John Morrison Barnes, 1913–1975

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The first director of the Toxicology Research Unit of the British Medical Council, was educated as a physician and spent his early years at the Sir William Dunn School of Pathology, University of Oxford.

One day in 1938—as he himself related the story to me and my wife, Christine, in 1966 during a relaxed evening in a Swiss mountain resort—he was approached by a colleague who had developed what looked to be a most promising drug. Before treating people, however, the investigator thought that some toxicity evaluation was in order, and so he asked Barnes to do a few rudimentary tests. Barnes took the compound, injected it intraperitoneally into three mice, found them alive and well the next morning, and reported his findings as “your drug seems not to be toxic.” He then was offered to participate in further evaluations of the drug, but declined because, as he told me, he did not really believe in miracle drugs. The investigator who had approached him was Howard Florey, the drug was penicillin, and as Barnes admitted somewhat ruefully, with his disbelief in miracle drugs, he simply had talked himself out of a Nobel Prize.

In 1942, Barnes joined the British Defense Research Establishment in Porton. A paper describing some of his research at the time deserves to be mentioned. (Barnes eventually would publish around 120 papers, half of which were original research and reviews, the other half concerning the safe use of chemicals and the hazards they present to man). This particular paper coming out of Porton, “The development of anthrax following the administration of spores by inhalation” (Barnes, 1947) would not have raised much interest a few months ago, but now certainly has some new actuality. Some of the conclusions seem not to fit with current perceptions of the disease and its threat to mankind: “Evidence obtained during the carrying out of the spore count on the lungs of exposed animals (rabbits, guinea pigs and mice) suggest that the anthrax spores find the lung a very uncomfortable medium in which to germinate” and “Much higher minimum lethal doses of anthrax spores are necessary to produce infection by inhalation than by subcutaneous injection.”

In 1947, the Medical Research Council established the Toxicology Research Unit, charged with experimental investigations of toxicological problems, with special reference to industrial hazards. Barnes was appointed its first director, a post he held until his untimely death in 1975. Other members were F. A. Denz, V. H. Parker, and W. N. Aldridge, eventually a winner of the Society of Toxicology Merit Award (Johnson, 2001). The first scientific problem studied in the unit was the toxicity of beryllium (Aldridge et al., 1949). During his entire career at the Medical Research Council, Barnes continued to maintain a high interest in beryllium, particularly its immunogenic properties, and was actually to some extent chagrined that research on beryllium toxicity mostly dealt with biochemical mechanisms of liver cell death rather than to address what seemed to be the real problem, pulmonary disease. Other early research efforts focused on dinitro-ortho-cresol (Parker et al., 1951), research that later led to some fundamental studies on the uncoupling of oxidative phosphorylation, and on the toxicity of new organic phosphorus compounds that were being developed as promising pesticides (Aldridge and Barnes, 1952).

After the unit moved to Carshalton, Barnes became instrumental in developing and maintaining an excellent research climate. He was very encouraging toward young people and fully supported their growth as truly independent investigators. He cared deeply for the quality of science that was conducted in the unit, but he also saw to it that the results of fundamental research were used for practical purposes wherever possible. Although he gave much encouragement to what might be called “mechanistic” research these days, he was truly a biologist and genuinely committed to pathology. He made several unexpected findings in his research and recognized their broader implications: delayed skin sensitivity caused by beryllium in guinea pigs, single-dose carcinogenesis by nitrosamines, behavioral changes caused by trimethyltin, and two types of poisoning caused by pyrethroid pesticides.

Beginning in the 1950s, Barnes had become a very much sought-after consultant for the World Health Organization, particularly in regard to the worldwide use of pesticides. He was firmly convinced that pesticides, responsibly used, would benefit mankind by improving food production and would not constitute an undue health hazard, particularly not at the low levels found as food residues. He believed that research eventually would enable toxicologists to deal with the problem of
minute amounts of pesticides in a rational way or, as he said in a 1955 talk at a National Crop Protection conference: "Meanwhile there are a number of laboratories interested in the poisonous properties of these substances and as their work proceeds it is hoped to be able to put a more intelligent interpretation on the data (i.e., residues in food) the analytical chemists can eventually gather" (Barnes, 1956). When Rachel Carson published *Silent Spring* in 1962, he was not to remain silent himself. His review of her book is titled "A most sensational saga" (Barnes, 1963). It starts with these two sentences: "In her first chapter, the author allows her imagination to run riot in depicting the future. Is this to be compared with H. G. Wells' *War in the Air* or his *Invisible Man*?"

