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Toxic Torts

The Newsletter of the Toxic Tort and Environmental Law Committee

July 26, 2012 Volume 15 Issue 1

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Leadership Notes

Letter from the Vice Chair

by Douglas M. Poland

As vice chair of DRI's Toxic Torts and Environmental Committee, I am pleased to introduce the summer 2012 issue of the TTEL Committee's newsletter. Dara Mann, Publications/Newsletter Chair, and Jeff Pypcznski, Publications/Newsletter Vice Chair, have solicited, reviewed, and selected two excellent and informative articles for this newsletter. If you have not taken advantage of the opportunity to write an article for the TTEL Committee newsletter, I strongly encourage you to do so. It is a great opportunity to share your recent experiences with toxic torts and environmental litigation and regulatory matters, give and receive practice tips in these areas, and share cutting-edge insights with your fellow committee members. It is also yet another opportunity to promote your practice and your law firm and to expand your network of contacts. Our committee will publish two more newsletters in 2012. If you are interested in being published, please contact Dara Mann at dmann@mckennalong.com or Jeff Pypcznski at jmpypcznski@pbn.com as soon as possible.

We also have an additional publishing opportunity: We currently are inviting committee members to submit article proposals for the January 2013 edition of *For The Defense* magazine, which has a nationwide audience of more than 40,000 readers. *FTD* articles must be original writings (i.e. not published elsewhere) and must be prepared by members of the DRI Toxic Torts and Environmental Law Committee. Generally, the articles should be between twelve to twenty (12-20) pages long, double-spaced, with no endnotes or footnotes. All articles must address subject matters of national interest to lawyers and corporate counsel practicing in the areas of toxic tort and environmental law. If you are interested in submitting a topic proposal or draft article for *FTD*, please contact Dara or Jeff by August 3. Final articles must be received no later than September 28 in order to be considered for publication.

Before moving to the content of this committee newsletter, I have one other order of business to address. TTEL Committee Chair Kevin Clark and I strongly encourage you to register for DRI's 2012 Annual Meeting, which will be held October 24-28, 2012, at the New Orleans Marriott. This year's Annual Meeting features keynote speakers Ambassador Karen Hughes and former White House Press Secretary Dee Dee Myers, who will present *A Point/Counterpoint – The Political Landscape*, and Niall Ferguson, internationally acclaimed author, whose most recent book, *Civilization: The West and the Rest*, is a global bestseller. Thursday afternoon, TTEL, in conjunction with the Alternative Dispute Resolution, Employment and Labor Law, and Medical Liability and Health Care Law Committees, will present a mainstage CLE session, *When the Players Are All In – Successfully resolving High Stakes Litigation in the Twenty-First Century.* TTEL committee member Diana Johnson put in many hours of hard work helping to organize and prepare this panel discussion, and she deserves our thanks and support.

You also will not want to miss our committee's Annual Meeting Business and CLE meeting to be held on Thursday morning from 8:00 a.m. to 9:30 a.m. After hearing from leaders and

Seminars

DRI 2012 Annual Meeting

October 24-28, 2012
New Orleans, Louisiana

DRI Publications

Exploring Toxic Torts and Environmental Liability Claims

representative of our various subcommittees about their accomplishments and future plans, we will turn the floor over to the following four committee members who were selected to offer CLE programming for the last hour of our meeting:

T. McRoy Shelley III – *Is Litigation Killing Us? Or Are We Killing Litigation?*

Joshua D. Shaw – *At the Intersection of International and Domestic Law – The Supreme Court to Address Corporate Liability for Violations of International Law*

Sean A. Simmons – *Subsequent Purchaser Doctrine – An Evolving Affirmative Defense in Toxic Torts or an Outlier?*

Melanie R. Edwards – *The Significance of Statistical Significance*

If you register for the Annual Meeting by **September 26, 2012**, you will receive $200.00 off the registration fee. **September 26** is also the deadline to receive the special discounted rate for a room at the New Orleans Marriott. To register or for more details, log on to www.dri.org, or call DRI at 312.795.1101. We look forward to seeing you in New Orleans in October!

