
Radiobiological Hormesis, Methodological Value Judgments, and Metascience

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Scientists are divided on the status of hypothesis H that low doses of ionizing radiation (under 20 rads) cause hormetic (or non-harmful) effects. Military and industrial scientists tend to accept H, while medical and environmental scientists tend to reject it. Proponents of the strong programme claim this debate shows that uncertain science can be clarified only by greater attention to the social values influencing it. While they are in part correct, this paper argues that methodological analyses (not merely attention to social values) also can help clarify uncertain science. The paper analyzes five measurement uncertainties, as well as seven methodological value judgments, relevant to H. Using criteria of internal and external consistency, as well as predictive power, it argues that metascience also helps resolve this debate. And if so, then value-laden, policy-relevant science may need, not only more attention to social values in order to resolve and to clarify disputes, but also more conceptual and methodological analyses of science. (This paper suggests what such methodological analyses might be like and uses the case of low-dose risks from radiation to illustrate its points, while a companion paper (“Chemical Hormesis, Conceptual Clarification, and the Warrant for Policy-Driven Science”) in this same issue of POS suggests what such conceptual analyses might be like and uses the case of low-dose risks from chemicals to illustrate its points.) If this paper’s thesis holds in the very politicized “hard case” of radiation hormesis, then it suggests that the metascientists may be right about what is also often necessary to clarify scientific disputes.

1. The Hormesis Debate in Radiobiology

At a 90-percent confidence level, biological effects of ionizing radiation from Chernobyl are likely to have caused, world-wide, 430,000 fatal premature cancers by the year 2000, roughly the same number caused by

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above-ground testing of United States nuclear weapons (Makhijani, Hu and Yih 1995, p. 75). UNSCEAR, the United Nations Scientific Committee on the Effects of Atomic Radiation, concluded recently that normal background radiation, alone, causes about 1 in 20 cancers, or roughly 30,000 cancer deaths annually in the United States (UNSCEAR 1994; Gonzalez 1994, p. 44). Despite the importance of these radiobiological fatalities, scientists are divided on their causes. One reason is the controversy over low-dose exposures and possible hormetic effects. (Hormetic effects are those that either benefit or, at least, do not harm an organism; taking 81 mg. of aspirin a day, for example, has the hormetic effect of reducing the probability of heart attack.) At the center of the conflict is hypothesis H that, although high doses of radiation (above approximately 20 rads) are harmful, low doses (up to about 20 rads) cause hormetic effects (Fry 1996). (A dose of radiation = E/dV , where E is the energy deposited, V is the volume of material hit, and d is the density of material; a rad is 100 erg/gram.)

Within the scientific community, there are two main positions on H. On one side are those who think H is more plausible than not-H. These are most of the representatives of the United States Department of Defense (DOD), the United States Department of Energy (DOE), the French government, and the nuclear industry. On the other side are those who think not-H is more plausible than H. These are most of the representatives of the medical and public-health communities, environmentalists, the United States Environmental Protection Agency (EPA), and other international and national radiation-protection groups. If H is correct, then likely the government will have to compensate many of the 400,000 atomic veterans and thousands of civilian downwinders; the United States can deregulate low-level nuclear waste; and many nuclear workers will not be awarded damages. If not-H is correct, then likely the government will have to compensate more atomic veterans and downwinders, the United States cannot deregulate low-level waste, and industry will have to provide damages to many nuclear workers.

2. Sociology versus Metascience: Two Strategies for Clarifying H

To many people, the debate over H appears to be more a matter of political values than scientific objectivity or rationality. That is, the quantitative risk assessment (QRA) debate over H seems to be influenced more by particular, interest-driven values of risk management than by the facts of epidemiology and QRA. To counter the way that risk-management values often subjectively influence risk-assessment facts, the United States National Academy of Sciences (NAS) has called for the separation of facts and values, of risk assessment from risk management (NRC 1983). But at least

two sorts of opponents, with quite different epistemological and methodological presuppositions, claim that such a separation is not possible. Although these opponents hold a variety of positions, they can be classified roughly by using the terminology of Mayo (1991) who divides them into “sociologists” and “metascientists.” The sociologists, advocates of the Strong Programme, such as Wildavsky and Douglas (1984), believe that it is possible to clarify hypotheses like H only by more attention to the social and political values that are inseparable from them. The metascientists, such as Mayo (1991) and Cranor (1993), believe that, although the positivists were wrong to say one can avoid all social and political values in science, nevertheless it is also possible to clarify scientific hypotheses like H by greater attention to metascience, that is, to developing a new set of tools for analyzing the scientific concepts, uncertainties, models, and inferences associated with methodological value judgments. Indeed, Mayo believes that, when it comes to questions of evidence and inference, the critique need not itself be a matter only of social and political values, but also of metascience.