He goes on to discuss how in both Europe and the United States the use of pesticides is carefully reviewed by competent committees and highly regulated; as a matter of fact, he points out that "the standard set by those working for the Food and Drug Administration of the (United States) Public Health Service for levels of pesticides permissible in food has been a model for many other countries." He then roundly dismisses any possibility that pesticide residues found in the current environment could be responsible for all the adverse health effects that Rachel Carson attributed to them. He is also quick to emphasize that in 1962, with the exception of aramite, no pesticide in general use had been found to be carcinogenic. On the contrary, toxicological investigations had precluded the use of potent carcinogens such as acetylamino fluorene. In short, in his review of Rachel Carson's book, Barnes is a staunch advocate of the use of pesticides – "the intelligent, restrained and well conceived use of these valuable tools devised by man could make life on this planet much better for all the living things which interest everyone of us."

In those years, Barnes was by no means the only toxicologist who believed that pesticides were not the health hazard Rachel Carson described. I remember the visit and a talk given by Wayland J. Hayes, Jr., a former president of the Society of Toxicology and author of the authoritative *Pesticides Studied in Man*. Asked during the discussion following his talk on pesticides whether they did represent a carcinogenic hazard, Hayes replied (if memory serves me well) in the negative, adding that "the molecules that killed my and your grandparent also will be the molecules that will kill me and you."

Barnes had similar views on the hazards of chemical carcinogens. In an essay, he described in detail the discovery of the nitrosamines in which he, together with his collaborator Peter Magee, had played an instrumental role (Barnes, 1974). He expresses some personal disappointment about the apparent preoccupation of what he called "alarmists" with the few parts per billion of nitrosamines present in certain foodstuffs. Rather, he believed nitrosamines should be used to study initiation of cancer and, above all, the evolution of cancerous lesions—what appeared to Barnes to be a much more important theme than any initial interaction of a carcinogen with some molecules. He perceived cancer to be a disease of the whole organism, and he defined it as "a disease in which cells with a disordered pattern of growth overwhelm the forces in the tissues which attempt to maintain ordered growth in the whole animal." He even went one step further in discounting the possible role of chemicals as environmental carcinogens: "Cigarette smoking kills hundreds of thousand of people a year, and a minority of these die of cancer as a result of exposing their bronchial epithelium to numerous toxic substances in concentrations that would be totally intolerable in the general atmosphere. To argue from the fate of a minority of cigarette smokers that the majority of human cancers is caused by environmental chemicals is a glaring example of the more thoughtless arguments of those who set themselves up as guides and advisers for a better and safer life."

John Morrison Barnes died several years before the landmark paper written by Doll and Peto (1981) took issue with the putative role of environmental carcinogens in the etiology of human cancer. One cannot help but wonder what his reaction would have been, or whether he would write today the following, also from the review of *Silent Spring*, where he deals with the question of DDT residues in human tissues, a fact to which Carson attributed disease: "The metal lead has been known for years to get deposited in human bones. What evidence is there that this has increased the incidence of human disease?" Barnes was acutely aware of the toxicity of metals, and much fundamental research was being done in his unit on the toxicity of beryllium organotin compounds and mercury. Tom Clarkson spent a few early years in Carshalton where, with active encouragement by Barnes, he did significant work on mercury compounds (Clarkson and Magos, 1966). The statement about lead is thus puzzling. Was it meant to indicate that lead, once deposited in bone, would no longer be harmful unless perhaps mobilized, thus supporting the notion that residues of foreign chemicals need not necessarily lead to disease?

Obituaries for Barnes appeared in the *Times* (London, September 30 and October 2, 1975), *Lancet* (October 18, 1975, page 777), and the *British Medical Journal* (October 18, 1975, page 170), whose editor wrote: "The subjects he made specially his own were often knocked about in public controversy" (e.g., toxicity of insecticides, food additives, lead, saccharin), and "to a discussion of the facts he brought scrupulous scholarship and dispassionate judgment. Where others strayed into enthusiasm or error, he was firmly grounded in common sense." But above all, he will best be remembered for his leadership of the Toxicology Research Unit in Carshalton, as was summarized by Peter Magee (*Times*, London, October 2, 1975): "His powerful intellect and outstanding capacity for getting on with people at all levels of the scientific hierarchy enabled him to build up the Toxicology Research Unit from very small beginnings into one of the larger establishments in the Medical Research Council. His own scientific output and reputation could undoubtedly have been greater if he had been less unobtrusive and unselfish in his help to others. It is certainly true to say that he contributed more to the establish-
ment of toxicology as a branch of science than anyone in this, and perhaps in any other, country.”

There is a John Morrison Barnes Memorial Lecture at each Annual Meeting of the British Toxicology Society.

REFERENCES


