

## Editorial

# A Case of Self-Experimentation

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In this issue of *Cancer Epidemiology, Biomarkers & Prevention*, Cheng *et al.* (1) report that two of the investigators in their study (M. Root and Z. Cheng) each ingested 1.0  $\mu\text{g}$  of AFB1,<sup>2</sup> a group 1 hepatocarcinogen (2). The purpose of their experiment was to monitor the urinary excretion, over a 10-day period, of a metabolite of AFB1, AFM1. This is the first reported instance in which humans were intentionally dosed with this toxin. Here, we examine the propriety of this experiment in the context of self-experimentation, in general.

Self-experimentation has a lengthy, though largely unpublicized, tradition in medical research. Over the years, self-experimenters have made many valuable contributions to medicine. For example, in 1929, Werner Forsmann made an incision in his own arm and inserted a catheter through his vein, directly into his heart, confirming his belief that the heart could be accessed directly without requiring invasive surgery (3). Although such a procedure could have resulted in severe complications or death, Forsmann came out of the procedure virtually unscathed. He ultimately won the Nobel Prize in Medicine and was praised by the Nobel Committee for his courage in using himself as his first subject. More recently, another important discovery through self-experimentation was made by Dr. Barry Marshall. Marshall was convinced that peptic ulcer disease had an infectious etiology, but his medical and scientific colleagues were skeptical. To test his hypothesis, Marshall ingested isolated *Helicobacter pylori* (4). Soon after, he developed gastritis, thus providing critical support for his theory. Fortunately for Marshall, he treated himself with antibiotics and apparently eradicated the infection. A less successful self-experiment was performed by John Hunter, who infected himself with gonorrhea to better understand the venereal disease, only to find that he had also inadvertently infected himself with syphilis (5). This self-administered infection led to a life-long illness with syphilis, as well as decades of confusion within the scientific community regarding the etiology and disease spectrum of gonorrhea.

As these examples illustrate, the ultimate success or failure of self-experiments often has more to do with the particular luck of the researcher than the validity of the hypothesis; a self-experiment gone awry may derail the progression toward scientific discovery for years, as well as cause irreversible harm

to the experimenter (and potentially many other persons). Thus, good fortune for self-researchers may be the difference between veneration and ignominy among colleagues.

Despite the precarious nature of the results of self-experimentation, it has several perceived advantages over typical research methods, the most obvious being convenience. The self-experimenter often begins conducting research on himself the moment an idea strikes, thereby avoiding the costly and time-consuming process of gathering and educating outside research subjects. In addition, self-experimentation may skirt controversial liability issues. In the eyes of some self-experimenters, it may also remove the need for obtaining informed consent and IRB approval. Finally, self-experimenters often see themselves as ideal subjects because they tend to trust the validity of their own observations over those of random research subjects (6).

For these and perhaps other reasons, self-experimentation is probably a much more widespread practice than generally imagined. It is difficult to make an accurate estimate of the prevalence of the practice, due to a dearth of research on the subject and probable underreporting on the part of researchers. However, one recent anonymous survey of the Dutch Society of Clinical Pharmacology found that over half of those who responded had engaged in some sort of self-experimentation, and of those, only about half had published the results of their experiments (7). Whether these numbers are representative of self-experimentation conducted in other medical specialties and in other countries is unknown. Nevertheless, it is safe to conclude that self-experimentation in medical research is not an anomaly, but rather, probably occurs with some regularity.

If self-experimentation is common and only the self-experimenter can suffer harm, why should the scientific community care? There are, we think, both ethical and scientific reasons for avoiding self-experimentation. First of all, an experiment that an investigator regards only of potential harm to himself could, in fact, affect others. Consider Dr. Marshall's experiment. He could have transmitted *H. pylori* to family members or close contacts. How *H. pylori* is transmitted is still unknown.

Secondly, as a research method, self-experimentation is usually not good science. By its very nature, it is not repeatable and therefore, not reproducible. Sample sizes of one or two cannot represent the general population. In the study by Cheng *et al.* (1), the percentages of the administered dose of AFB1 recovered in the urine of the two subjects as AFM1 appear similar because the recovery percentages were low, 5.6-6.3% after 5 days. The mean difference in recoveries of AFM1 between the two subjects was about 12%, but the SD was 30%. Because the ultimate goal of the research by Cheng *et al.* (1) was to be able to estimate AFB1 exposure by measurement of AFM1 in urine samples collected in field studies, basing such estimates on their self-experiments could yield large errors. Thus, the observations made in self-experiments may yield skewed results that mislead rather than inform the scientific community.

Another problem with self-experimentation is that it tends

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<sup>2</sup> The abbreviations used are: AFB1, aflatoxin B<sub>1</sub>; AFM1, aflatoxin M<sub>1</sub>; IRB, Institutional Review Board; OPRR, Office for Protection from Research Risks.

to be narrowly focused only on the outcome of interest to the investigator. Therefore, the information derived from the experiment may be considerably less than what could have been observed with a similar research design, but with a broader definition of outcomes. Again, using the study of Cheng *et al.* (1) as an example, it would have been interesting to know what happened to the 94% of the AFB1 dose that did not end up as AFM1 in the urine. Even more important would have been measures of AFB1 toxicity, *e.g.*, alanine aminotransferase levels and complete blood counts before and after exposure to AFB1. The investigators believed that ingestion of 1  $\mu\text{g}$  of AFB1 was safe, but then they failed to monitor themselves to prove that it was safe.

Finally, what role, if any, should IRBs take in evaluating self-experiments? [The experiment by Cheng *et al.* (1) was approved, without comment, by his university's IRB.] The mission of the IRB is to protect human research subjects from undue risk. In the case of self-experimentation, however, IRBs are at a considerable disadvantage. There are no specific guidelines to cover their actions. The OPRR does not include self-experimenters among its special classes of research subjects. On the other hand, the OPRR considers normal volunteers to be a vulnerable population. Hence, IRBs could consider self-experimenters simply a subclass of normal volunteers. If this were so, then the IRB governing the protocol of Cheng *et al.* (1) might have insisted on eligibility criteria for participation in the experiment (absence of liver disease, absence of infection with hepatitis B or C viruses, and normal physical examination) and monitoring of the subjects throughout the experiment. The IRB could also have considered the possibility of long-term effects. Although such effects are difficult to recognize, the IRB could

have required follow-up physical examinations and laboratory tests for several months or even years after the self-experiment.

Western views of autonomy tend to allow people to do what they wish with their own bodies, up to some unstated point. Nevertheless, we believe that the IRB must exercise its same best judgment on self-experimentation, as it does on all other human research, particularly research on normal volunteers. Injury to a self-experimenter, if it should occur, is just as bad as an injury to any other normal volunteer. Self-experimentation should not be the equivalent of walking a tightrope without a net.

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