For the most part, the sociologists appear to have captured public opinion regarding H. They say, for example, that the debate over H is really about the virtues of honesty and trust, not science (Dunlap et al. 1993), and that many people, including scientists, reject H in part because military-industrial groups support H and have lied in the past about damage from radiation. Higher numbers of breast and thyroid cancers have appeared around the Hanford nuclear installation, elevated leukemias near the Nevada test site, and statistically significant increases in brain cancers around Rocky Flats and Los Alamos; yet experts both said all these sites were safe and then spent 40 years covering up their knowledge of the increased fatalities (see D’Antonio 1993). Support for H, the sociologists say, comes from groups like the French, who receive most of their electricity from nuclear power, who denied for many weeks the presence of Chernobyl fallout (Lambert 1987), and who continue above-ground nuclear testing. Moreover, the sociologists point out, government studies of nuclear-worker safety are not to be trusted, because “practically all” of them have been controlled by promoters (like the DOE) of military and civilian nuclear technologies (Nussbaum and Kohnlein 1995, p. 203).

Contrary to the dominant sociological view of H, this paper argues that more attention needs to be paid to metascientific analyses of H. That is, one ought neither invoke only social or ethical values, nor impute motives, to show where the scientific debate over H goes wrong. Instead, one also ought to help resolve this debate by practicing metascience, conceptual and methodological analyses of science. And if so, the paper suggests, metascience ought to play a greater role in helping to adjudicate disagree-

ments over scientific hypotheses in QRA. Although facts and values cannot be completely separated, nevertheless metascientists have an important role to play in conceptual analysis of scientific terms and in criticizing methodological value judgments in science. This paper suggests what such *methodological* analyses might be like and uses the case of low-dose risks from radiation to illustrate its points, while a companion paper (“Chemical Hormesis, Conceptual Clarification, and the Warrant for Policy-Driven Science”) in this same issue of POS suggests what such *conceptual* analyses might be like and uses the case of low-dose risks from chemicals to illustrate its points.

3. Measurement Problems: the Heart of the Case for the Sociological View

What is it about debates over hormesis hypothesis H that suggests they can be resolved *only* through more or better consideration of social values, as opposed to both more or better science, as well as consideration of social values? One answer is that measurement of radiobiological effects is empirically underdetermined, and so scientists use social values to fill the gaps. Consider five ways measurement problems associated with H underdetermine the science. For one thing, there is an infinite number of *mathematical functions* that pass through all the human data points representing observations of radiobiological effects at high exposures. Yet each of these curves behaves differently in the low-dose region, and there are no uncontroversial low-dose data points to adjudicate among the curves, in part because one cannot engage in controlled experiments on humans to obtain the low-dose data. A second measurement problem is *technical apparatus*. There are different filters used to detect radiation, and there is controversy over which is best. The EPA, for example, uses filters that detect only about 15 percent of the atmospheric radioiodine of that detected in the filters that the Finns use (Caufield 1989, pp. 238–239).

A third difficulty is *uncontrolled data collection*. Even the most reliable high-dose data points, reliable because of the large sample size, have been obtained under uncontrolled conditions, e.g., at Hiroshima, Nagasaki, and Chernobyl. Given such uncontrolled and often unstudied conditions, it is unclear whether alleged low-dose effects were obscured, for example, by high naturally occurring rates of cancer; by individual variations in nutrition, lifestyle, and genetic susceptibility; or by external and internal selection effects (Trosko 1996).

Correlating particular *exposures and doses* presents a fourth problem. It is virtually impossible to affirm, confidently, that specific radiobiological doses to humans are associated with given releases. This is, in part, because dose uptake varies from individual to individual, because of previous exposures, and because there are many undetected radiation hot spots that

have radiation levels thousands or millions of times greater than average (Robbins, Makhijani, and Yih 1991, pp. 16–17). Even wearing dosimeters would not resolve all these difficulties, since internal exposures often are far greater than external.

A fifth measurement problem is *scale*. In order to use epidemiological methods to detect low-probability cancers from increments of radiation as small as 10 or 20 rem, one would have to use not only extraordinarily large sample sizes, but also extremely long follow-up times. As the doses became lower and approached background, however, the sample sizes needed for reliable results would exceed that available, even from the Japanese studies (MacLachlan 1995; Parsons 1994; Nussbaum and Kohnlein 1995, pp. 202–205). Yet lengthy epidemiological studies are necessary because there is no unique fingerprint in the DNA from radiation-induced, as opposed to other, disturbances (Trosko 1996, pp. 815–817). As a result, short-term studies tend to support H, while long-term studies tend to refute it.

