SACRED BOVINES

IS SCIENCE SELF-CORRECTING?

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Science is tentative, we often hear. Which means that scientists can make mistakes (*Sacred Bovines*, Oct., 2008; Feb., 2009; Sept., 2012). At the same time, we have great confidence in and vigorously defend evolution and climate change as undeniably true. How do we reconcile these apparently conflicting claims about the nature of science?

The conventional wisdom – how could one believe otherwise? (hence, this month's Sacred Bovine) – is that science is *self-correcting*. Errors may arise. But researchers supposedly examine each other's results critically. Any mistake is soon exposed. It cannot persist for long. Progress toward truth is restored. So they say.

If self-correction works, then when a new theory that corrects earlier mistakes finally becomes available, biologists should endorse it and accept it immediately. Yet, in several historical cases, the consensus actively *rejected* such new theories – the same theories that we now accept as unquestionably correct. What do such examples tell us about when one should trust science – or doubt it as tentative? A proper understanding seems essential if our students, as future citizens and consumers, are to learn how to address claims about, say, the safety of GMOs or vaccines, healthy diets, or the environmental impacts of development projects.

What Causes Pellagra?

Consider the history of pellagra, a disease sometimes described by three Ds – dermatitis, diarrhea, and dementia. Death once loomed as a possible fourth 'D'. In the early 1900s, as economic conditions worsened in the southern United States, the disease became epidemic in just a few short years.

What caused pellagra, and what could be done to treat it or prevent it? The history tells us something about scientific errors – and if, when, and how they are corrected (Rajakumar, 2000; Marks, 2003; Mooney et al., 2014).

Everyone seemed to acknowledge, even without systematic research, that pellagra was closely related to poverty. But that could hardly be regarded medically as a cause. In the next several years, many theories emerged. Pellagra was due to poor sanitation (some sort of infection), consumption of corn (moldy, spoiled?), poor environmental conditions, or seasonal influences. Because the first set of cases had been reported in an insane asylum, and pellagra was found frequently in prisons, orphanages, and cotton mill villages, and given that it shared features with tuberculosis, infection seemed most likely.

To help resolve the uncertainty, in 1912, mining baron Robert Thompson and cotton broker Henry McFadden commissioned a report from the New York Post–Graduate Medical School. The team traveled to Spartanburg, South Carolina, to collect epidemiological data firsthand. They issued their first report in 1914. They confirmed the contexts of poverty and sanitation. Having examined the role of diet, they excluded the possibility of any particular dietary item, such as corn. Their overall conclusion confirmed the earlier assumption of an infectious agent.

In the meantime, Casimir Funk introduced the concept of vitamins, and hinted in 1913 that pellagra, like scurvy and beriberi, might be a vitamin deficiency, too. Today, of course, we are inclined to celebrate his insight. Pellagra, we now know, is a niacin (vitamin B3) deficiency. But in the context of the time, without clear evidence, his proposal could only be regarded as speculative. Niacin was not yet known. Funk's "correction" was not truly effective.

In a separate 1914–15 study, initiated by the U.S. Public Health Service, Joseph Goldberger focused on diet and tried generally more varied diets in four different institutions. The effect on reducing pellagra was favorable. Goldberger's conclusions reflect our modern views, so his work tends to be rendered intuitively as groundbreaking. A classic study overturning the earlier misconceptions. Self-correction at work. Yet Goldberger's data were very broad. While the results indicated diet as a possible factor, Goldberger could not identify any particular deficiency, whether amino acid, mineral, or another factor. Ironically, he gave low probability to the role of any unknown vitamin. So, even though Goldberger was "right," his conclusions were justly regarded as incomplete and inconclusive. Correction is not as easy as identifying an alternative or producing a handful of confirming evidence.

A few years later, in 1916, the Thompson Commission published its final report. Drawing on additional research – and despite Goldberger's findings – they strongly echoed their earlier conclusions that pellagra was infectious. The tentativeness seemed resolved. End of story? Ironically – perhaps paradoxically – the apparent resolution to the theoretical uncertainty by a prestigious commission rejected the (ultimately) correct answer.

