

# BELLE NEWSLETTER

*Biological Effects of  
Low Level Exposures*

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## TOXIC TORTS

### HORMESIS AND THE LAW: *Introduction*

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*The emergence of hormesis as a serious scientific challenge to the traditionally used dose response models (i.e., threshold and linear at low dose) in hazard and risk assessment (Calabrese and Baldwin, 2003; Calabrese, 2005a,b) has encouraged detailed evaluations on the implications of hormesis in a broad range of disciplines. Hormesis is now becoming a central research focus in the area of biogerontology (Rattan, 2004a,b), neuroprotection (Mattson and Cheng, 2006), adaptive response in radiation (Mitchel, 2006; Scott, 2005), behavioral pharmacology (Grundmann et al., 2007), bioethics (Elliott, 2004), risk communication (Renn, 2003) and generalized stress responses (Calabrese et al., 2007).*

*The interest in hormesis is not likely to fade as independent researchers have incorporated this concept into grant proposals, dissertations (Zalizniak, 2006; Sykora, 2007), textbooks (Beck et al, 2000) and monographs (Calabrese, 2006) while books are now being written for the general public on this topic (Hiserodt, 2005). The reason why hormesis is growing in interest is not only because of its wide reaching societal implications but also because it is based upon thousands of*

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replicable scientific studies that have been published in peer-reviewed journals. Numerous recent publications have now culled these studies from diverse biological and biomedical disciplines, using all sorts of descriptive terms such as biphasic, bell-shaped, U-shaped, J-shaped, bitonic, hormesis, Yerkes-Dodson Law, dual effects, biomodal effects and others and have created a scientific scaffolding for improved evaluation of the dose response (Calabrese, 2005a,b). This integration of thousands of studies showing evidence of hormesis from numerous biological subdisciplines has led to the belief that not only is hormesis real and reproducible but that it represents a previously unrecognized basic principle that has been missed by the broad biomedical community (Calabrese, 2005b).

This issue of the BELLE Newsletter represents a continuing effort to explore some of the legal implications of hormesis. An earlier BELLE Newsletter devoted an entire issue to legal implications of hormesis (Cross, 2001). The current issue of the BELLE Newsletter extends that effort by exploring what hormesis might mean for the area of toxic torts. To accomplish this goal Professor Gary Marchant, Arizona State University, a law Professor as well as having earned a Ph.D. in genetics at an earlier stage of life, developed a white paper on the topic. This paper was then sent to a number of recognized experts in environmental law/toxic torts and risk assessment for their expert commentary. Following the receipt of these expert commentaries they were sent to Professor Marchant for a final response and possible rebuttal. The results of these efforts constituent this issue of the BELLE Newsletter.

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# HORMESIS AND TOXIC TORTS

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## ABSTRACT

Policy implementation of hormesis has to date focused on regulatory applications. Toxic tort litigation may provide an alternative policy venue for real-world applications of hormesis. Businesses and government entities who are sued by individuals claiming to have been injured by exposure to very low levels of toxic substances may defend those cases by deploying hormesis to argue that such exposures were unlikely to be harmful. The threshold issue in using hormesis in toxic tort defense is whether such evidence will be admissible under applicable standards for scientific evidence, which will likely turn on whether hormesis is deemed to be "generally accepted" in the relevant scientific community. Given the relatively novel status of hormesis, its admissibility will likely be a close call, but is likely to be held admissible in favorable circumstances. If admissible, hormesis is likely to receive a fairer and more even-handed consideration than in regulatory decisions, where regulatory agencies are bound by policy-based default assumptions that limit their receptivity to new concepts such as hormesis. The perception of hormesis by juries will likely be the critical factor for determining the utility of hormesis in toxic tort litigation, and this perception is likely to be affected by the presentation and circumstances in the individual case.

## I. INTRODUCTION

Over the past decade, major progress has been made in understanding the existence and generalizability of hormesis.<sup>1</sup> Studies across a wide variety of biological systems and toxic agents demonstrate a biphasic or U-shaped dose-response curve consisting of a protective effect at very low doses that becomes a toxic effect at higher doses.<sup>2</sup> Unfortunately, this scientific advance has not been accompanied by a corresponding increase in real-world application of the hormesis concept in the policy world. To date, policy and legal implementation of hormesis has focused primarily on regulatory agencies, whose cautious approach to new scientific concepts and evidence have predisposed them against open-minded consideration of hormesis in risk analysis and regulatory decisions.<sup>3,4,5</sup>

A different legal venue in which hormesis may have both relevance

and greater prospects for implementation is toxic tort litigation. A recent Fortune magazine article on hormesis began with this teaser: "Toxic-tort lawyers aren't going to like this: Evidence is growing that most hazardous chemicals, as well as radiation, not only are harmless at low doses – but may actually do a body good."<sup>6</sup> Will hormesis have a significant impact on toxic tort litigation? This commentary analyzes the potential application of hormesis in toxic tort litigation, including both the promise and hurdles of its implementation. Part I provides a brief background of toxic tort litigation. Part II analyzes how hormesis might be used in toxic tort litigation. Part III explores the admissibility of hormesis evidence under the existing judicial standards for the introduction of scientific evidence. Finally, Part IV evaluates more broadly the prospects for the introduction and acceptance of hormesis evidence in toxic tort litigation.

## II. BACKGROUND ON TOXIC TORT LITIGATION

In toxic tort litigation, one or more individuals ("plaintiffs") who are allegedly injured by exposure to a toxic substance or agent produced or released by a corporation or other entity ("defendant") file a lawsuit seeking compensation for their injuries. In addition to compensatory damages, the plaintiffs may also seek and be awarded punitive damages if the defendant acted willfully or recklessly in exposing the plaintiffs. While most toxic tort cases seek recovery for existing injuries such as cancer, birth defects, neural effects or other manifest injuries, in recent years it has become more common for exposed plaintiffs to seek recovery for "latent risks" that have not yet developed into clinical injuries. Examples of such claims by people who are at an increased risk of disease due to toxic exposures include attempts to obtain compensation for increased risk of disease, fear of developing disease, or medical monitoring.<sup>7,8</sup> The major incentives for bringing such claims before injury is manifest are concerns that the defendant may no longer be solvent or the proof may be stale by the time latent diseases develop many years or even decades after exposure. Courts are divided on whether they recognize such claims and the requirements for bringing such a claim.

Typical scenarios for a toxic tort lawsuit, whether it be for compensation for existing disease or latent risks, include exposure to groundwater contaminated with toxic substances that have leached from a toxic waste site, toxic substances released into the environment by an industrial accident or explosion, pesticide exposure in a residence or workplace, or use of a product with a toxic ingredient or component. These toxic tort cases often involve relatively low, chronic exposures that possibly may be in the hormetic range.

Plaintiffs in a toxic tort bear the burden to prove by a preponderance of the evidence all elements of their case. Proof of causation is probably the most serious impediment that most toxic tort plaintiffs face, and the outcome of many toxic tort cases turn on the resolution of the causation dispute. Both sides use expert witnesses to present their cases for or against causation. The trial judge usually makes an initial determination on whether each proposed expert's testimony is admissible and thus can be presented to the jury based on factors such as relevance, reliability and credentials. Many toxic tort cases are dis-

missed because the plaintiffs are not able to offer sufficient admissible expert testimony on causation, but in those cases where the plaintiffs' case is allowed to proceed and be presented to the jury, they are often awarded large damages in compensation. Toxic tort liability is therefore a major economic risk to companies and governmental entities that produce, use, or dispose of toxic substances. Those potential defendants therefore have strong incentives to consider the introduction of hormesis evidence in appropriate cases.

### III. USES OF HORMESIS IN TOXIC TORT LITIGATION

The primary potential application of hormesis in toxic tort litigation would be to help a defendant argue that the toxic substance for which it was responsible could not have caused injury to plaintiff because the low level of exposure would likely have been health protective rather than harmful due to hormesis. The ultimate goal is not to prove that a particular toxic exposure was actually beneficial, but rather to suggest such an effect for the purpose of buttressing the defendant's central argument that very low exposures may not be harmful.<sup>9</sup> For this argument to have any chance of success, the exposure at issue in the particular case would have to be very low, which probably excludes most cases involving occupational exposures or acute exposures from accidents or similar mishaps where exposure levels tend to be higher. Cases involving low-level environmental contamination of soil, water or air by chemicals or radiation would be the most likely scenarios for successful use of a hormesis defense. The defense could be used in cases involving actual injury, where the issue is what caused the plaintiff's illness, or in cases where plaintiffs who have been exposed to a toxic substance but who have not yet developed any clinical disease seek a remedy such as ongoing medical monitoring. While the standards for medical monitoring cases differ from jurisdiction, most courts require that the plaintiff demonstrate that medical surveillance is necessary because the exposure caused "a significantly increased risk of contracting a serious latent disease."<sup>10</sup> A defendant may be able to block this showing by proffering evidence that the low exposure levels experienced by the plaintiff is likely to produce a hormetic rather than toxic response, obviating the need for medical monitoring,

Cases involving very low exposures would seem to be the ones in which defendants are most likely to prevail in any event even without hormesis evidence, which is partly true. Nevertheless, there are a significant number of cases that are litigated and even successful that involve low-level exposures. In some cases, these low level exposures may indeed be harmful if the exposed population is large or includes very susceptible individuals, but in other cases the likelihood of harm is likely to be very low. Yet jurors, like other lay persons, tend to think qualitatively rather than quantitatively, and thus are likely to perceive any toxic exposure as potentially likely to cause injury even when statistical analysis and scientific models suggest that the likelihood of harm may be very low or even negligible.<sup>11</sup> Cass Sunstein, who refers to this heuristic as "probability neglect," notes that "jury behavior is not likely to be affected greatly by assurance that the risk was unlikely to come to fruition, even if the issue of probability is

legally relevant."<sup>12</sup> Hormesis offers the potential of an entirely different framework for perceiving risks. Instead of trying to argue quantitatively that low level exposures correspond to very low probabilities of harm, hormesis can be used to argue that low level exposures are qualitatively different in that they do not present risks and may even be beneficial. The implications of this different perceptual framework on the public, including juries, could be substantial.<sup>13</sup>

Some actual cases in which hormesis evidence could possibly have been utilized are provided below in Box 1.