Now we turn to the substantive articles in this newsletter. In our first article, *Island Hopping Among the Chromosomes: Are Chromosomal Aberrations the Trump Card in Toxic Tort Causation?*, Erik Falk, Julie Nord Friedman, and Dr. Howard Sandler address the role that the study of chromosomal/cytogenic aberrations may play in toxic tort litigation. As they note, science does not know the precise mechanisms involved in carcinogenesis for most cancers, and as trial lawyers, we turn to inferential scientific tools such as epidemiology, animal studies, in vivo studies, in vitro studies, industrial hygiene exposure assessments, etc., to infer or rebut cancer causation. They then examine whether the study of chromosomal aberrations and their role in carcinogenesis has advanced far enough to be of use in toxic tort litigation and whether they can replace the inferential tools that we have traditionally used.

In our second article, *Lone Pine Procedure Successful in Hydraulic Fracking Case*, Dan Dunn, Andrew Lillie, and Anna Edgar summarize the strategy that they used to present a complex case management procedure to a Colorado state court in a recent toxic tort case involving the natural gas extraction process known as hydraulic fracturing. Recognizing that many courts may be unfamiliar with or reluctant to use the Lone Pine method of case management, they explain the strategy that they followed to identify the inadequacies of the plaintiffs' allegations, provide the court with substantial legal authorities supporting the entry of a Lone Pine order, and present evidence calling into serious question the plaintiffs' claims, resulting in complete dismissal of the plaintiffs' case.

We hope that you find these articles insightful and helpful to your practice.

Featured Articles

Island Hopping Among the Chromosomes: Are Chromosomal Aberrations the Trump Card in Toxic Tort Causation?

by Eric K. Falk, Julie Nord Friedman, and Howard M. Sandler

I. Introduction

Science does not know the precise mechanisms involved in carcinogenesis for

most cancers. By definition, cancer is uncontrolled cell proliferation, i.e. abnormal cell growth which escapes the "regulatory process" of the body's defense mechanisms. But the exact chromosomal process by which those initial cells become abnormal and continue to spawn abnormally, and what caused them to do so, is mostly unknown.

Much of toxic tort litigation involves claims of exposure to various substances, allegedly causing various cancers. As trial lawyers, we turn to various scientific fields such as epidemiology, animal studies, in vivo studies, in vitro studies, industrial hygiene exposure assessments; etc, all to infer the causation of the cancer, or to rebut the inference of causation. However, at bottom, the fields that we turn to as trial lawyers are inferential tools. They are inferential because we simply do not know the precise mechanisms of carcinogenesis.

In the last 25 to 30 years, the study of chromosomal/cytogenetic aberrations (hereafter referred to as "chromosomal aberrations"), and their role in carcinogenesis, has become cutting edge science. Chromosomal studies have provided valuable insights into the mechanisms of certain cancers, and also in the study of treatment modalities. But can these studies result in "cutting edge toxic tort law?" Can they replace the inferential tools that we have traditionally used? Are they simply another inferential tool? Has the study of chromosomal aberrations advanced far enough to be of use in toxic tort litigation or are these studies not yet ripe? See e.g. Goldstein; Chapter 29—Benzene, §29:33, "Specific Causation—Hematological Manifestations: Chromosome Abnormalities in Cytogenetics, in *Modern Scientific Evidence: The Law and Science of Expert Testimony*; David L. Faigman, David H. Kaye, Michael J. Saks, Joseph Sanders, Editors; found at 3 Mod. Sci. Evidence §29:33 (2010-2011 Edition).

With all due deference to Lewis Carroll, this article will attempt to peer "through the looking glass" and see what we find just as Alice did in Carroll's sequel to *Alice's Adventures in Wonderland*, albeit on the issue of chromosomal aberrations and causation.

II. The Molecular Genetics of Cancer

Cancers arise from the accumulated defects in certain genes, which in turn cause uncontrolled cell proliferation. See e.g. Fearon, "Progressing from Gene Mutations to Cancer," Chapter 15 in *Clinical Oncology*, Abeloff, et al. Editors, 3rd Edition (2004). The study of chromosomal aberrations dates back to the 1950's. For example, between 1956 and 1960, researchers identified certain specific chromosomal aberrations associated with congenital abnormalities such as Down's Syndrome. As noted in one leading cancer textbook, "The opening salvo in cancer clinical cytogenetics was finding a characteristic marker for chronic myelogenous leukemia (CML): the Philadelphia Chromosome." Qumsiyeh & Yilmaz, Chapter 1.5, "Cytogenetics," in C *ancer*: *Principals & Practice of Oncology*, DeVita, et al. Editors, 7th Edition (2005).

