context of present-day ecological analyses of communicable disease. One recent proposal comes from Timothy Inglis of the University of Western Australia in Nedlands, Australia. His purpose, as explained in the *Journal of Medical Microbiology* (56:1419, 2007), is to take account not only of advances in molecular genetics and ecology but also of developments in scientific method and the philosophy of science. These include “growing ethical objection to the use of laboratory animal models for incremental scientific gain” which “places a restraint on the use of animal models for pathogenesis research or clinical diagnostic work.”

Conscious of the wider range of strategies now used to build an argument for a causal relationship, Inglis proposes what he calls a more inclusive approach to establish proof of causality. He builds up his argument from a series of assertions. The first is “congruence or reproducible correlation of a taxonomically defined life form with the clinico-pathological and epidemiological features of infection.” The second is “consistency of the demonstrable biological response in the subject to an encounter with the prospective infective agent.” The third is “progressive or cumulative dissonance as an explanation for pathophysiological processes at every known level of biological organisation in the subject.” And lastly: “curtailment of that pathophysiological process on the deliberate introduction of a specified biomedical intervention.”

Inglis asks us to recognize a subcategory of microorganisms to be called “priobes” based on “evidence to implicate the candidate biological entity as an initiator or primer for cumulative dissonance.” A priobe is “the sufficient and necessary antecedent cause of a pathophysiological process evident as an infectious disease.”

I have studied carefully, and wrestled with, these notions. I have even found them conceptually enticing. But Koch’s postulates were not devised as intellectual diversions. They were intended, and indeed served robustly for some years, as explicit guidelines for research. Having tried to apply Inglis’s proposals to several currently unresolved issues in disease aetiology, I find it hard to see where they take us.

Can they, for instance, be of any practical help to the research group in Venezuela which has been battling to understand the significance of *Helicobacter*, already familiar for its association with gastritis and gastric ulcers in humans, in Thoroughbred racehorses? The background to their work is a clutch of recent findings: isolation of a new enterohepatic *Helicobacter* species from two healthy horses, a report on a significantly raised prevalence of *H. equorum* DNA in hospitalized horses, and studies demonstrating a high incidence of gastric ulcers in racehorses in training.

The aim of the new research was to assess the presence of *Helicobacter* DNA in the gastric mucosa of 20 Thoroughbred horses in Caracas, Venezuela. None of the animals had shown any symptoms of gastrointestinal disease. The results of PCR tests on squamous and glandular mucosa samples (M. Contreras et al., Lett. Appl. Microbiol. 45:553, 2007) show that seven of the horses had gastric ulceration, five had gastritis, and six had both conditions. *Helicobacter*-like DNA was evident in two of the horses with gastric ulceration, in three of those with gastritis, in five of those with both pathologies, and in one with normal gastric mucosa.

Overall, therefore, 10 of the 11 infected animals showed gastric lesions, with just one of them having normal mucosa. “This suggests that *Helicobacter* species are present in the stomach of Thoroughbred horses,” the investigators conclude. “However, 39% of our horses with gastric pathologies did not show *Helicobacter* or other bacteria, indicating that lesions also may be due to other causes. . .This is the first report of *Helicobacter*-like DNA in the gastric mucosa of horses. The pathogenic potential of these organisms requires further investigation.”

I struggle to see how Inglis’s proposals could have helped to clarify this picture, or indeed could help to shape the next phase of research. Yet once we start pondering the issue, we are confronted with a wider question. In an age of molecular genetics, viable but not culturable organisms, biofilms, polymicrobial communities, transmissible spongiform encephalopathies, and highly sophisticated microbial ecology, is there a place for Koch’s postulates at all?