#### Box 1: Examples of Cases in Which Hormesis Might Have Been Utilized

*Kemner v. Monsanto Company*, 576 N.E. 2d 1146 (Ill. App. 1991), *appeal denied*, 584 N.E.2d 130 (Ill. 1991): This case arose from a train derailment in which a tank car containing a Monsanto chemical feedstock contaminated with a small amount of dioxin spilled its contents onto the tracks. Some 65 nearby residents brought lawsuits claiming personal injuries and property damage from the dioxin exposure. The total amount of dioxin spilled allegedly was less than one teaspoon. After a trial that lasted 3.5 years, the jury returned a judgment finding very little actual harm, but awarding over \$16 million in punitive damages against Monsanto. Given the extremely small amount of dioxin released, Monsanto might have reassured the jury by introducing evidence of hormesis to argue that any exposure to extremely low levels would not have been harmful. The jury's decision was subsequently overturned on appeal.

*Nonnon v. City of New York*, 819 N.Y.2d 705, 2006 WL 1529293 (N.Y.A.D. June 6, 2006): This case in one of a series of lawsuits brought by residents in neighborhoods near the now inactive Pelham Bay landfill owned and operated by the City of New York. The lawsuits include claims by individuals that the toxic chemicals leaching from the landfill caused their cancers. Although a New York State study found no increase in cancer in the affected neighborhoods, the plaintiffs' experts claim that there is an increased rate of cancer and that the landfill was the likely cause of those cancers. The City attempted to have the lawsuits dismissed based in part on an argument that any toxic exposure to the plaintiffs would have been too low to cause their cancers, but the court refused to dismiss the case and held that the issue must be resolved by a trial, which was affirmed on appeal. In a dissenting opinion, one appellate judge suggested that the plaintiffs' reliance on the linear dose-response model to argue that any level of toxic exposure will be harmful is scientifically unreliable and should be "flatly rejected." At the upcoming trial, the City could use evidence of hormesis to reassure the jury that any very low exposures to toxic chemicals from the landfill leachate were unlikely to be harmful.

*Sutera v. Perrier Group of America*, 986 F.Supp. 655 (D. Mass. 1997). In 1990, some lots of Perrier sparkling drink-

ing water were found to contain trace amounts of benzene, resulting in an expensive recall and a public relations disaster for the company, even though the FDA and many scientists concluded that the small amount of benzene contamination was unlikely to pose a significant health threat. Charles Sutera, a regular Perrier drinker, brought a lawsuit contending that the benzene in Perrier caused his leukemia. The trial court granted summary judgment for the defendant after excluding the plaintiff's proposed expert testimony, in part based on its finding that "there is no scientific evidence that the linear no-safe threshold analysis is an acceptable scientific technique used by experts in determining causation in an individual instance." Although no trial was necessary in light of the court's dismissal of the case, if a trial had been held, the defendant might have introduced evidence of hormesis to help persuade the jury that the low level of benzene was unlikely to have caused Mr. Sutera's cancer, and given the court's rejection of the linear dose-response model, it seems likely that this judge would have admitted the hormesis evidence. More recently, another set of lawsuits were filed in 2006 alleging harm from trace amounts of benzene in soft drinks, again raising an opportunity to raise hormesis evidence.<sup>14</sup>

*In re Hanford Nuclear Reservation Litig.*, 292 F.3d 1124 (9th Cir. 2002). The Hanford Nuclear Reservation was an Atomic Energy Commission facility in Hanford, Washington that was used to make plutonium for the U.S. nuclear weapon arsenal. Over the more than four decades it was in operation, the facility released gaseous radioactive pollution that exposed hundreds of thousands of people living downwind. Multiple class action lawsuits involving many thousands of plaintiffs were filed in federal court, which were consolidated into one massive case. Some of the plaintiffs are seeking compensation for actual injuries such as cancers, while others are suing to recover for their fear of disease or increased risk of disease. The exposure levels for many of the plaintiffs in the case was very low. According to at least some experts, the indisputable radioactive pollution and exposure created by the Hanford facility has not resulted in any detectable increase in radiogenic cancers in the surrounding population, and two experts affiliated with the facility have suggested that the lower than expected cancer rates found in several studies may be an example of hormesis in action.<sup>15</sup> The defendants in the case could use hormesis to argue that is unlikely that very low levels of radioactive pollution could have caused the disease of plaintiffs with existing cancers, and do not present any serious risk or cause for concern to those plaintiffs seeking damages for their fear of developing cancer.

*Rhodes v. Dupont*, W. Va. Cir. Ct., Wood Country, No. 06-C-264, filed May 23, 2006. In this recently filed class action lawsuit, residents are suing Dupont for contaminating the water supply in Parkersburg, West Virginia with ammonium perfluorooctanoate (PFOA), also known as C-8,

which is used to make Teflon. The remedy plaintiffs are seeking include funds for medical monitoring and alternative drinking water supplies. The lawsuit was filed after tests showed the drinking water contained trace amounts of PFOA at levels above 0.05 parts per billion. The company responded to the lawsuit in the media by claiming that "[t]hese levels are far below any established regulatory guidance for drinking water and have not been shown to pose a health risk."<sup>16</sup> Again, hormesis evidence could potentially be useful here for reassuring the jurors that such low exposure levels are harmless.

The hormesis argument could be used by a defendant in a toxic tort suit in either an affirmative or defensive posture. In an affirmative use, the defendant's own expert would affirmatively argue that the toxic exposure the plaintiff incurred was of a nature and level that would have a hormetic effect, and thus more likely than not could not have caused the plaintiff's illness. In such a use, the defendant's expert would be required to establish the admissibility of the hormesis evidence, which as discussed below, would require establishing the validity and scientific acceptance of hormesis generally and making a sufficient showing that hormesis was applicable in the specific context of plaintiff's exposure, which may require some data about the specific substance, individual susceptibility, and quantitative exposure level at issue in the case.<sup>17</sup> This could be a substantial impediment for many substances, because as even the most ardent scientific proponents of hormesis concede, proving the existence of hormesis in a specific exposure context is an arduous and burdensome undertaking.<sup>18</sup>

In the defensive use, the defendant's lawyer would seek to undermine the plaintiff's causation case by raising hormesis in her cross-examination of the plaintiff's causation witness, asking whether the plaintiff's expert had adequately considered the possibility of hormesis in forming his causation opinion. It is well-established that an expert's testimony may be excluded from admission if it failed to consider a relevant factor or alternative explanation.<sup>19,20</sup> The plaintiff's expert would likely respond that hormesis is neither credible nor relevant, and thus does not call into question his causation expert opinion. The defendant would then need to introduce a rebuttal expert witness to argue that hormesis is a generally-occurring and well-established phenomena. If this argument is successful, the burden would again shift to the plaintiffs and their expert to show that they had adequately excluded hormesis as a relevant factor in causation. Because plaintiffs have the ultimate burden of proof in a toxic tort suit, the plaintiff would be required to demonstrate that hormesis did not apply under the specific facts of the particular case once a defendant had successfully persuaded the judge or jury that hormesis was a generally-occurring effect and thus potentially relevant. As one court stated the relevant standard, "[s]cientific knowledge of the harmful level of exposure to a chemical, plus knowledge that the plaintiff was exposed to such quantities, are minimal facts necessary to sustain the plaintiffs' burden in a toxic tort case."<sup>21</sup> The defendant argue that a plaintiff had not succeeded in demonstrating exposure to a harmful level of a chemical until the plaintiff had proven that the exposure level was indeed harmful, which necessarily means proving that no hormetic effect existed in the relevant exposure scenario.

Because this defensive use of hormesis to undermine the plaintiff's expert witness would put the burden of proof on the plaintiff to show that hormesis was inapplicable, it has a greater chance of success for the defendant. In both an affirmative and defensive application, however, the defendant would be initially required to offer admissible expert evidence that hormesis is indeed credible and potentially relevant to the case.