> As one article puts it:
>
> > …it is now well established that every tumor type that has been studied in a sufficient number to permit conclusions may be subdivided on the basis of characteristic, often specific, and sometimes even pathognomonic balanced chromosomal rearrangements. This is true for hematological disorders, malignant lymphomas as well benign and malignant mesenchymal, germ cell, neuroglial, neuronal, neuroectodermal, and epithelial tumors.

Mitelman, *Recurrent Chromosome Aberrations in Cancer*, Mutation Research 462 (2000) 247-253.

In their form, "Chromosomal aberrations are usually considered to derive from unrepaired or misrepaired DNA lesions induced by exogenous or endogenous exposure to DNA damaging agents." Boffetta, et al.; *Chromosomal Aberrations and Cancer Risk: Results of a Cohort Study from Central Europe*; 165 American Journal of Epidemiology 36 (2007).

Well what does all this mean in plain English? We are all familiar, from elementary and high school science classes, with the principal that cells divide, creating what are called "daughter" cells. One cell becomes two, two cells become four, etc. When a cell divides, the chromosomes divide with it. Tumors, whether benign or malignant, arise when a chromosome divides improperly. Such cells are called "aneuploid" cells. This process actually occurs in almost all of our organs, all the time. We have improper cell division going on in our bodies as we write this, and as you read this. However, our genes have "programmed" defense mechanisms which regulate and control the abnormal cells, and essentially kill them before they proliferate. We also have a wonderful immune defense system that can kill aneuploid cells which escape this programmed death. Nevertheless, on rare occasions, an abnormal cell escapes these processes, and then continues to divide and replicate its own cytogenetic abnormalities. At some point, when it does so, it becomes cancer. An excellent scientific summary of this process can be found in Fearon, *supra*. Abnormalities in chromosomes that are a result of this process can be numerical abnormalities, which entail having the loss or gain of certain chromosomes; or structural abnormalities, which involve changes in part of one or more chromosomes. Structural abnormalities can be classified as either translocations, deletions, duplications, inversions or amplifications. A more detailed discussion of these abnormalities can be found in Qumsiyeh & Yilmaz, *supra*.

III. A Quick Review of Certain Studies of Chromosomal Aberration and Their Implication for the Causation Analysis

In this section we will examine certain, selected studies on chromosomal aberrations with regard to benzene exposures and hematopoetic cancers. This section is not meant as a comprehensive review of *all* such literature. It is a review of *selected* articles, and naturally reflects that bias.

Benzene is an important industrial chemical that is known to cause Acute Myeloid Leukemia (AML). See e.g. *Twelfth Report on Carcinogens*, United States Department of Health and Human Services (2011). Whether benzene exposure can be associated with other forms of leukemia, various lymphomas, multiple myeloma, etc., remains controversial, with various studies providing support for both positions.

Upon absorption following exposure, benzene is metabolized within the liver, where it is converted primarily to phenol, which in turn is subsequently metabolized to various polyhydroxylated metabolites. See e.g. Zhang, et al; *Detection of 1, 2, 4 Benzenetriol Induced Aneuploidy and Microtubule Disruption by Fluorescence In Situ Hybridization and Immuno Cytochemistry*; Mutation Research 320 (1994) 315-327. However, the mechanism of benzene induced carcinogenesis is not well understood. Indeed, as one study put it:

> Unfortunately, there is no convenient model for studying the mechanisms by which benzene produces neoplastic effects in animals. Although each of these effects, i.e., aplastic anemia, chromosome damage, and carcinogensis, are indicative of the ultimate impact of benzene on bone marrow, the relationship between these phenomena and the mechanisms by which they are initiated remain to be fully understood.

Snyder, et al.; *The Toxicology of Benzene; 100 Environmental Health Perspectives*, 293 (1993).

Nevertheless, there are "many reported observations of chromosome aberrations in blood from workers exposed to benzene." *Id*. A brief review of some of these articles follows, but bear in mind, many of these articles report chromosomal aberrations associated with benzene exposure but fail to link to them to carcinogenesis. Other articles note chromosomal aberrations found in various leukemias and lymphomas, but failed to establish them as a result of benzene exposure.