4. Using Analysis of Methodological Values to Rescue Objectivity

The upshot of these five areas of uncertainty is that, given problems such as exposure-dose correlation and temporal scale, scientists often can choose to use or to interpret flawed studies in ways that serve their anchoring biases. Should one then agree with the sociologists that the debate over H is determined mainly by social values used to fill the uncertainty gaps? There are a number of reasons that the sociologists seem wrong on this point, one of which is that criticizing questionable methodological value judgments also can help provide a rational and objective analysis of H.

What are some of these methodological value judgments? One is that scientists need not stratify populations for age at exposure. This value judgment seems questionable, in part because the younger the organism, all things being equal, the more susceptible it is to various physical threats. Not to stratify a population by age, when age differences account for susceptibility differences, is to dilute the effects of exposure, to aggregate individuals in ways that presuppose they manifest similar epidemiological effects when, in reality, they differ in significant ways. In the case of low-dose radiation, studies that stratify populations for age at exposure show much higher and statistically significant risks from low-level ionizing radiation, while research that ignores *age stratification* finds hormetic effects in the form of no dose-related cancer risk for low-level radiation (Stewart and Kneale 1993; Nussbaum and Kohnlein 1995, pp. 202–204). Because proponents of H tend not to stratify their research populations and to make the methodological value judgment that they need not do so, their results are more open to question.

A second questionable methodological value judgment is that epidemiologists ought to compare the number of deaths of radiation workers (exposed to low-dose radiation) to fatalities in the general population, rather than to other worker fatalities. This judgment is questionable because comparing radiation-worker deaths to those in the general population is comparing apples and oranges. Because workers are much healthier than either retirees or children, comparing them to the entire population results in a bias that overestimates workplace safety, a bias known as the “*healthy-worker effect*.” Because so many proponents of H subscribe to this methodological value judgment, their results are likewise problematic.

Another questionable methodological value judgment is that stimulation or beneficial effects at only a few *biological endpoints*, rather than all relevant biological endpoints, provides sufficient evidence for the hormetic effects of low-dose radiation. This judgment is questionable because, from the point of view of objectivity, one is interested in net, not partial, biological effects. For example, a number of researchers who support H argue that low-dose radiation stimulates the organism with respect to two biological endpoints: weight gain and growth rate (Goldman 1996, pp. 1821), but they ignore all other endpoints such as carcinogenesis and lifespan. Other researchers did a year-long study and reported that small doses of radiation enhanced germination of birch seeds near Chernobyl, but they failed to control for other factors affecting germination, and they ignored important biological endpoints such as lifespan and mutagenetic effects (Yushov, Chueva, and Kulikov 1993). Still other researchers affirmed H after several years of studying minnows. They detected a tripling of mutagenetic effects from low-dose radiation but ignored them (because the effects did not increase, after the first few generations), and then claimed the radiation exposure was hormetic (Blaylock, Theodorakis, and Shugart 1996).

The length of the minnow study raises another important methodological value judgment, that one can evaluate H by performing *short-term studies* of days/weeks/years rather than life-span studies. For example, after a four-day study, Lee and Ducoff (1994) concluded that chicken red blood cells were able to repair radiation damage. Their analysis, however, relied not only on the methodological value judgment about short-term study but also on questionable judgments such as the acceptability of their removing the blood from the chickens, irradiating it under laboratory conditions, and then considering only the endpoint of hemolysis (dissolution of the red blood cells with the liberation of hemoglobin). They concluded that, at doses below 3000 rads, hemolysis was indistinguishable in the exposed group and in the controls. Had Lee and Ducoff done longer studies

that considered other biological endpoints such as immune-system suppression and lifespan, they likely would have been unable to allege that they had shown radiation hormesis. If one is attempting to assess hormesis, it seems more reasonable to employ life-span studies, in part because alleged short-term gains may be offset by long-term losses, and few people would prefer the former. Responses such as avoidance, removal, neutralization, or repair of low-dose damage may seem hormetic, but these strategies for combating harmful effects of low-dose exposures are likely to be metabolically very costly for the organism. As Calow (1991) argues, if metabolic costs increase after low-dose exposures but energy income remains the same, there will be tradeoffs, and the organism's production, reproduction, or some other aspect of its health will be affected negatively. For example, some recent studies on dogs allege hormesis and radioresistance after "priming doses" of low-level ionizing radiation. However, the animals that initially appeared to be radioresistant exhibited higher-than-normal rates of anemias, cancers, leukemias, and other diseases later in life (Fry 1996, p. 826). The methodological value judgment about short-term studies clearly is troublesome, in part because, if scientists examine organisms over a sufficiently long time period, they typically discover negative effects of all low-dose radiation (Parsons 1994; Muller 1956).