#### IV. ADMISSIBILITY OF HORMESIS EVIDENCE

The threshold question for hormesis evidence in toxic tort litigation will be whether such evidence is admissible. Trial judges must review proposed scientific expert testimony prior to its presentation to the jury to ensure that it meets applicable evidentiary rules. In 1993, the U.S. Supreme Court issued its "Daubert" decision which adopted a new standard for admitting scientific and other technical evidence in federal courts.<sup>22</sup> Many (although not all) state courts have subsequently adopted a similar standard. Daubert requires the trial judge to act as a "gatekeeper" in ensuring that scientific and other technical testimony is reliable and relevant before it can be presented to a jury. The Supreme Court provided a non-exclusive list of four factors a trial judge should consider in determining whether proffered scientific evidence is reliable, including whether the evidence: (i) can and has been empirically tested; (ii) has a known rate of error; (iii) has been peer-reviewed and published; and (iv) is generally accepted within the relevant scientific field.

The admissibility of hormesis in a case where such evidence may be relevant will therefore likely turn on a trial court's consideration of the four Daubert factors identified above. The first two factors are whether hormesis has been empirically tested and has a known rate of error. A defendant seeking to introduce hormesis will rely primarily on the exhaustive work of Edward Calabrese who has surveyed the scientific literature and created several large databases to empirically test the prevalence and generalizability of hormesis in the toxicological literature.<sup>23</sup> For example, one study evaluated over 20,000 toxicology studies and, using rigorous entry and evaluative criteria, found a hormetic response in approximately 40 percent of the 668 dose-response relationships from 195 published studies that met the a priori entry criteria.<sup>24</sup> This prevalence rate likely represents a significant under-estimate of its frequency given the data and technical limitations that would preclude detecting the effect in many of the studies in which hormesis could not be demonstrated.<sup>25</sup> Most importantly for purposes of the admissibility inquiry, the hormetic model was more often consistent with the published toxicological data than was the standard threshold model of toxicology generally used by plaintiffs' experts in reaching their opinions.<sup>26</sup> Another database has collected approximately 5600 dose-response relationships from 1000 toxicological studies demonstrating hormesis across a broad range of toxic agents, target organisms, and health endpoints.<sup>27</sup> Few scientific concepts introduced into evidence in toxic tort litigation have such extensive empirical support.

Plaintiffs would not be without counter-arguments, however. First, plaintiffs would try to undermine the empirical studies of Calabrese,

arguing that such analyses do not show that hormesis is a generalizable or common phenomenon.<sup>28</sup> For example, they are likely to argue that these studies are retrospective literature reviews rather than predictive, empirical testing of hormesis.<sup>29</sup> The plaintiffs' experts would also likely focus on the specific facts of the case at issue, and argue that the vast majority of studies showing hormesis in animals, plants and microorganisms are not relevant to whether the toxic agent in *this* case produces hormesis in these individual human plaintiffs under the exposure circumstances of *this* particular case. They would likely attempt to introduce additional uncertainties and doubt by pointing to factors such as whether there were genetic or other susceptibilities in the human population that may cause any alleged hormetic effects to occur at different exposure levels in different people, how exposures to other toxics might affect the hormetic level for the toxic exposure at issue, and how different health endpoints may have different doses at which they exhibit a hormetic response.<sup>30,31,32</sup> In many cases, these questions will be largely unanswerable.

In important ways, these legitimate concerns about hormesis will have less cogency in a litigation context than in a regulatory context. For example, a regulatory agency must be concerned about the entire range of susceptibility within the general population in determining a hormetic level, struggling with the likelihood that different people may have different levels at which hormetic and toxic effects occur from a given type of exposure due to differences in intrinsic susceptibilities and other environmental exposures. In a toxic tort lawsuit, however, the only relevant focus is on the individual plaintiffs *in that case*, and so there is no need to be concerned with the effect that recognizing a hormetic level would have on the most susceptible individuals within the entire population. To be sure, it is certainly possible that an unusually susceptible individual will be included in the plaintiff class, but that may be unlikely and therefore a lesser concern than in regulation which directly encompasses the entire population and thus definitely includes the most susceptible individuals within the population. Similarly, a regulator's task is complicated by the fact that a given toxic agent may cause several different health endpoints with different dose levels at which a hormetic effect occurs. In a toxic tort case, the plaintiff usually seeks compensation for a specific health endpoint, again simplifying the analysis to that single endpoint.

Moreover, hormesis need not be universal or absolutely certain to be admissible. No toxicological model or theory accepted in litigation has absolute certainty and complete applicability. Rather, the applicable standard is whether the argument or evidence is "more likely than not." According to Calabrese, empirical testing demonstrates that the hormetic model is more likely than any competing model: "the data indicate that the hormetic dose-response model clearly out-competes its most serious competitors in head-to-head competition and is generalizable, being independent of biological model, endpoint measured, and chemical/physical stressor."<sup>33</sup> This is all that is required for admission of other types of scientific evidence, and a higher standard should not be imposed for hormesis than competing toxicological models that are less likely to apply based on empirical head-to-head testing against hormesis.

The third *Daubert* factor, which is whether the theory has been peer-reviewed and published, would likely be the easiest for the defendant to satisfy. There is now a substantial body of published, peer-reviewed studies supporting hormesis. The published literature need not be unanimous in supporting a theory before it is admissible - there simply needs to be some published, peer-review studies supporting the theory about which the expert seeks to testify. That condition seems easily satisfied by hormesis. The plaintiff might try to argue that there needs to be published, peer-reviewed studies on the specific toxic substance and exposure scenarios at issue in the instant case, but especially if the defendant is using hormesis in a defensive manner as explained above, such specificity may not be necessary for the testimony to be introduced since it is the plaintiff who bears the ultimate burden of proof.

The biggest hurdle to the admissibility of expert testimony on hormesis will likely be the fourth *Daubert* factor, which is whether the evidence is “generally accepted” in the relevant scientific community.<sup>34</sup> Historically, hormesis has been marginalized from mainstream toxicological thought and practice, for a variety of complex reasons, including data availability, its perceived association with homeopathy, and political opposition.<sup>35,36,37</sup> In recent years, however, there has been a resurgence in attention to and acceptance of hormesis.<sup>38</sup> For example, a substantial number of peer reviewed studies supporting hormesis have recently been published in prominent toxicology journals,<sup>39</sup> prestigious scientific journals such as *Science*,<sup>40</sup> *Nature*<sup>41</sup> and *Scientific American*<sup>42</sup> have recently published mostly favorable commentaries or news articles remarking on the reemergence of hormesis, major professional scientific organizations such as the Society of Toxicology and the Society of Risk Analysis have recently held sessions on hormesis at their annual meetings, and leading toxicology textbooks have recently added sections on hormesis.<sup>43,44</sup> All of these developments could be marshaled in support of the “general acceptance” of hormesis.

To be sure, some recent articles have recently criticized the scientific and evidentiary support for hormesis.<sup>45,46</sup> Of course, general acceptance does not require uniform and unanimous support in the scientific community, and in at least some jurisdictions, it does not even require the support of a majority of qualified scientists. In the words of the Illinois Supreme Court, “[s]imply stated, general acceptance does not require that the methodology be accepted by unanimity, consensus, or even a majority of experts.”<sup>47</sup> Rather, the issue would be whether hormesis has the support of a substantial portion, perhaps even a majority of, the relevant scientific community, which likely would be defined here as the field of toxicology although opponents may seek to broaden the relevant disciplinary boundaries to include public health and environmental science. Part of the battle in determining general acceptance would be in defining the relevant scientific field in which the acceptance should be determined.

Another focus of the admissibility contest will be on the credentials, objectivity, motivations, and influence of the scientists on both sides of the debate. Lawyers for defendants advocating for the admissibility of hormesis evidence would likely argue that many if not most of the scientists who have published criticisms of hormesis are public health advocates with a strong commitment and record of supporting greater

regulation of toxic substances, and thus who predictably would be ideologically opposed to any theory that could potentially be used to relax regulatory requirements. Conversely, lawyers for plaintiffs would likely argue that most of the published studies in support of hormesis was authored by a single scientist (Edward Calabrese) and his colleagues, and that Dr. Calabrese is a committed advocate for hormesis and thus lacks objectivity. While these types of ad hominem attacks are generally considered inappropriate and out-of-place in a scientific forum, they are common in litigation “battle of the experts.” The common objective of both sides will be to try to paint the experts testifying on the other side, and the published scientists on whose research they rely, as ideological advocates for a minority position in the scientific community.