What the literature seems to suggest is that we have two

"islands," one island noting benzene exposure and chromosomal aberrations, another island noting various cancers with chromosomal aberrations, but no "bridge" fully connects these two islands.

Zhang, et al., *supra*, found that the benzene metabolite, 1, 2, 4-benzenetiol induced aneuploidy in chromosomes 7 and 9 in HL60 cells, and that this was dose related. Chen, et al., demonstrated that chromosomal breakage was an early genotoxic event induced by benzene and its metabolites. Chen, et al; *Chromosomal Loss and Breakage in Mouse Bone Marrow and Spleen Cells Exposed to Benzene Vivo*; 54 Journal of Cancer Research, 3533 (1994).

Zhang, mentioned above, in particular, has been a prolific researcher on the issue of benzene induced chromosomal aberrations. In a series of studies since the 1994 study, *supra*, Zhang and colleagues have reported the association of benzene exposure to the frequency of aneuploidy in a diverse variety of chromosomes, including chromosomes 1, 2, 4, 5, 6, 7, 8, 9, 11, 12, 14, 18, 21 and 22. See Zhang, et al., *Interphase Cytogenetics of Workers Exposed to Benzene*,104 Environmental Health Perspectives, 1325 (1996); Zhang, et al., *Increased Aneusomy and Long Deletion of Chromosomes 5 and 7 in the Lymphocytes of Chinese Workers Exposed to Benzene*, 19 Carcinogenesis 1955 (1998); Smith and Zhang, et al., *Increased Translocations And Aneusomy In Chromosomes 8 And 21 Among Workers Exposed To Benzene*, 58 Cancer Research 2176 (1998); Zhang, et al., *Benzene Metabolites Induce the Loss and Long Arm Deletion of Chromosomes 5 and 7 in Human Lymphocytes,* 22 Leukemia Research 105 (1998); Zhang, et al., *Benzene Increases Aneuploidy in the Lympho Sites of Exposed Workers*: *A Comparison of Data Obtained by Fluorescence In Situ Hybridization in Interphase and Metaphase Cells;* 34 Environmental Molecular Mutagenesis 260 (1999); Zhang, et al., *Aberrations in Chromosomes Associated with Lymphoma and Therapy Related--Leukemia in Benzene Exposed Workers*; 48 Environmental and Molecular Mutagenesis 467 (2007); Zhang, et al, *Chromosome-Aneuploidy Study (CWAS*) *In Workers Exposed to an Established Leukemogen, Benzene*; 32 Carcinogenesis 605 (2011).

Another set of studies has examined chromosomal aberrations with regard to certain cancers. For example, Yunis published in 1983 an article entitled *The Chromosomal Basis of Human Neoplasia,* 221 Science 227 (1983). In tables one and two of this article, Yunis set forth the various chromosomal aberrations that are associated with numerous cancers, including the various leukemias, and a small number of the lymphomas. Mohamed, et al., published on chromosomal aberrations in multiple myeloma. *Chromosome Aberrations in a Series of 120 Multiple Myeloma Cases with Abnormal Karyotypes*, 82 American Journal of Hematology 1080 (2007).

Bowen and colleagues reported that the CYP1A1*2B Allele may predispose a person to the development of AML. Bowen, et al., *CYP1A1*2B Allele is Over Represented in a Subgroup of Acute Myeloid Leukemia Patients with Poor Risk Karyotype Associated with NRAS Mutation, But Not Associated with FLT3 Internal Tandem Duplication;* 101 Blood 2772 (2003).

Some articles do attempt to link specific exposures, specific leukemias, and specific chromosome damage, thus attempting to build "the bridge" between the exposure and causation of carcinogenesis.. Aberrations involving chromosome 8 in patients with Acute Nonlymphocytic Leukemia (ALL) has been specifically associated with smoking, although the confidence interval demonstrated that the association was not statistically significant, in Davico, et al.; *Chromosome 8, Occupational Exposures, Smoking and Acute Nonlymphocytic Leukemias: A Population Based Study*, 7 Cancer Epidemiology, Biomarkers and Prevention 1123 (1998). Despite the fact that the confidence interval included 1.0, the author stated that the association between smoking habits and chromosome 8 aberrations was "strong". The authors also noted that 3 of the 5 patients with chromosome 8 aberrations who were smokers also were "occupationally exposed to solvents or [polycyclic aromatic hydrocarbons]." The authors then stated:

> "We can hypothesize that exposure to PAH's that occurs through tobacco

> smoking, particularly of unfiltered cigarettes, or for occupational reasons, can induce nonlymphocytic leukemia by interfering with chromosome 8."