Other questionable methodological value judgments used in assessing H are that only a *small sample size* is necessary in epidemiological studies. For example, one group (Blayklock, Theodorakis, and Shugart 1996) studied only 28 organisms and then made claims for low-dose hormesis. Similarly Spengler et al. (1993) in *Pediatrics* alleged no increase in childhood leukemia, and therefore hormesis, even though their sample size was too small to detect most statistically significant effects. Likewise, the French Academy (see MacLachlan 1995; Duport 1996), in arguing for hormesis, admitted that the studies (on which it relied) were not powerful enough to exclude health effects at single doses below 200 mSv (20 rem). When the sample sizes for radiation studies increase, all things being equal, then alleged support for H disappears. For example, research on approximately 40,000 subjects (who received doses of 200 mSv or less) indicates that there are no beneficial effects of low-level radiation and that there is no threshold for risk from exposure (Pierce and Preston 1996). And if not, then the judgment to use small samples is problematic.

Still other questionable methodological value judgments are that one can posit support for H even if the relevant experiments rely on *counterfactual conditions*, as in Lee and Ducoff's 1994 study on chicken blood removed from the animals. Obviously the judgment (that such experiments provide reliable information about hormesis) is questionable

because there is no hormesis if it does not occur under real-world conditions. Yet many proponents of H employ this judgment. For example, some researchers said that if one lowers the viscosity of the intermolecular medium or if one allows that not all DNA breaks can or ought to be repaired (Vysotskii et al. 1996), then one can claim that low-dose radiation has hormetic effects at the molecular level. A significant amount of research alleging support for H fails because it presupposes unrealistic experimental conditions on the basis of which to make claims about adaptation or hormesis (see Zach, Hawkins, and Shepard 1993).

Perhaps the most common methodological value judgment made by proponents of H is that one can assert H on the basis of studies that *ignore confounders*. Yet, in principle, objective scientific conclusions ought not fail to take account of confounders. The Davis, Boice, Kelsey and Monson (1987) study alleged no effects of low-dose exposure, but it failed to take account of a confounder (smoking) causing lung cancer in the control group, and it was able to verify only one-third of its data. Another often-ignored confounder is caloric restriction. Scientists know that organisms with reduced calories or weight gain also enjoy a reduced likelihood of cancer (Trosko 1996, p. 818; Hart and Turturro 1996, pp. 15–16). In areas of high background radiation, such as in India, poverty and nutritional deficiencies could explain such alleged lower cancer rates. But without examining the confounders, some scientists simply allege that these areas provide evidence of hormesis. Instead, the radiation-induced “signal” (cancer) may be drowned out by the “noise” of other non-radiation effects that cause the same “signal.” Once researchers take account of confounders, alleged adaptive or hormetic effects of radiation disappear (Nussbaum and Kohnlein 1995). Some populations in India, for example, have higher numbers of Down’s Syndrome cases, ostensibly as a result of higher levels of background radiation (Rytomaa 1996), and there are a number of correlations between different levels of background radiation and childhood cancers (Knox et al. 1988; Hatch and Susser 1990). Some scientists likewise have documented that, 100 miles downwind, even the relatively low levels of radiation released at Three Mile Island have increased childhood cancers and doubled the number of cases of congenital hypothyroidism in the first nine months after the nuclear accident (Mangano 1996; Hatch and Susser 1990). If such studies are accurate, then any study of H that ignores confounders is highly questionable.

5. Using Analysis of Categorical Values to Rescue Objectivity

In addition to critically evaluating alternative methodological value judgments, another way to use metascientific techniques to help resolve the de-

bate over H is to assess how well the alternative approaches to H cohere with various categorical judgments of value. Such categorical values include, for example, internal consistency, external consistency, simplicity, heuristic power, and predictive power.

Hypothesis not-H, rather than H, appears better able to serve the value of *coherence* or *internal consistency* with other recognized aspects of radiobiological theory, particularly the theses of additivity, cumulativeness, and convertibility. Calculating any radiation risks, for individual lifetimes or for populations, requires additivity of dose, and this, in turn, requires that radiation have no threshold for biological effects and no hormetic effects; otherwise additivity would not “work.” Without not-H and additivity, it also would be impossible to show established cumulative radiobiological effects, such as the fact that radiation-induced cancer risk increases with age. Likewise, without not-H, it would be impossible to have *convertibility* between individual and population measures of dose, as current theory presupposes. (On average, the same number of illnesses will result if 1,000 people are exposed to 10 cGy or if 10,000 people are exposed to 1 cGy. See Nussbaum and Kohnlein 1995; Lindell 1996.) Thus, one could accept H, but only at the price of rejecting three of the most fundamental concepts of radiation dosimetry. As a result, internal consistency and coherence seem to argue for not-H over H.