Even more remarkable, perhaps, were two supplemental sections to the final report by independent researchers invited by the commission to contribute their views. The first was by Charles Davenport, a noted biologist from Cold Spring Harbor Laboratory in New York. How did Davenport address the diet-versus-infection

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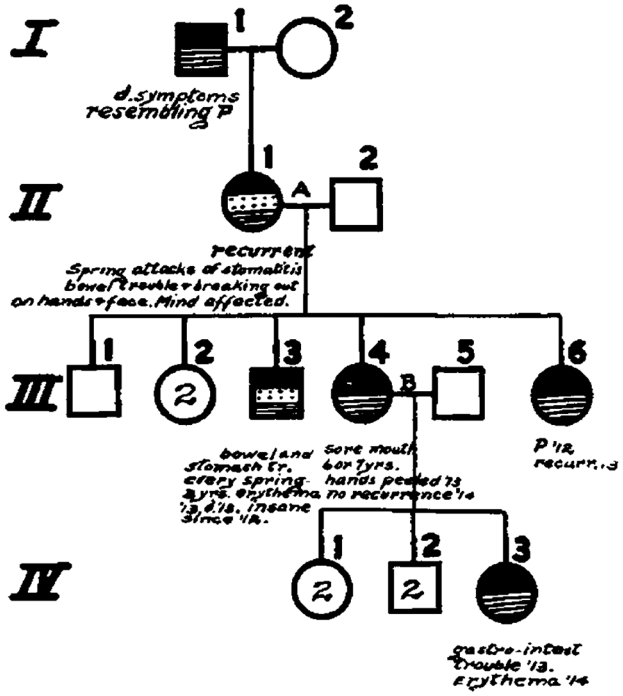

Figure 1. Amid the controversy about whether pellagra was caused by diet or infection, Charles Davenport presented this pedigree as evidence that pellagra had, instead, a significant hereditary factor. Davenport's error further confounded the debate, rather than contributing to a "self-correcting" process in science.

controversy? By dismissing both! The significant cause of pellagra, he concluded, was, instead, hereditary! Davenport presented over three dozen pedigrees, mapping the occurrence of pellagra across generations in families (Figure 1). Davenport acknowledged that the disease was "probably communicable," as the Thompson Commission contended, but he stressed that "constitutional factors" shaped the spread of the disease:

> When both parents are susceptible to the disease, at least 40 per cent., probably not far from 50 per cent., of their children are susceptible; an enormous rate of incidence in a disease that affects less than 1 per cent., of the population on the average. . . . We can understand this on the ground of inheritable differences in constitution of the children, just as brown eyes and blue eyes occur in the same family.

For Davenport, family differences (for example, whether mental, dermal, or intestinal symptoms of pellagra predominated) reflected biotypes or bloodlines that "afford the best proof that there is, indeed, a hereditary factor in pellagra" (Davenport, 1916, p. 15). More evidence, then. But it hardly promoted correction. Davenport's interpretation (we may easily observe in retrospect) was surely influenced by his belief in eugenics. For him, many undesirable human conditions could be attributed to genetics, rather than discomforting social inequities or politics. He thus discounted the correlation of pellagra with economic impoverishment. And poverty was surely "inherited" – culturally. Historically, Davenport's high-profile pronouncement led away from, not towards, correction.