Judicial decisions on whether hormesis is “generally accepted” will likely turn on how the hormesis debate is framed. One framework, likely to be argued by plaintiffs, is that the linear dose-response model is the standard model that has been accepted and applied by the vast majority of scientists for many decades, and that hormesis represents a novel theory that is attempting to challenge the well-settled consensus in favor of the traditional linear model. While hormesis advocates have provided some interesting data and arguments that may warrant more study, the theory of hormesis is still very speculative and preliminary, and is not even close to displacing the dominant linear paradigm. A different framework likely to be advocated by defendants is that the shape of the dose-response curve at low exposure levels has always been very controversial and uncertain to experts in the field. Although hormesis is a relative newcomer to mainstream theories on the shape of the dose-response curve at low exposures, this is a very unsettled question and hormesis is empirically-based and as well-accepted as any other theory to most qualified experts who have carefully reviewed the data. In support of this conception, defendants could quote the Federal Judiciary Center’s *Reference Manual on Scientific Evidence* which states that “[t]he question whether there is a no-effect threshold dose is a controversial one in a variety of toxic substances areas” and “[e]ven the shape of the dose-response curve—whether linear or curvilinear, and if the latter, the shape of the curve—is a matter of hypothesis and speculation.”<sup>48</sup>

The admissibility of hormesis evidence in federal courts and state courts that have adopted the *Daubert* standard would be made on a case-by-case consideration of the four factors discussed above by the presiding trial judge in each trial. Not all of the four factors must be satisfied for evidence to be admitted; rather the judge makes a judgment on the overall reliability of the evidence based on consideration of the four factors. In addition, a court is permitted to consider other relevant factors in making its admissibility decision, such as whether the evidence at issue was generated for litigation purposes and whether the evidence is relevant, which do not appear to be decisive factors here. Given the powerful arguments likely to be made by both sides summarized above, different courts could quite conceivably make different decisions in different cases based on factors such as the judge’s own perspective, the credentials and credibility of each side’s expert witnesses, the strength of the legal advocacy on each side, and the availability of published data directly related to the chemical and exposure scenario at issue in the particular litigation. In other words,

there is a good possibility that hormesis evidence would be held admissible in an appropriate case.

The States that have not adopted the *Daubert* standard generally apply the earlier *Frye* standard, which bases admissibility of scientific testimony solely on the general acceptance of the evidence in the relevant scientific community (i.e., the fourth prong of the *Daubert* standard). *Daubert* has generally resulted in higher standards for the admission of scientific evidence relative to the pre-*Daubert* practice under *Frye*, leading to a greater rate of rejection of proposed expert testimony. In cases such as hormesis, however, that involve relatively new scientific theories or concepts that have not yet fully percolated into scientific consciousness and understanding, *Frye* may create a higher hurdle to admissibility because of its sole focus on “general acceptance,” while downplaying the other *Daubert* criteria such as peer review and publication and whether the theory has been tested.<sup>50</sup> Because the general acceptance is probably the weakest of the four *Daubert* factors for hormesis, state courts that still apply the *Frye* standard are likely to be the most hostile to acceptance of hormesis testimony and evidence.

A more definitive resolution of the admissibility issue would likely result from a scientific review of hormesis by a prestigious scientific body such as the National Academy of Sciences (NAS). Given the lack of their own scientific training, most trial judges tend to give great weight to authoritative scientific expert reports. For example, in the silicone breast implant litigation, the admissibility of plaintiffs’ expert testimony dropped precipitously after the NAS Institute of Medicine issued an expert scientific report which concluded that most of the evidence and arguments that plaintiffs were relying on were not scientifically reliable and credible.<sup>51</sup> Thus, if a prominent scientific organization such as the NAS was to produce an expert report on hormesis, the conclusions of that report, whether pro or con, would be highly influential if not determinative of admissibility decision for hormesis in both federal and state courts.

## V. PROSPECTS FOR USE OF HORMESIS IN TOXIC TORT LITIGATION

If evidence of hormesis is admissible, what impact would it have in toxic tort litigation? A major advantage of such litigation relative to regulatory proceedings is that the private parties have much greater control of the issues in contention. Regulatory agencies have so far been very reluctant to consider hormesis evidence, consistent with their generally conservative and cautious approach to considering new types of evidence, especially where such evidence might suggest less stringent regulatory standards.<sup>52</sup> Even when hormesis evidence is presented to an agency in a regulatory proceeding by a private party, agencies have tended to summarily dismiss that evidence with a perfunctory comment.<sup>53,54</sup> Given the high deference reviewing courts give to regulatory agencies on such scientific issues,<sup>55</sup> a proponent of hormesis has relatively little recourse for forcing a regulatory agency to give serious consideration to hormesis.<sup>56</sup>

In contrast, in litigation the parties control the evidence and the focus of the dispute, and thus have greater power to insert hormesis directly

into the decision-making calculus. Moreover, toxic tort litigation is likely to be more receptive to hormesis than the regulatory context because there is less commitment to institutionalized default assumptions that restrict regulatory agencies’ openness to new ideas and evidence. For example, while regulatory agencies apply a standard conservative assumption that animal studies are relevant to humans, judges and juries are less bound by such a precautionary assumption.<sup>57,58</sup> Perhaps the most pertinent example is the skepticism some toxic tort decisions have shown towards the linear, no-threshold dose-response model, which at least until very recently has been applied dogmatically by regulatory agencies.

For example, one federal district court, noting that the linear dose-response model “is not proven fact,” held that the linear model may be an appropriate assumption for more precautionary regulatory decisions but is not acceptable in lawsuits which “must be resolved by reasonable conclusions based on the evidence, not by educated guesses.”<sup>59</sup> Another court recently held that “there is no scientific evidence that the linear no-safe threshold analysis is an acceptable scientific technique used by experts in determining causation in an individual instance.”<sup>60</sup> Yet another federal district court was even harsher in rejecting the linear model: “It fails all of the *Daubert* reliability factors. The linear non-threshold model cannot be falsified, nor can it be validated. To the extent that it has been subject to peer review and publication, it has been rejected by the overwhelming majority of the scientific community. It has no known or potential rate of error. It is merely a hypothesis... In sum, it has no capacity to be of assistance to a jury in resolving the ultimate issues of the case.”<sup>61</sup> Regardless of whether one agrees with these decisions or not, they demonstrate that courts provide a fresh and unencumbered look at evidentiary issues that is not bound by the precedent and political sensitivity of the regulatory world, and which open a door to fair consideration of hormesis on its merits.

Another factor favoring the litigation forum is the very different objectives of regulation and litigation, with regulation representing a prophylactic, precautionary protection of the general public from future risks, whereas litigation is a fact-specific inquiry into what is the responsible cause for injury that has already occurred in a specific individual or groups of individuals.<sup>62</sup> This difference in objective results in different approaches to evidence, as described by one court:

Regulatory [agencies] ... make prophylactic rules governing human exposure. This methodology results from the preventive perspective that the agencies adopt in order to reduce public exposure to harmful substances. The agencies’ threshold of proof is reasonably lower than that appropriate in tort law, which ‘traditionally make[s] more particularized inquiries into cause and effect’ and requires a plaintiff to prove ‘that it is more likely than not that another individual has caused him or her harm.’<sup>63</sup>

The difference in objectives and methodologies corresponds to a less policy-driven and more data-driven approach to evidence in courts relative to regulatory agencies, which makes courts more of an even playing field than regulatory agencies to consider new evidence such as hormesis that might be perceived as threatening to a regulatory agency’s core mission.

A final consideration is how juries are likely to respond to hormesis evidence. Many people react incredulously to the concept of hormesis when first presented with the idea. This perception is validated by the fact that hormesis was included in the popular book *Nine Crazy Ideas in Science: A Few Might Even Be True* by Robert Ehrlich.<sup>64</sup> Juror response to the introduction of hormesis might be even more hostile in the litigation context if a culpable corporate defendant who has allegedly acted recklessly or irresponsibly in exposing the plaintiffs to a toxic substance turns to the jury and argues that plaintiffs have nothing to worry about because the toxic agent they have released is actually good for the plaintiffs. As Ortwin Renn has written, “[i]f hormesis is a being perceived as a new strategy of industry to avoid risk reduction measures and to gain points in court, the hypothesis will be rejected by most observers ....”<sup>65</sup> Hormesis therefore has the potential to backfire against a defendant in terms of jury perception.

On the other hand, if presented in a careful and modest manner as part of an overall defense, hormesis could be beneficial to a defendant in the right circumstances. Even if jurors are skeptical towards hormesis on first impression, they can be persuaded by an effective scientific presentation by a credible expert witness who summarizes the extensive body of scientific evidence supporting hormesis and its acceptance by mainstream toxicology as evidenced by, for example, its inclusion in some of the field’s leading textbooks. If presented successfully, hormesis may provide a more effective defense than quantitative arguments based on the low statistical probability of risk from low exposures by blocking the “probability neglect” heuristic of lay persons (including most jurors and judges) to think qualitatively not quantitatively by ignoring probabilities and applying a yes/no dualism on whether an agent is toxic or not.<sup>66</sup> If a defendant can demonstrate that an exposure is likely to be not toxic and may even be beneficial at very low levels, the jurors are likely to apply a much different and more favorable framework to adjudging causation and liability.

## VI. CONCLUSION

Most trial lawyers, whether they primarily represent defendants or plaintiffs, will concede that juries usually “get it right.”<sup>67</sup> Given the mounting scientific data and opinion validating the concept of hormesis, toxic tort litigation may provide a promising forum for the real-world application of hormesis. Judges and juries may be more receptive and open-minded to considering hormesis relative to regulatory agencies constricted by political and programmatic restraints. Nevertheless, there will be significant obstacles to the admissibility and effectiveness of hormesis as evidence in toxic tort litigation. Reliance on hormesis evidence is likely to be most effective in appropriate cases involving very low exposures to toxic agents whose hormetic potential has been directly studied, and where the defendant has not engaged in flagrant or egregious wrongdoing.