How well does assuming H or not-H allow one to serve the value of *predictive power*? If one assumes not-H, and instead that all doses of ionizing radiation are harmful and linearly related to response, and that there is no threshold for increased probability of harm, then one is able to predict the observed effects of American and British studies of nuclear workers covering about 36,000 and 95,000 people respectively (Schull 1996, p. 799). Similarly, if one assumes not-H, and that dose and response are linearly related at all doses, then one is able to predict why, at several hundredths of a rad, there have been clear increases in cancer, early infant mortality, and Down’s syndrome that can be correlated with background radiation, with low-level emissions of ionizing radiation from weapons testing, from the Sellafield nuclear facility fire, and from the Chernobyl accident (Hatch and Susser 1990; Nussbaum and Kohnlein 1995; Caufield 1989). For example, scientists have documented “super clusters” of cancers near nuclear plants in Scotland, England, and Wales, and leukemia rates near the Sellafield nuclear reprocessing plant are 10 times greater than normal (Urquhart 1987). Researchers also have documented clear increases in cancer from prenatal X-ray exposures, from increases in background radiation, and from exposures because of the Three Mile Island nuclear accident (Nussbaum and Kohnlein 1995; Gofman 1990; Hatch and Susser 1990, p. 813; Fry 1996, p. 825). However, assuming H would make it impossi-

ble to predict any of these effects. Provided the studies cited are reliable, not-H rather than H, appears to do a better job of serving the value of predictive power.

Hormesis hypothesis H also appears to serve the value of *external consistency* less well than does not-H when one considers several established facts. These are that even the slightest amounts of ionizing radiation (35 eV) produce an ionization track through a cell; that not all such potentially carcinogenic particle-track alterations are repaired; that such alterations in the DNA are capable of producing mutations; that the vast majority of mutations are detrimental (Muller 1956, p. 394); that mutations cause cancers (Trosko 1996; Beninson 1996; Fry 1996; Muller 1956); that cancers increase as a function of dose (Stewart, Webb and Hewitt 1958; Stewart and Kneale 1993; Gofman 1990); and that cancer begins in a single cell (Beninson 1996, p. 123).

Other considerations of *external consistency* also support H, rather than not-H. For example, although radiation sometimes appears to provide beneficial effects at low doses, when one moves to even lower doses, these allegedly beneficial effects disappear. In experiments subjecting Chinese hamsters to cobalt-60 gamma rays, Crompton, Barth, and Kiefer (1990) discovered that when they reduced the dose rate from high (8400 rads/hour, or 84 Gy/hour) to low (20 to 3.9 rads/hour, or 200 to 39 mGy/hour), the frequency of mutations induced by a given dose decreased, just as proponents of H suggest. However, further reduction to a very low dose rate (2.9 to 0.45 rads/hour, or 29 to 4.5 mG/hour) caused an increase in the mutation frequency; at the lowest doses, they found that the dose-response curve was quadratic. They postulate that, at the lowest doses, damage does not induce the repair mechanism. They also say that even at the higher "low doses," where there is repair, radiation-induced mutational lesions cause observable, heritable changes in the genetic material, changes likely rendering the genes more susceptible to a second mutation. Other researchers have replicated their results and concluded that, per unit dose, low levels of ionizing radiation may induce more damage than higher levels (Nussbaum and Kohnlein 1995; Kiefer, Muller, and Gotzen 1988). Hypothesis not-H appears better able than H to explain these apparent inverse-dose effects, and these effects, in turn, could explain some of the apparent hormesis observed by other researchers in the low-dose region where some repairs take place. Thus, on these particular grounds of external consistency, not-H appears superior to H.

6. Conclusion

If the previous assessments of methodological and categorical value judgments are correct, then they suggest that, contrary to the sociologists, un-

certain, value-laden science may need not only more attention to social values in order to resolve and to clarify disputes. Instead it may need also more attention to metascience, to methodological and conceptual analyses of science. Moreover, if this paper's thesis holds in the very politicized, policy-relevant "hard case" of radiation hormesis, then it suggests that the sociologists may be wrong, and that metascientific analysis also may be necessary to clarify disputes in other areas of science.

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