The second addition to the commission's 1916 report was from Edward Vedder, who had worked earlier on beriberi, recently identified as a vitamin deficiency. Vedder vigorously defended the skeptical position that "much of the evidence that has been presented as a proof of the infectious nature of pellagra can be reasonably explained in accordance with a deficiency hypothesis" (Vedder, 1916, p. 172). Still, while maintaining that "the hypothesis that pellagra is caused by a deficiency is very plausible and must be taken into consideration in subsequent studies of this disease," he refrained from endorsing it fully. He regarded "the question as to whether pellagra is an infection or a deficiency disease to be entirely open" (p. 137). Unfortunately, perhaps, that caution was not widely accepted in the shadow of the Thompson Commission's and Davenport's strong claims. It may seem to us, now, that Vedder was correcting science at this point. But in the context of the time, this required knowing (anachronistically, in advance of the future history) to trust Vedder, not Davenport or the commission, as the voice of science (*Sacred Bovines*, May, 2012). That is the conundrum or error. Based on the 1916 report, science seemed to have just "self-corrected." But, ironically, it had not.

Meanwhile, Goldberger had continued his work under the Public Health Service. In a new study also published in 1916, he and labor economist Edgar Sydenstricker echoed the diet deficiency hypothesis. But now they linked poor diet directly to low wages and the high cost of food, which they presented as the root cause:

> [T]he proportion of families affected with pellagra declines with a marked degree of regularity as income increases.

They further blamed the agricultural system in the South, which was focused on cotton as a cash crop, at the expense of growing local vegetables, which, where available, tended to alleviate the risk of pellagra. That is, the problem was fundamentally or primarily socioeconomic, not biological. Their emphasis on the social system – faulting the tenant system and agricultural economy – would continue at least until 1927 (Marks, 2003, quotation on p. 45). That did not really help foster understanding of any specific nutritional dimension of pellagra. Even Goldberger and his colleagues (heroes, today) seemed not always to contribute methodically to correcting the science.

Because most scientists considered the question resolved, they did not seek further evidence. That was due to Goldberger's work alone. In 1922, he finally narrowed down the apparent deficiency to an amino acid – either tryptophan or cysteine – while simultaneously rejecting a role for vitamins. Again, what appears as self-correction supports the wrong conclusion. By 1924, Goldberger reversed himself again, accepting vitamin H as a factor. The subsequent publications (in 1927) began to gain some traction among other scientists. Goldberger had found a simple nutritional supplement, yeast, that seemed effective in treating pellagra in both dogs and humans. Hospitals and other institutions had a concrete (and affordable) remedy that could be implemented. Scientific opinion followed. But still without full clarity on what caused pellagra. Goldberg died of cancer in 1929, and without his effort, the search for dietary clues to pellagra waned.

Although Goldberger was largely correct, nicotinic acid (vitamin B3) was not identified until 1937. In summary, correcting early theories about spoiled rice and infection was anything but straightforward. Many opportunities to shift closer to the ultimate solution were missed. Equally important, perhaps, was the

challenge of any policymaker during the period. Could they have effectively relied on a scientific consensus to identify with certainty the cause of pellagra? The Thompson Commission, in the implicit role of a panel of experts resolving errors, was wrong. Davenport introduced yet more error. Vedder's cautions were overshadowed. Goldberger's claims were vague or inconsistent. Correcting the rejections itself took time. The process hardly conjures an image of systematic or methodical "self-correction." Nor any explicit test for knowing when corrections might *finally* be done.

Yes, correction did occur. But not *self*-correction. The convoluted history of pellagra does not exhibit any uniform progress towards a solution. One should consider the many particular factors that did yield gains. Substantial effort separated Funk's proposed explanation of a vitamin deficiency and general acceptance of the corrected theory over two decades later. Corrections are not guaranteed, and sometimes the new, corrected theory is, ironically, actively rejected.