More broadly, successful application of hormesis in toxic tort litigation could serve as a wedge to open doors to greater receptivity and application of hormesis in the scientific, medical, regulatory and policy realms. A useful analogy is provided by the “paradigm shift” currently underway in forensic identification science.<sup>68</sup> For many years, forensic scientists and courts had simply assumed the accuracy and

accepted as reliable many types of forensic identification evidence such as handwriting, bite mark, tire mark, and even fingerprint analysis, even though there was very little empirical data to validate these methods. In significant part because of the Supreme Court’s 1993 adoption of the more empirically-based *Daubert* standard for admission of scientific evidence, the empirical basis of forensic evidence is now being critically analyzed by courts and is often being found wanting. The consequences of this revolution include not only more scientifically rigorous and empirical treatment of forensic evidence in the courts, but has also resulted in “scientists [beginning to] question the core assumptions of numerous forensic sciences,” “federal funding materializ[ing] to support research that examines long-asserted but unproven claims,” and greater and more balanced news coverage of the limitations of the previously “venerated” forensic methods.<sup>69</sup> In much the same way, testing hormesis head-to-head against the traditional linear dose-response model under the empirically-driven *Daubert* standard in toxic tort litigation may not only open the door to hormesis evidence in the courts, but may also stimulate greater responsiveness to hormesis by scientists, regulators, funding agencies and the media.

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# COMMENTARY: HORMESIS AND TOXIC TORTS - TRADITIONAL TORTS AND CLAIMS FOR SUBCLINICAL HARM

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Professor Marchant presents a fascinating analysis of the way in which hormesis might be applied in toxic tort cases. His article provides a fulsome discussion of the relevant standards that experts presenting evidence of hormesis may have to satisfy in court.

In particular, Professor Marchant's analysis shows that the standards for admission of expert testimony may shift in the context of hormesis:

The plaintiffs' experts would also likely focus on the specific facts of the case at issue, and argue that the vast majority of studies showing hormesis in animals, plants and microorganisms are not relevant to whether the toxic agent in this case produces hormesis in *these* individual human plaintiffs under the exposure circumstances of *this* particular case.

Marchant, *Hormesis and Toxic Torts* at 11 (emphasis in original). In other words, plaintiffs would be arguing that particular studies do not support a specific causation finding for purposes of the litigation. Such argumentation is more typical of a defendant's position.

In a traditional toxic exposure case, a plaintiff must show both that a toxicant is capable of causing the injury at issue (general causation) and that the toxicant did in fact cause the injury to the plaintiff (specific causation).<sup>2</sup> Hormesis may present an additional evidentiary burden for plaintiffs in this context.

Even more interesting may be the effects of hormesis on efforts to define within the traditional tort system more recent claims of sub-clinical harm. In addition to the general causation and specific causation standards that have long been relevant to traditional toxic torts, the legal system has more recently grappled with how to address low dose issues, or situations in which a physiological change can be identified, but no current harm can be directly traced to that change. Some of these discussions echo the evidentiary considerations articulated by Professor Marchant.

Medical monitoring claims, in which plaintiffs seek recovery for health monitoring after alleged harmful exposure to a hazardous substance, are one arena in which evidence of hormesis may substantially affect the legal calculus, because the exposures in medical monitoring cases typically are low-level in nature and subclinical effects are at issue.

Medical monitoring claims involve, by definition, a plaintiff with no current injury -- and with no ability to show that an injury traceable to some allegedly negligent exposure will ever occur. Under traditional principles of tort law, medical monitoring claims brought in the 1960s and 1970s were routinely denied in the absence of any physical injury.<sup>3</sup>

In the 1980s and 1990s, however, several courts presented with sympathetic toxic tort plaintiffs began to be persuaded to award medical monitoring costs as a remedy for alleged environmental exposures.<sup>4</sup> Indeed, the first six state supreme courts to address the issue found that medical monitoring costs could be awarded to any plaintiff who had shown exposure to a harmful substance and an "increased risk" of harm.<sup>5</sup> Several of these courts further recognized medical monitoring as an independent cause of action, substantially expanding its original role as remedial relief for a properly pled and proven negligence claim.<sup>6</sup>

The formulation provided by the Pennsylvania Supreme Court in *Redland Soccer Club v. Department of the Army* is typical:

[A] plaintiff must prove the following elements to prevail on a common law claim for medical monitoring: (1) exposure greater than normal background levels; (2) to a proven hazardous substance; (3) caused by the defendant's negligence; (4) as a proximate result of the exposure, plaintiff has a significantly increased risk of contracting a serious latent disease; (5) a monitoring procedure exists that makes the early detection of the disease possible; (6) the prescribed monitoring regime is different from that normally recommended in the absence of the exposure; and (7) the prescribed monitoring regime is reasonably necessary according to contemporary scientific principles. Proof of these elements will naturally require expert testimony.<sup>7</sup>

The language used by the *Redland Soccer Club* court -- discussing a "common law claim" under which "elements" must be proven -- illustrates the manner in which courts began to accept medical monitoring as a "claim," while ostensibly maintaining a direct connection between that claim and the "elements" of exposure and negligence providing a basis for the claim. Under these standards, a court may award medical monitoring costs so long as some expert testimony supports an "increased risk" of harm, even if the exposure is only marginally above "background" levels, and may not ever result in physical disease.

Independent medical monitoring claims thus may substantially lower the threshold of compensable exposure (anything above "background", with no requirement of any adverse effect), while simultaneously encouraging courts to apply less rigor to a plaintiff's negligence

showing, since negligence is merely one of the “elements” of the medical monitoring claim, rather than the foundational tort for which medical monitoring may be one remedy. Some decisions have confused the situation by using the terms “remedy,” “claim,” and “cause of action” interchangeably.<sup>8</sup>

“Lumping” the negligence showing in with the medical monitoring claim may, indeed, have adverse medical consequences, because the court has no defined phase at which to evaluate medical alternatives proposed and to award a remedy tailored to specific plaintiff needs.<sup>9</sup> When evidence of harm is already marginal,<sup>10</sup> hormetic evidence may substantially affect the outcome of these sorts of cases.

Some courts have rejected medical monitoring claims as inconsistent with traditional tort principles. Among other things, defendants have shown that medical monitoring claims are a new back door for old-style “increased risk” claims. Such increased risk of disease claims seek recovery for the present value of future physical harms based on the possibility that plaintiffs may develop certain diseases in the future. Such claims have been widely rejected as speculative,<sup>11</sup> and even courts permitting the claims have required plaintiffs to prove that their chances of getting the disease are greater than 50 percent, or more likely than not.<sup>12</sup>

Likewise, medical monitoring claims may be shown to be a new version of “fear of disease” claims, which courts have allowed only under far more exacting standards than those articulated by cases in which medical monitoring claims have more recently been accepted. Fear of disease claims typically seek recovery for a plaintiff’s present fear about his or her future well-being, based on the tort of negligent infliction of emotional distress. Most jurisdictions allow recovery for fear of disease, but require that the plaintiff have suffered a present physical injury or impact.<sup>13</sup> Courts have stated that the rationale for requiring physical injury or impact is to “guarantee the genuineness” of the claim.<sup>14</sup>

Accordingly, some courts have relied on fear of disease and related precedent to reject medical monitoring claims. Other courts similarly have recognized that medical monitoring costs are most appropriately considered, if at all, as a remedy, based on traditional principles of tort law.

For example, the Sixth Circuit recently noted that it viewed medical monitoring as a remedy for a tort action and not an independent claim, explaining that “[i]nstead of ‘the injury in an enhanced risk claim [being] the anticipated harm itself’ and ‘[t]he injury in a medical monitoring claim [being] the cost of the medical care that will, one hopes, detect that injury’ we think it more accurate to find the increased risk of future harm is the injury in both types of cases. The difference lies in the remedy sought by the plaintiff.”<sup>16</sup>

The Michigan Supreme Court provided an even more detailed discussion, concluding:

Plaintiffs advance their [medical monitoring] claim as if it satisfies the traditional requirements of a negligence action in Michigan. In reality, plaintiffs propose a transformation in tort law that will require the courts of this state -- in this

case and the thousands that would inevitably follow -- to make decisions that are more characteristic of those made in the legislative, executive, and administrative processes. . . . [W]e are not prepared to acquiesce in this transformation.<sup>17</sup>

Rather, the Michigan court found, a plaintiff asserting a claim for a court-supervised medical monitoring fund for “equitable” relief must first establish a valid cause of action, based on a present physical injury: “It is a *present* injury, not fear of an injury in the future, that gives rise to a cause of action under negligence theory.”<sup>18</sup>

The U.S. Supreme Court has endorsed a similar analysis outside the common law tort context, reversing a ruling that allowed an exposed - but uninjured -- asbestos plaintiff to pursue a medical monitoring claim under the Federal Employers’ Liability Act, because (i) the plaintiff, despite a “massive, lengthy, and tangible” exposure, had no injury that would allow medical monitoring costs as a traditional element of damages; and (ii) allowing recovery for medical monitoring costs in the absence of physical injury would create a number of “systemic harms” for courts, the tort system, and society. Three state supreme court decisions issued in 2001 and 2002 adopted this rationale to reject tort-based medical monitoring claims.<sup>19</sup>

In this legal climate, acceptance of hormesis is likely to face a uphill battle with lawyers and judges who may view the concept as unnecessarily complicating an already Byzantine situation. In the right circumstances, however, hormesis could provide an additional window into assessing responsibility for the subclinical effects that have begun to arrive in court.