Exposure to organic insolvents, AML and chromosome aberrations was explored again by Albin and her colleagues in *Acute Myeloid Leukema and Clonal Chromosome Aberrations in Relation to Past Exposure to Organic Solvents*, 26 Scandinavian Journal of Work and Environmental Health 482 (2000). Here, 372 cases of AML diagnosed between 1976 and 1993 were studied. Information on exposure was obtained, along with cytogenetic investigations from bone marrow or peripheral blood samples taken before the start of treatment. In terms of occupational exposure, the authors noted that "Exposure to all organic solvents was associated with a moderately increased overall risk for AML (odds ratio of 1.6, 95% confidence interval ranging from 1.1—2.4)." However, when it came to the analysis of the chromosomal aberrations, the authors found:

> Analyses by the presence of clonal chromosome abnormalities did not
>
> indicate that the increased overall risk associated with exposure to all
>
> organic solvents was predominantly associated with AML with an abnormal karyotype. In fact, the risk of AML with a normal karyotype in association with exposure to all organic solvents was somewhat higher than that for an abnormal karyotype."

The authors did find that a high odds ratio was observed in association with abnormalities of chromosome 8, but this "strong estimated effect for trisomy 8 was not due to benzene exposure alone."

Prior to Albin, Ciccone and colleagues also examined the issue of chromosomal aberrations in patients with AML, Chronic Myeloid Leukemia (CML) and Myelodysplastic Syndromes (MDS). Ciccone, et al.; *Myeloid Leukemia and Myelodysplastic Syndromes: Chemical Exposure, Histological Subtype and Cytogenetics in a Case Control Study,* 68 Cancer Genetics and Cytogenetics 135 (1993). Interestingly, Ciccone noted that chromosomal aberrations were not associated with chemical exposures, although a non-statistically significant excess risk was evident for those who had been exposed to electromagnetic fields, although this was reportedly found only for chromosomal aberrations in AML cases.

Suffice to say, with articles providing scientific evidence for both camps in the attempt to "build the bridge between the two islands," the best summary of the state of the science is, perhaps, taken from a 2008 article by Cliona M. McHale and her colleagues, *Chromosome Translocations in Workers Exposed to Benzene,* 39 Journal of the National Cancer Institute 74 (2008):

> In conclusion, there are limitations to the use of translocations by biomarkers of early effect for hematologic malignancies. Current detection methodologies may lack the necessary sensitivity for their detection at biologically meaningful levels. Also, although translocations are thought to be initiating events in leukemia, their presence alone does not cause leukemia. Additional cooperating mutations are required for disease.

Essentially, we are back to where we started—the precise mechanism of carcinogenesis is poorly understood.

IV. What Does All This Mean in Toxic Tort Litigation?

Studies of chromosomal aberrations, when they are used in toxic tort litigation, are used by either party in an attempt to prove or disprove the cause and effect relationship between an alleged exposure and an end result, in what is often termed the "battle of the experts." Such studies may be used in a localized exposure case such as a community living near a landfill, see e.g. *Nonnon v. City of New York*, 2011 WL 4089536 (N.Y.A.D. 1 Dept.) or a more generalized exposure

such as the SV40 vaccine, see e.g. *Gannon v. United States*, 571 F. Supp. 2d 615 aff'd 292 Fed. Appx. 170, 2008 WL 4151665 (C.A.3 (Pa.). Such studies can also be found in benzene or solvent litigation, generally involving leukemia and other hematoepoetic cancers. This is best summarized by *Goldstein*, supra:

> There is much interest in the possibility that cytogenetics findings may distinguish those individuals with hematological cancers due to benzene. Two general observations are the basis for this interest. Benzene has long been known to produce chromosomal abnormalities in the bone marrow and circulating white blood cells of exposed workers. Cytogenetics abnormalities, found to occur in about half of patients with [acute myelogenous leukemia] have been noted to be more common in those with history of work place exposure to potential leukemogenic agents.