○ Reassessing the Image of Self-Correction

The dynamics in the history of pellagra are not an isolated case. Other biological theories correcting past errors have been rejected when introduced. For example, in 1849, John Snow provided evidence supporting the idea that cholera was caused by a waterborne agent. Before that, doctors, statisticians, and public health officials had focused on miasmas, or poisonous fumes, emanating in various geographic districts. Snow's correction was read, considered, and rejected – and rejected for roughly 17 years (Eyler, 2001; Johnson, 2006). In 1847, Ignaz Semmelweis presented evidence that puerperal fever, affecting mothers after childbirth, was caused by putrid matter on the hands of physicians themselves, and could be prevented by simple antiseptic hand-washing. While practices changed in some hospitals, Semmelweis battled unsuccessfully for recognition of his theoretical interpretations, generally accepted only two decades later (Carter, 1983). Similarly, Barry Marshall and Robin Warren struggled to persuade their colleagues that stomach ulcers were caused by a bacterium, *Helicobacter pylori*, and not by stress, as had been assumed by doctors for decades. Their eventual Nobel Prize stands in stark contrast to the initial skepticism and sometimes dismissive criticism (Thagard, 1999).

Other cases abound. Acupuncture as an effective analgesic was rejected by U.S. physicians in the 1970s as so much Chinese quackery, although later endorsed by a National Institutes of Health consensus panel in the 1990s (Bowers, 1979; Allchin, 1996). The concept of prions – one of several corrections to the central dogma of molecular biology – was reviled for years (Prusiner, 2003). The endosymbiotic origin of mitochondria and chloroplasts was proposed in the 1920s, as a correction to the assumption that organelles originated autogenically. Now taught in textbooks, that revised theory was ridiclued at the outset (Hagen, 1996). So, while scientific theories may be corrected – ultimately – the many examples where corrections were initially rejected indicate that the practice of science offers no clear promises. Moreover, those rejections were often sustained over time.

Certainly, correction in science can occur. But science is not homoeostatic, or self-correcting. There is no feedback mechanism, such as one finds in a thermostat, or in the physiological processes that regulate metabolism, blood sugar, oxygen levels, and so on. Some corrections are even rejected at first. Errors are corrected by other means.

How, then, are errors remedied? Above all, error correction takes work. First, contrary evidence does not magically and conveniently appear on its own. Errors rarely announce themselves. They can go completely unnoticed without the appropriate perceptual filters. Or they can be dismissed as artifacts or unusual exceptions. Alternative ideas must take hold, allowing one to identify possible blind spots and where, precisely, relevant new evidence might be telling.

Second, someone must have the personal motivation to pursue the prospect of developing new, possibly contrary, evidence. That interest may depend on cultural context. It may depend on an individual's biographical background. For example, Goldberger's family upbringing sensitized him to the plight of the poor who suffered from pellagra. At the same time, it oriented him as much to the socioeconomic causes as the biological ones. Science is indeed a thoroughly social and human endeavor.

Third, researching errors involves collecting more data. That requires more time, more materials, more resources. Who pays for that? Someone must have a concrete stake in correcting the error. Ironically, the investments by wealthy merchants and the Public Health Service may have had as much to do with maintaining a healthy workforce and local economies as with caring about the welfare of the disadvantaged who suffered from pellagra.

Fourth, conceptual change is not easy. Human mindsets, once established, are quite resilient. It seems to be how our brains work (*Sacred Bovines*, Aug., 2010). Once a solution or scientific explanation has been found acceptable, why think twice about it? When someone else finds an error, it requires cognitive restructuring. More work: communication, education, persuasion. Again, this is not an automated or easy process.

In summary, error correction in science requires many concrete factors, not some abstract ideal. Correction does not occur without noticing, motivation, funding, and conceptual context. If any of these many conditions fail (and the historical case here shows that sometimes they do), errors are likely to persist. Science is far from automatically *self-correcting*. Like science itself, finding and fixing errors requires persistent delving and the people and resources to do so.

Errors occur not only in science, but also in *understanding the nature of science*. Hence, one may perceive that the very image of science as self-correcting has its own history, sources, and biases. It certainly seems convenient in appealing to the authority of science. But the inherent promise may not be fully informed or fully informative, as exemplified in the rejection of the proper cause of pellagra and of other ultimately accepted concepts. Citizens and consumers need a full understanding of how scientific errors occur and persist, in order to make informed decisions. Articulating when and why correction occurs – namely, clarifying just how and in what ways science is tentative – will help empower students as scientifically literate citizens.

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