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3. *See, e.g., Morrissy v. Eli Lilly & Co.*, 394 N.E.2d 1369, 1376 (Ill. App. Ct. 1979) (possibility of developing cancer due to DES exposure found “an insufficient basis upon which to recognize a present injury”).
4. *See, e.g., Bourgeois v. A.P. Green Indus., Inc.*, 716 So. 2d 355, 360-61 (La. 1998), *superseded by* LA. CIV. CODE ANN. art 2315 (2005); *Potter v. Firestone Tire & Rubber Co.*, 863 P.2d 795, 831 (Cal. 1993).
5. *Ayers v. Jackson Twp.*, 525 A.2d 287, 311-12 (N.J. 1987); *Hansen v. Mt. Fuel Supply Co.*, 858 P.2d 970, 979 (Utah 1993); *Potter*, 863 P.2d at 823, 824-25 (Cal. 1993); *Redland Soccer Club, Inc. v. Dep’t of Army*, 696 A.2d 137, 145-46 (Pa. 1997); *Bourgeois*, 716 So. 2d at 360-61; *Bower v. Westinghouse Elec. Corp.*, 522 S.E.2d 424, 426, 432-33 (W. Va. 1999). The New Jersey Supreme Court has subsequently amended the *Ayers* holding to require physical injury.

- Theer v. Philip Carey Co.*, 628 A.2d 724, 733 (N.J. 1993) (“[M]edical surveillance damages are not available for plaintiffs who have not experienced direct and hence discrete exposure to a toxic substance and who have not suffered an injury or condition resulting from that exposure and whose risk of cancer cannot be limited and related specifically and tangibly to that exposure.”).
6. See, e.g., *Redland Soccer Club*, 696 A.2d at 145-46; *Hansen*, 858 P.2d at 979; *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829, 849 (3d Cir. 1990). Cf. *Friends For All Children v. Lockheed Aircraft Corp.*, 746 F.2d 816 (D.C. Cir. 1984) (originally recognizing concept of medical monitoring as relief for evacuated Vietnamese orphans who suffered aircraft cabin decompression and crash).
  7. *Redland Soccer Club*, 696 A.2d at 145-46 (footnote omitted).
  8. See, e.g., *Bower*, 522 S.E.2d at 428-29.
  9. Considering medical monitoring to be a remedy, a New Jersey court in 2005 thus recognized the limits of the doctrine, evaluated the relevant facts, and refused to extend medical monitoring to a proposed class of Vioxx users who sought EKGs to determine if they had experienced an unrecognized myocardial infarction or other unrecognized injury. See *Sinclair v. Merck & Co.*, No. ATL-L-3771-04-MT, 2005 WL 1278364, at \*7-8 (N.J. Super. Ct. Law Div. May 19, 2005) (“[B]ecause medical monitoring is a remedy that ‘is not easily invoked,’ this Court declines to find the New Jersey Supreme Court would extend medical monitoring to the proposed class in this particular situation.”) (footnote and citations omitted).
  10. See, e.g., Jamie A. Grodsky, *Genetics and Environmental Law: Redefining Public Health*, 93 Cal. L. Rev. 171, 234 (noting, for example, that “[t]here are many barriers to treating gene expression changes as adverse effects,” not least because “not all changes in gene expression imply toxicity”).
  11. *Eagle-Picher Indus., Inc. v. Cox*, 481 So. 2d 517, 521, 525 (Fla. Dist. Ct. App. 1985) (rejecting claim for increased risk of cancer damages in asbestos case where plaintiff had asbestosis and stating that “[w]e have come to our decision that any recovery for cancer damages must await the actuality of cancer . . .” and that “public policy requires that the resources available for those persons who do contract cancer not be awarded to those whose exposure to asbestos has merely increased their risk of contracting cancer in the future”). See also James A. Henderson, Jr. & Aaron D. Twerski, *Asbestos Litigation Gone Mad: Exposure-Based Recovery for Increased Risk, Mental Distress, and Medical Monitoring*, 53 S.C. L. REV. 815, 822 (2002) (“Courts that have abolished the single-action rule have flatly rejected claims based on increased risk.”).
  12. See, e.g., *Hagerty v. L & L Marine Servs., Inc.*, 788 F.2d 315, 319 (5th Cir. 1986) (holding that in accord with “other courts . . . a plaintiff can recover only where he can show that the toxic exposure more probably than not will lead to cancer”) (citing several cases adopting the “greater than fifty percent” rule) (emphasis in original).
  13. See, e.g., *Eagle-Picher Indus.*, 481 So. 2d at 528 (“The physical injury requirement is consistent with Florida law, necessary and fair. . . . Imposing a requirement that there be a physical injury as a predicate to recovery for mental distress arising from a fear of cancer is not an arbitrary act.”) (footnotes omitted); *Rustvold v. Taylor*, 14 P.3d 675, 680-81 (Or. Ct. App. 2000) (rejecting plaintiff’s negligence claim for emotional-distress damages based on her fear of contracting Hepatitis B or HIV where plaintiff’s physical injuries had nothing to do with her claimed emotional distress).
  14. See, e.g., *Eagle-Picher Indus.*, 481 So. 2d at 529 (“[T]he physical injury requirement will insure that the claims permitted are only the most genuine.”).
  15. See *Hinton ex rel. Hinton v. Monsanto Co.*, 813 So. 2d 827, 829 (Ala. 2001) (relying on *Pfizer, Inc. v. Farsian*, 682 So. 2d 405, 407 (Ala. 1996)); *Wood v. Wyeth-Ayerst Labs.*, 82 S.W.3d 849, 852-53 (Ky. 2002) (relying on *Capital Holding Corp. v. Bailey*, 873 S.W.2d 187, 195 (Ky. 1994)); *Abusio v. Consol. Edison Co. of N.Y., Inc.*, 656 N.Y.S.2d 371, 372 (N.Y. App. Div. 1997); *Broich v. Nabisco, Inc.*, slip op. (N.Y. Sup. Ct. May 16, 2002) (Werner, J.) (unpublished decision).
  16. *Sutton v. St. Jude Med. S.C., Inc.*, 419 F.3d 568, 572 (6th Cir. 2005) (citation omitted; brackets in original).
  17. *Henry v. Dow Chem. Co.*, 701 N.W.2d 684, 692 (Mich. 2005).
  18. *Id.* at 689 (emphasis in original).
  19. *Metro-North Commuter R.R. Co. v. Buckley*, 521 U.S. 424, 428, 439, 442-44 (1997). See *Badillo v. Am. Brands, Inc.*, 16 P.3d 435, 440-41 (Nev. 2001) (finding that Nevada does not recognize a cause of action for medical monitoring because (i) “[a]ltering common law rights, creating new causes of action, and providing new remedies for wrongs is generally a legislative, not a judicial, function,” and (ii) “[e]xposure to environmental tobacco smoke raises many complex issues of legal causality. . . .”); *Hinton*, 813 So. 2d at 829-30 (rejecting medical monitoring claims related to PCB exposure because (i) “Alabama law has long required a manifest, present injury before a plaintiff may recover in tort,” (ii) “recognizing a cause of action based upon nothing more than an increased risk . . . would result in . . . cases [being decided] based upon nothing more than speculation and conjecture,” and (iii) the reasons stated in *Metro-North*); *Wood*, 82 S.W.3d at 852, 857-58 (refusing to establish medical monitoring fund because (i) Kentucky law had “consistently held that a cause of action in tort requires a present physical injury to the plaintiff,” (ii) the issue presents “significant public policy problems” and matters “best left to the legislatures,” and (iii) the reasons stated in *Metro-North*).

# COMMENTARY ON “HORMESIS AND TOXIC TORTS”

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Professor Marchant's paper on hormesis and toxic torts is a timely and scholarly discussion of what may revolutionize toxic torts as we know them today. Plaintiffs in toxic tort cases typically point to the hazardous substance to which they have been exposed and argue that whatever physical ailments they may experience must have come from the exposure. In other words, any exposure, no matter how minimal, is bad. As Professor Marchant points out, if hormesis is generally accepted by the scientific community, it will then be used as a defense to many toxic tort claims. The burden on plaintiffs' lawyers will be increased enormously, since they will then be required to prove that their client or clients were exposed to a level of toxins sufficient to actually cause physical harm. As juries become familiar with the concept of hormesis, they can be expected to reject plaintiffs' claims where the exposure falls in the non-harmful hormetic range. We can only hope that Professor Marchant's paper, together with the ever-growing scientific literature on hormesis, receives wide distribution, particularly within the legal community.

No doubt there will be serious challenges in the courts to the admissibility of defenses based upon hormesis. Proponents must meet the requirements of *Daubert*,<sup>1</sup> or the parallel requirements under the laws of those states which have not adopted the *Daubert* rule.<sup>2</sup> The work carried out by Dr. Edward Calabrese and his colleagues has gone a long way to establish the validity of hormesis.