Judges, when presented with challenges to the sufficiency of or reliance on such studies by a particular party's expert, often turn to and utilize the factors for evaluating whether a substance or a particular exposure can cause disease as set forth by Sir Austin Bradford Hill in his seminal 1965 presentation, *The Environment and Disease: Association or Causation?* 58 Proceedings of the Royal Society of Medicine 295 (1965). Those factors, well known to toxic tort lawyers, are:

- Strength
- Consistency
- Specificity
- Temporality
- Biologic Gradient (Dose Response)
- Plausibility
- Coherence
- Experiment
- Analogy

These factors have been erroneously referred to by both some courts and some experts as "criteria". The difference is not just semantics and it must recognized that while some courts accept the Bradford-Hill factors as an aid to assist in determining causation, other courts have found them unnecessary. Further, some courts acknowledge that failure to satisfy one factor does not necessarily in and of itself defeat an expert's opinion. See, *In Re Neurontin Marketing, Sales Practices, and Products Liability Litigation*, 612 F. Supp. 2d 116.

Courts that do discuss the Bradford-Hill factors in connection with chromosomal aberrations acknowledge that these studies only address one of the nine factors —the biological plausibility; i.e., the mechanism of the cancer. "The concept of biologic plausibility, which numbers among the nine Hill viewpoints, asks whether the hypothesized link is credible in light of what is known from science and medicine about the human body and the potentially offending agent." *Milward v. Acuity Specialty Products Group*, 639 F.3d 11 [Court found that the sum of expert testimony addressed many of the Bradford-Hill factors, including biologic plausibility, to support the inference that the association between benzene exposure and APL is causal.]. Of course, fulfillment of this one criterion is not sufficient to substantiate causation. Hill himself cautioned, "none of my nine viewpoints can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be required as a sine qua non."

At least one court has specifically addressed whether biologic plausibility alone could prove causation and found the answer to be "no." In *Gannon*, supra, plaintiffs, Jamie and Rebecca

Gannon, sued the United States under the Federal Tort Claims Act alleging that the government negligently licensed Lederle Laboratories to produce Orimune (an oral polio vaccine) and that the United States failed to confirm that SV40, a monkey virus, was not present at each stage of production. Plaintiffs allege that Jamie Gannon received an SV40 contaminated vaccine and developed a medulloblastoma as a result thereof.

The bench trial commenced with a Daubert examination of plaintiffs expert, Dr. Adi Gazdar. For convenience at the time, Dr. Gazdar also gave his theory on causation at the hearing. The trial court denied the Daubert motion. Defendant's then filed a motion pursuant to F.R.C.P. 52(c) as to causation, specifically challenging whether SV40 causes human medulloblastoma. Plaintiffs argue that said motion was premature as they had not yet presented all evidence. The trial court ultimately held that the Gannons did not meet their burden of proof on causation. This was upheld by the Third Circuit Court of Appeals. *Gannon*, supra.

The Eastern District set forth extensive findings of facts. First and foremost, the court recognized that to prevail, plaintiffs had to prove that SV40 causes cancer in humans generally *and* that it in fact caused Mr. Gannon's medulloblastoma (i.e. general causation and specific causation). *Gannon*, supra. Dr. Gazdar's opinion was based on biological evidence, as Dr. Gazdar conceded that there were no epidemiological studies that supported the proposition that SV40 causes cancer, let alone medulloblastomas. *Id.* The court further stated that in order to prove causation one would need to have *both* supporting epidemiological evidence as well as biological evidence. *Id.* The Court noted that National Academy of Sciences established the Institute of Medicine to examine policy matters pertaining to public health, and in 2002 the IOM had conducted a review concerning the possible link between SV40 contamination of polio vaccines and human cancer. *Id.* As they had in the past, IOM evaluated both biological and epidemiological evidence well as applied the Bradford-Hill criteria. *Id.*

> While the IOM (Institute of Medicine) Report concluded that based on the biological evidence, it is plausible that SV40 could contribute to some human cancers, the IOM specifically emphasized that any conclusion that SV40 causes human cancer must also be supported by epidemiological evidence.
>
> *When other evidence of causality is available, biological data add supportive evidence, but they cannot prove causality on their own*.

