Thank you Ron for an introduction that only my mother would believe. So, I want to cover a century of tort litigation and the education of the judiciary in the biomedical sciences and do that all in my allotted twelve minutes.

I’d like to start with a case that those who teach torts know pretty well, *Stubs v. City of Rochester.*¹ That case is a forerunner to what most of us call toxic torts. To quickly recall the facts, Mr. Stubbs contracted typhoid fever allegedly due to the intermingling of two water systems—one for drinking; one for wastewater. Mr. Stubbs’ difficulty was that there were multiple competing causes that may have been responsible for his disease and he had the burden of proof to show that it was the intermingled water rather than those other causes.² There was unquestionably negligence by the city of Rochester, and Mr. Stubbs developed typhoid. He sued the city, but confronted a difficult causation question. And the problem is that there are many competing causes of typhoid.³

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¹ Williams Professor of Law, Wake Forest University School of Law.
² 124 N.E. 137 (N.Y. 1919).
³ So, the basic factual causal model I want to invoke is exemplified in Slide 1. See infra Slide 1. As revealed in this slide, there are numerous but-for causes of any outcome; here, Stubbs’s typhoid. The causal question is whether the intermingled water is one of those necessary factors for that outcome. As this slide reveals, there are always multiple causes for any outcome, although tort law focuses only on the tortious ones.
⁴ Multiple competing causes is a concept different from multiple necessary causes and is depicted in Slide 2. See infra Slide 2. Multiple competing causes are the bane of determining factual causation in toxic torts because the vast majority (though not all) of the diseases involved in toxic torts can be caused by different factors, e.g., smoking, asbestos exposure, and unknown factors that also cause lung cancer.
What Stubbs was facing was about eight different competing (potential) causes, and what he had to show was that the intermingling of the two water systems was the cause of his typhoid rather than any of those other lurking causes. Interestingly, the drinking water came from what was called the “Hemlock System.” Somebody in Rochester invoked more than a bit of irony in naming it the Hemlock System, while the Holly system was the one for sewage. So, Stubbs’s problem was to demonstrate that the cause of his typhoid was from the intermingled water as opposed to other potential causes.

And that exemplifies the difficult issues that exist in toxic torts today. It is demonstrating that the defendant’s agent was a cause of the plaintiff’s harm, not any of the other competing causes for plaintiff’s disease. Interestingly, Mr. Stubbs used some very primitive statistics to show that it was the intermingled water that was responsible for his disease as opposed to those other causes. We could critique them and they’re quite critique-able, but time is short and I will save the critique for when I have the luxury of an hour of class with which to pursue this matter. Nor, I would suggest, would an expert proffering them today in response to a Daubert motion have a chance of succeeding. Yet, the New York Court of Appeals pulled them from the record and put them in its opinion in support of its decision that Stubbs had met his burden of production on causation and was entitled to a trial.

Nevertheless, Stubbs was the beginning of the use of statistics to prove that the cause of disease is an environmental agent for which the defendant is responsible. To assess the state of judicial engagement with the biosciences, there are two conditions that must be met:

1. We need bioscience; and
2. We need toxic injury and for those injuries to get into court.

On the first score, although the enlightenment began the search for physical laws to explain natural phenomena and there were some crude efforts to employ statistical evidence to identify the source of epidemics, most famously in John Snow’s nineteenth century study of cholera in London.

4. Stubbs, 124 N.E. at 140.
5. There are a few pathognomonic or “signature” diseases for which there are no competing causes to an environmental agent and, thus the existence of the disease points to the environmental agent as causal. Vaginal adenocarcinoma in young women is one such signature disease for in utero DES exposure. Asbestosis in another.
6. For those who are curious, I have provided the data presented by Stubbs in Slide 3. See infra Slide 3. For those who want to know the critique of these statistics and why they are far less persuasive, in light of modern scientific methodology, come to class when I teach Stubbs.
7. Stubbs, 124 N.E. at 140.
that led him to the conclusion there was a “cholera poison” in polluted water, it wasn’t until after World War II that epidemiology came into its own with a “systematized body of . . . principles by which to design . . . studies” to determine the cause of a disease.