Much will depend upon the attitude of the trial judge called upon to rule on the admissibility of a hormesis defense. Under *Daubert*, as Professor Marchant points out, the trial judge is the "gatekeeper" when it comes to the admissibility of expert scientific evidence. The defense lawyer arguing for the admission of expert testimony based on hormesis must overcome two hurdles: first, the trial judge must rule that the proffered testimony meets the *Daubert* test, i.e., under the Federal Rules of Evidence, the court must ensure that the scientific expert is relevant and reliable. Presumably the greater latitude of admissibility under Rule 702 will make it easier to mount a hormesis defense in federal courts than in those states which adhere to the *Frye*<sup>3</sup> rule.

Under the *Frye* rule it will be necessary to establish that the particular scientific theory or principle must be sufficiently established to have gained general acceptance in the particular field in which it belongs.<sup>4</sup> Courts have usually interpreted that to require acceptance by peer reviewed scientific journals or similar publications.

While it is true that plaintiffs' attorneys will argue that the client in each particular case has genetic predispositions or other characteristics which make the client susceptible to a "zero threshold" exposure level, the burden will fall on the plaintiff to prove any such claims. Once the court has accepted the principle of hormesis, the burden will shift to the plaintiff to prove why hormesis should not apply in the particular case. That may turn out to be a formidable task.

In the final analysis, general acceptance of the principle of hormesis may be a blessing not only to defense lawyers, but to society as a whole.

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1. *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 113 S. Ct. 2786, 125 L. Ed. 2d 469 (1993).
2. For example, California follows the *Kelly-Frye* approach to expert scientific evidence. See, e.g., *People v. Kelly*, 17 Cal. 3d 24, 549 P.2d 1240 (1976) and *Frye v. United States*, 293 F. 1013 (D.C. Cir. 1923).
3. *Frye v. United States*, 293 F. 1013 (D.C. Cir. 1923).
4. For a complete discussion of the *Daubert* and *Frye* positions, see Lathrop, Mitchell L., "The Changing Face of Expert Evidence," 52 *F.D.C.C. Quarterly* 409 (2002).

# COMMENTARY ON "HORMESIS AND TOXIC TORTS

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In the article entitled "Hormesis and Toxic Torts", Dr. Gary E. Marchant proposes that the concept of hormesis could be used as a defense strategy in the context of toxic tort litigation. Hormesis is typically defined as a U or inverted U-shaped dose response curve, due to stimulation of a response at low doses vs. inhibition of this response at high doses. Dr. Marchant postulates that hormesis could be used to argue that a specific chemical is not responsible for a plaintiff's injury because low levels of exposure would likely have been health protective, rather than harmful, for the plaintiff. While the idea of using hormesis in the context of toxic tort litigation is certainly intriguing, its successful use in toxic tort litigation will likely be limited, at least given the current state of knowledge regarding hormesis.

Dr. Marchant provides several examples where the concept of hormesis could have been invoked to obtain a more favorable outcome for the defendant, including cases involving a dioxin spill, individuals with cancer who lived near a landfill, benzene in Perrier sparkling water, and radioactivity at the Hanford nuclear reservation. However, it is not clear that there is sufficient evidence for any of these examples to demonstrate that hormesis would have occurred under the specific circumstances of the case. Even for dioxin, which has been cited as an example of *in vivo* hormesis for carcinogenesis (Calabrese et al, 2001),<sup>1</sup> the hormetic dose-response curve is most apparent for all tumors combined, and possibly for pulmonary tumors and pituitary tumors, but only in male rats. For other tumor sites, tumor incidence either increased or decreased linearly with dose, and was not hormetic. Because the dioxin example involved a claim of property damage rather than actual injury, it would not be possible to determine with any certainty whether any potential future injuries would have a hormetic dose-response. Given that a hormetic dose-response was observed only for two tumor endpoints, and only in males, it could be argued, with this particular example, that any potential future injuries would likely not have a hormetic dose-response.

Although hormesis has been demonstrated for a wide variety of agents (*e.g.*, heavy metals, pesticides, drugs), which operate by a variety of mechanisms (*e.g.*, enzyme-induction, receptor-mediated, DNA reactive), most examples of hormesis have been derived from studies in plants or non-mammalian species (such as yeast or bacteria) or *in vitro* in cell systems. The implications of a hormetic dose-response in plants or non-mammalian species, or even in a mammalian cell system for the whole animal, much less in humans, is unclear.

Because of the lack of evidence of generalizability of hormesis for the most likely endpoints and species in toxic torts cases (*i.e.*, chronic diseases such as cancer in humans), chemical-specific evidence will be required for successful use of hormesis as an argument by the defense. We are unaware of studies confirming the hormetic dose-response for chronic diseases and specific chemicals in humans. Moreover, there is evidence to suggest that hormesis is not generalizable across endpoints, at least for some chemicals. For example, in addition to the example of dioxin discussed above, cadmium chloride has also been used as an example of an agent that demonstrates a hormetic dose-response for a cancer endpoint (Borak et al, 2005).<sup>2</sup> However, the hormetic dose-response curve for cadmium-induced tumors has been observed only for testicular tumors, but not for prostate tumors.

Another consideration regarding the use of hormesis in a toxic tort venue is that in some cases, observations of hormesis in certain test systems suggest the potential for adverse rather than beneficial effects at low doses. For example, a hormetic effect involving enhanced cell proliferation *in vitro* at low doses *vs.* cell killing at higher doses does not necessarily support a conclusion that low doses would be health protective in humans, since uncontrolled cell proliferation is a hallmark of the carcinogenic process. In this example, careful consideration would have to be given to the nature of the proliferative response in the system being studied and its extrapolation to humans.

Dr. Marchant postulates that hormesis is more likely to be accepted in the context of a toxic tort litigation than in a regulatory setting. This is in part because, in a toxic tort setting, the plaintiffs may not necessarily include the most susceptible individuals in the population. It remains to be known, however, the extent to which individuals vary in their "susceptibility" to hormesis (assuming in *arguendo* that such variability does exist). An individual "less susceptible" to hormesis would actually be at greater risk from low dose exposures. Data are also limited (if existent at all) regarding the variability in the hormetic dose-response among individuals. Thus, a defendant would be unlikely to know the extent to which the exposed individuals in toxic tort litigation were "susceptible" to hormesis, or at what doses hormesis would be observed in specific individuals. The lack of such information would weaken a defense claim for hormesis.

Dr. Marchant is correct in saying that "the theory of hormesis is still very speculative and preliminary, and is not even close to displacing the dominant linear paradigm." Because of this, we believe claims of hormesis will probably have limited use in a toxic tort setting, in particular for making the argument that the chemical may have actually been health protective rather than harmful. However, hormesis is likely to have utility in terms of a general discussion regarding the nature of the dose-response curve. That is, the hormetic model could be used to illustrate the considerable uncertainty in extrapolating from high dose to low dose effects and to demonstrate that the linear no-threshold model is a hypothetical construct, that may be appropriate (in some cases) for regulatory decision-making, but not for making inferences regarding toxicological causation.

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2. Borak, J; Sirianni, G. 2005. "Hormesis: Implications for Cancer Risk Assessment." *Dose-Response.* 3:443-451.

# COMMENTARY: HORMESIS AND TOXIC TORTS

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While I find Professor Marchant's consideration of hormesis in the toxic tort context to be insightful, I disagree with a number of his assumptions – many of which are generally consistent with the Belle generated literature. I am not a scientist, which puts me at a distinct disadvantage in this forum. Nevertheless, the application of hormesis in legal proceedings raises a number of concerns, many of which are addressed herein.

Hormesis is generally understood to stand for the proposition that low-level exposures to known toxic chemicals could be "beneficial" to human health. In his paper, Professor Marchant asserts the obvious – application of hormesis in litigation could be a powerful tool in denying liability for alleged injuries deriving from low levels of exposure. I am skeptical as to Professor Marchant's proposed application of this hypothesis.

As an initial matter, there appears to be significant concern in the scientific community about hormesis. For example, some scientists who have reviewed this issue have found, *inter alia*, that, "even if certain low-dose effects were sometimes determined to be beneficial, this finding should not be used to influence regulatory decisions to increase environmental exposures to toxic agents, given factors such as variability in individual susceptibility, variability in individual exposures, and the public's regular exposure to complex mixtures."<sup>1</sup> As suggested below, many of these same concerns are relevant in toxic tort litigation.

Moreover, it appears that many low level exposures causing an hormetic effect can actually be detrimental to human health. According to Dr. John Peterson Myers:

[h]ow can exposure to something that isn't overtly toxic be a problem? Altered gene expression in development changes the path taken by the developing organism. A good example is work by Ho et al., on how exposure to bisphenol A during development causes prostate cancer in adult rats. At birth there is nothing obviously wrong with the rat, but by adulthood it is at high risk to prostate cancer. According to Ho et al., the low dose of bisphenol A prevents a gene from shutting down, something Calabrese would regard as stimulatory because this gene is involved in promoting cell division.