Gannon v. United States, 571 F. Supp. 2d 615 aff'd 292 Fed. Appx. 170, 2008 WL 4151665 (C.A.3 (Pa.). [emphasis supplied] Thus the court ultimately found that Dr. Gazdar's opinion that SV40 causes cancer and that it caused Mr. Gannon's medulloblatoma failed to satisfy the Bradford-Hill criteria. *Id.* More specifically, Dr. Gazdar relied solely on biological evidence; he acknowledged that the IOM had found that the available epidemiological data was inadequate, and his opinion was inconsistent with multiple studies on the issue. *Id.*

Yet another court, while viewing the biologic plausibility viewpoint as one of the particularly crucial viewpoints, first required that plaintiffs' expert be able to prove evidence of an association, in this case between neurontin and an increased risk of suicidality, before the court then took into account biologic plausibility. See *In re Neurontin*, supra.

In *In Re Neurontin Marketing, Sales Practices, and Products Liability Litigation*, 612 F. Supp. 2d 116, plaintiff allege that they or their decedents suffered suicide related injuries as a result of taking Neurontin. Defendants moved to exclude plaintiffs' expert testimony on question of whether Neurontin has the capacity to cause the alleged suicide events. The motion was denied after a three day hearing and said ruling was upheld by the United States District Court for Massachusetts.

Plaintiffs offered three experts, who in combination opined that Neurontin could increase a patient's risk of suicidality. All three relied on a variety of scientific evidence including human

and animal studies, case reports and scientific literature. The District Court went through an extensive scientific primer reviewing the power of both epidemiological studies and non-epidemiological evidence. With respect to epidemiological evidence, the District Curt acknowledged that association was the starting point for the Bradford-Hill criteria. *In Re Neurontin*. In the instant case, the court found an association, albeit not a statistically significant one, based on an FDA epidemiological study on the issue. *Id.* Plaintiffs, however, were able to extrapolate data from the same class of drugs to support their causation theory. *Id.* The District Court found that plaintiff did establish an association between Neurontin and increased risk of suicide, thus satisfying the prerequisite for causation using the Bradford-Hill criteria. Only at this point did the District Court consider and discuss the biologic plausibility argument of the plaintiffs.

In *Nonnon v. City of New York*, 2011 WL 4089536 (N.Y.A.D. 1 Dept.), actions were filed against a municipality for personal injuries arising from exposure to hazardous substances emanating from a landfill. Plaintiffs relied on various experts, including Dr. Neuberger, an epidemiologist, who prepared a study and opined that persons residing in close proximity to the landfill experienced higher incidence rates of acute lymphoblastic leukemia (ALL), as compared to persons further away from the landfill. Plaintiffs then relied on Dr. Bernard to analyze Dr. Neuberger's study and issue an opinion using the Bradford-Hill factors. While Dr. Bernard found strength of association and biological plausibility to Dr. Neuberger's study and opinion, the court specifically noted that the "strength of the epidemiological data alone permit and inference of causation. *Id.*

At best, studies of chromosomal aberrations currently address, conceivably, only one of the nine Bradford-Hill causation factors—biological plausibility, i.e. the mechanism of the cancer. Of course, that leads us right back to the question of whether the mechanism of the cancer is adequately understood. If it is poorly understood, then that, of necessity, impacts the use of genetic based carcinogenesis studies under the Bradford-Hill factors. One ultimately has to demonstrate, using validated, reliable, scientific methodology, which specific chromosomal aberrations are involved in the actual carcinogenesis process for the particular cancer at issue. One then has to relate those particular chromosomal aberrations back to the exposure. Relating the chromosomal aberrations back to the exposure inevitably takes us back to epidemiology, which is still the best indicator of the association and possible causal association of an exposure in a particular cancer in human beings.

Studies of chromosomal aberrations can help us to more precisely diagnose the disease, but they do not necessarily link the disease to the toxic agent. These studies can help us diagnose the disease by analyzing the basic biological error(s) which initiated, promoted, etc in essence, caused the disease, and how it may respond to specific treatments.. But do they help us identify what caused the genetic cascade of events that lead to a clinically detectible cancer? Do they help us identify the necessary dose that is required to initiate and/or facilitate the causal mechanism?

That is why we must return to the field of epidemiology. In fact, "[r]eview of the criteria themselves, as set forth in the seminal remarks of Dr. Bradford-Hill, shows that an epidemiologic foundation is a prerequisite for application of his criteria. 'The Bradford-Hill criteria *start with an association demonstrated by epidemiology* and then apply such criteria as the temporal sequence of events, the strength of the association, the consistency of the observed association, the dose-response relationship, and the biologic plausibility of the observed association.'" *Soldo v. Sandoz Pharmaceuticals Corp*. 244 F.Supp.2d 434 citing *In re Breast Implant Litig.,* 11 F.Supp.2d at 1233 n. 5. [emphasis supplied]

If human epidemiology has not demonstrated an association between the exposure and the disease, then the mechanistic studies, while interesting, are simply not relevant. See e.g. Surgeon General of the United States*, The Health Consequences of Smoking*, noting that the Bradford Hill criteria*, including* the biologic plausibility/mechanistic criteria, can only be applied *after* a statistical association has been demonstrated. See also Goodman and Samet, Chapter 1:

"Cause and Cancer Epidemiology," in *Cancer: Epidemiology and Prevention*, edited by Schottenfeld and Fraumeni, 3rd Edition (2006).

At the end of the day, chromosomal aberrations do not provide the "end game" on the causal inquiry. They do not trump epidemiology. Epidemiology remains the pre-requisite foundational point for the causal inquiry. The two islands, one noting exposure and chromosomal aberrations, the other noting certain cancers with certain chromosomal aberrations, remain unconnected.

Lone Pine Procedure Successful in Hydraulic Fracking Case

by Daniel J. Dunn, Andrew C. Lillie, and Anna K. Edgar

Introduction

In a recent toxic tort case involving the natural gas extraction process known as hydraulic fracturing, the defense pursued an unconventional case management strategy that resulted in complete dismissal of the plaintiffs' case. This article summarizes the case and lessons learned for toxic tort defendants.

Toxic tort cases are fundamentally dependent on expert testimony, particularly in the areas of exposure, dose and medical causation. Plaintiffs often file these cases, however, without securing experts in advance to ensure their claims meet minimum legal and scientific standards. Nonetheless, liberal pleading requirements and rules governing motions to dismiss and for summary judgment can prevent deserving defendants from achieving early dismissal. Moreover, toxic tort cases are often exceedingly expensive due to the need for multiple experts, the expansive time periods over which relevant events occurred, and voluminous evidentiary data and documents. Defendants often settle even weak claims simply to avoid the high cost and distraction of prolonged litigation.

The Lone Pine Procedure

Under the traditional approach to case management, plaintiffs do not disclose their expert case until late in the process after the close of fact discovery, which can take years and cost enormous sums of money. Late expert disclosure may make sense in ordinary civil cases. But in complex toxic tort cases, where expert opinion is the foundation of the case, reversing the traditional order should be considered.

Many courts have done just that by requiring plaintiffs to make a prima facie showing of exposure and causation through qualified expert opinion at the outset of the case, before full discovery and other pre-trial activities may proceed. Such orders follow *Lore v. Lone Pine Corp.*, 1986 WL 637507 (N.J. Sup. Ct. Nov. 18, 1986). They have been used in myriad toxic tort cases, from mass torts to claims of a few plaintiffs, "to identify and cull potentially meritless claims and streamline litigation in complex cases." *Baker v. Chevron USA, Inc.*, No. 1:05-CV-227, 2007 WL 315346, at *1 (S.D. Ohio Jan. 30, 2007). *See, e.g.*, *Abuan v. Gen. Elec. Co.,* 3 F.3d 329, 334 (9th Cir. 1993); *McManaway v. KBR, Inc.*, 265 F.R.D. 384, 385 (S.D. Ind. 2009); *Acuna v. Brown & Root, Inc.*, No. SA-96-CA-543-06, 1998 WL 35283824, at *5–6 (W.D. Tex. Sept. 30, 1998), *aff'd*, 200 F.3d 335 (5th Cir. 2000); *Schelske v. Creative Nail Design, Inc*., 933 P.2d 799, 802 (Mont. 1997); *Wilcox v. Homestake Mining Co.,* No. CIV 04-534, 2008 WL 4697013 (D.N.M. Oct. 23, 2008), *aff'd,* 619 F.3d 1165 (10th Cir. 2010).

Typically, *Lone Pine* orders require plaintiffs to provide an expert affidavit by a specific date that states (1) the identity and amount of each chemical to which each plaintiff was exposed; (2) the precise disease or illness from which each plaintiff suffers; and (3) evidence supporting allegations that exposure to the defendant's chemicals caused the alleged