Think of it this way. If you were a pilot steering a boat from New York to London, it would be toxic if someone blew up your engine. But if they altered the compass so that it led you 3 degrees off course from the very start of the trip, by the time you reached Europe you'd be on the shores of France. Small shifts in the course of development can have profoundly adverse impacts even though they may not be overtly toxic at the time of exposure.<sup>2</sup>

It is in this context that I find Professor Marchant's willingness to champion the utilization of hormesis in toxic torts of concern.

In his article, Professor Marchant discusses some of the problems with relying on hormesis in litigation, primarily as a result of *Daubert* and its progeny – a series of cases that establish the requisite showing for admissibility of scientific evidence at trial.<sup>3</sup> These problems warrant a more detailed and focused discussion. For example, as Professor Marchant points out, this type of evidence usually must be established to a "reasonable degree of medical certainty" before it can be considered in litigation. Dr. Calabrese estimates "that a U-shaped (or j-shaped) dose-response relationship may be reliably expected in about 40% of experiments with appropriate study design."<sup>4</sup> Thus, even if we assume, *arguendo*, the existence of a hormesis friendly environment, an hormetic response can be expected to convey less than half of the time. This generally does not meet the "reasonable degree of medical certainty" standard for the admission of medical/scientific evidence.<sup>5</sup>

Moreover, even if we assume a non-linear dose response is appropriate, at what level of exposure does the curve change to indicate harm. Hormesis applies to very low levels of exposure. In the modern world people are likely continuously exposed to hormetic levels of myriad toxins – without the additive (even low level) exposure that could form the basis for a toxic tort based claim. While I am not a proponent of the blind, unwavering application of a linear non-threshold model, it is important to note that the watchful eye and heavy regulatory hand of the government is not preventing the general public from exposure to massive amounts of regulated and unregulated chemicals.<sup>6</sup> With more time and research it may be established that background levels of toxins in our daily environment already occupy the lower end of the J-shaped curve.<sup>7</sup>

If we assume further, *arguendo*, that there are no background toxins under normal conditions, toxic tort plaintiffs often live in a "toxic soup" environment. This relatively common environmental condition can also impact the potential availability of hormesis as a viable evidentiary theory. By way of example, it is not clear to me that the hormetic effect measured in low level exposures to some metals would remain constant when combined with, for example, an acidic environment. Before hormesis can influence a particular piece of litigation, it should be studied in light of, *inter alia*, life-time acquired individual susceptibilities, genetic heterogeneity, cumulative exposures of a particular toxic tort plaintiff, and the pre-existing burden of all the toxins found in our daily lives.

Finally, hormesis proponents, including Professor Marchant, lament over the perceived unfair consideration of hormesis by the U.S.

Environmental Protection Agency. Thus, the agency is faulted for “policy-based default assumptions that limit their receptivity to new concepts such as hormesis.” As discussed briefly above, hormesis appears to apply in only specialized conditions and in a minority of cases – it should not, at this time, be relied on to upset generalized regulatory policy-based default assumption, nor should it be allowed as admissible scientific evidence. The proposition that hormesis would be more likely to gain acceptance in litigation than by the regulatory agency charged with reviewing the efficacy and impact of chemicals is cause for concern, not rejoice.

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2. Myers, “Hormesis is a Flawed Theory”, *Environmental Science & Technology* (2006).
3. Belle certainly seems to be addressing the “peer review publication” element of *Daubert*.
4. E. Calabrese, Precautionary Principle and Hormesis, *Belle Newsletter*, Vol. 12, No 2, Sept 2004 at 5.
5. *E.g.*, *Wood v. Gutierrez*, 2006 WL 2935253 at \*6 (Ohio App. 3 Dist. 2006) (reasonable degree of medical certainty means greater than 50%); *Silica Products Liability Litigation*, 398 F. Supp.2d 563, 604 (S.D. Tex. 2005) (same); *Kellan v. Board of Trustees*, 551 N.E.2d 264, 267 (Ill. 2005) (same); *Hunter v. Harvil*, 1999 WL 318065 at \*2 (Ark. App. 1999); *Robinson v. Group Health Association*, 691 A.2d 1147, 1150 (D.C. App. 1997).
6. GAO, Testimony before the Committee on Environment and Public Works, U.S. Senate, “Actions Are Needed to Improve the Effectiveness of EPA’s Chemical Review Program,” Statement of John B. Stephenson, GAO-06-1032T (August 2, 2006) (“... EPA has used its authorities to require testing of fewer than 200 of the 62,000 chemicals in commerce when EPA began reviewing chemicals under TSCA in 1979. . . Since Congress enacted TSCA in 1976, EPA has issued regulations to ban or limit the production of only five existing chemicals or groups of chemicals.”); *see also*, e.g., Myers, “Hormesis is a Flawed Theory”, *supra*. (“the notion that widespread observations of hormetic responses justifies weakening health standards is naïve and wrong. Calabrese is right that current regulations should recognize the ubiquity of non-monotonic dose response system. But the appropriate response to this observation is not to weaken standards but to strengthen them, because the adverse impacts of low dose stimulation of gene expressions can’t be predicted by today’s regulatory testing.”).
7. *See, e.g.*, CDC, “Third National Report on Human Exposure to Environmental Chemicals,” (2005); National Geographic, “The Chemicals Within Us,” Vol. 210, No. 4 at 116 (October 2006).

# RESPONSE

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The commentaries on my article represent divergent, but uniformly valuable, insights and views on the potential application of hormesis in toxic tort litigation. Two of the commentaries (Robin Juni and Mitchell Lathrop) are generally in agreement with my thesis that hormesis may be relevant and useful evidence in a limited set of toxic tort cases. Both contribute additional insights that strengthen my argument.

Lathrop emphasizes the important role of the burden of proof, which is ultimately on the plaintiff, in applying hormesis evidence. It may indeed be the case that some individual plaintiffs are more susceptible to low level exposures of hazardous substances than others in the population, and thus perhaps less likely to benefit from a hormetic response at such exposure levels. Lathrop correctly points out, however, that the burden to establish this individual susceptibility will be on the plaintiff, once the defendant has established the general proposition of hormesis. This is consistent with the existing case law where plaintiffs alleging a unique susceptibility to a hazardous exposure cannot rely on evidence of the existence of such susceptibility in the population generally, but must produce specific evidence that the individual plaintiff at issue in fact has that susceptibility.<sup>1</sup>

Juni makes an excellent point in focusing on the potential role of hormesis in claims for "subclinical" harm, also sometimes called "latent risk" claims. Such claims by asymptomatic plaintiffs seeking funds from a defendant responsible for a toxic exposure for medical monitoring or as compensation for increased risk of disease or fear of disease often (but not always) involve low exposure levels for all or many members of the plaintiffs' class. These cases therefore may be promising contexts for applying a hormesis defense, as Juni suggests. The application of hormesis to fear of cancer claims may be particularly intriguing. These claims tend to be somewhat circular and self-fulfilling, in that a plaintiff is told he or she might be at an increased risk of cancer from their exposure, and then seeks compensation for the fear that results from that information. If the plaintiff is informed that hormesis may provide some protection against low-level exposures, the plaintiff's fear, and basis for bringing a fear of cancer claim, may be dissipated.

Howard Shanker and Mara Seeley & Barbara Beck are more skeptical of the utility of hormesis in toxic tort litigation, and succinctly raise the key arguments that a good plaintiff's attorney will surely raise

against hormesis evidence. I certainly agree with these commentators that hormesis arguments will not be valid or relevant in many toxic tort claims, but believe these commentators are overly pessimistic about the role of hormesis in other toxic tort cases. Both sets of commentators raise legitimate points about the difficulty that a defendant may face in proving hormesis in a given case. Specific evidence of the hormetic effect of the particular toxin at issue and information about the susceptibility of the individual plaintiff would be needed to prove affirmatively a hormetic response in a specific context. But the commentators fail to address a key point of my argument which is that a defendant could use a hormesis argument in a more defensive mode, arguing that the plaintiff, who has the ultimate burden of proof, will fail to meet that burden unless the plaintiff demonstrates that hormesis does not apply to their circumstances. In other words, as Lathrop's commentary recognizes, once hormesis is generally established as a relevant toxicological consideration, which arguably has now been achieved given its coverage in leading toxicology texts, the plaintiff must adequately take account of and rebut the possibility of hormesis to meet their burden of proof in demonstrating causation. The bottom line is that the placement of the burden of proof on the defendant or plaintiff will often be outcome-critical in addressing hormesis.

Both sets of commentators also correctly point out that a hormetic response may not always be beneficial to health, and in some cases may be a detrimental or adverse effect. Fair enough, but in those cases the defendant would not (and could not) assert a hormetic argument (and it may be the plaintiff that seeks to rely on the evidence of an adverse hormetic response). In most cases, however, the hormetic response appears to tilt in the direction of a protective effect, and those are the circumstances in which hormesis would be potentially useful to defendants.

Finally, a technical point to set the record straight, Seeley & Beck quote me out of context when they assert that I state that "the theory of hormesis is still very speculative and preliminary...." If my statement is read in context, it refers to one of two main viewpoints that are likely to exist on hormesis, and is the one likely to be advanced by plaintiffs' lawyers, but it is not my position.

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