On the second score, we find no cases using the biosciences in tort litigation nor any major congregations of toxic torts where such evidence would be useful until the 1960s, and, even then, the toxic soup is quite thin. Sam Estep, a professor of law at the University of Michigan, was the first academic to engage with the problem of toxic causation in a 1960 article that addressed radiation injury. Estep was remarkably advanced in his analysis, appreciating the difficulties of competing causes, latency periods, the need for statistical evidence, agents that accelerate the occurrence of disease, and the difficulties of using statistical evidence for particular cases. Want to know how many courts cited his work in the few years after it was published? How about in the sixty years since it was published? The answer is the same: Zero. The answer to the first question may have been influenced by the fact that the early 1960s was before courts were confronted with bioscience to prove causation and that by the time tort litigation required such, the article was long forgotten.

Understanding this period before the late 1970s and 1980s when the Agent Orange and Bendectin litigations burst onto the scene requires confronting a perdurable myth about scientific evidence entering the courtroom: Before the pathbreaking Supreme Court decision in Daubert v. Merrell Dow Pharmaceuticals, Inc., in 1993, Frye was the sheriff determining which experts could bring scientific precepts into the courtroom. Maybe on the criminal side, but in civil cases, invocation of Frye was

11. In re “Agent Orange” Prod. Liab. Litig., 611 F. Supp. 1223 (E.D.N.Y. 1985), aff’d, 818 F.2d 187 (2d Cir. 1987). The Agent Orange litigation was brought by military members who served in Vietnam who claimed that their exposure to a by-product of the defoliant known as Agent Orange was responsible for a wide variety of ailments from which they suffered. See generally PETER H. SCHUCK, AGENT ORANGE ON TRIAL: MASS TOXIC DISASTERS IN THE COURTS (1st ed. 1988).
12. Bendectin was a drug sold for morning sickness of pregnancy that was associated with birth defects and resulted in a mass toxic tort roughly contemporaneously with the Agent Orange litigation. See generally MICHAEL D. GREEN, BENDECTIN AND BIRTH DEFECTS: THE CHALLENGES OF MASS TOXIC SUBSTANCES LITIGATION (1996); JOSEPH SANDERS, BENDECTIN ON TRIAL: A STUDY OF MASS TORT LITIGATION (1998).
virtually non-existent until the late 1970s and 1980s when the Agent Orange and Bendectin litigation surfaced, with the latter providing the fodder that led to the Supreme Court’s decision in Daubert. The period before those cases emerged is characterized by courts deferring to the substance of an expert’s opinion, so long as the expert had appropriate credentials in the field in which she was opining.15

Typical is a case in the first round of tobacco litigation, in which the Third Circuit Court of Appeals responded to the defendant’s claim that lack of proof of causation justified granting its motion for judgment as a matter of law: Plaintiff’s expert stated that causation existed in his opinion and that is not only sufficient, it also requires no further examination,16 the court summarily responded.

MER/29 was one of the first mass toxic torts—the drug was the initial anti-cholesterol drug brought to market in the early 1960s, but it also brought cataracts and other adverse events to those who used it. Over 1,500 plaintiffs sued the manufacturer, and its wrongdoing in testing the drug brought punitive damages and convictions of a number of company officials.17 But what MER/29 did not bring was any judicial consideration of the sciences that would address causation. Typical was the attitude of Judge Friendly in a leading MER/29 case. On appeal, defendant challenged the sufficiency of the plaintiff’s evidence of causation. Judge Friendly responded that the only witness, a doctor, who testified for the plaintiff on causation “was of the opinion with a reasonable amount of medical certainty that these were caused by the taking of MER/29; he relied on ‘medical literature’ and ‘conversations’ that many persons who developed skin and hair changes like [the plaintiff’s] after taking MER/29 also developed cataracts.” That, declared, Judge Friendly, was sufficient for leaving the matter of causation to the jury.18

A vaccine case in the same time frame is similar: Plaintiff received the Salk polio vaccine and later developed polio. One of the investigators involved in the largest ever epidemiology study,19 which assessed the effectiveness of Salk polio vaccine, testified in what was one of the earliest cases in which epidemiologic evidence was employed. He explained that a

small number of vaccines might develop polio, which plaintiff had, but that “it was impossible to prove that any individual case was caused by vaccine.” Nevertheless, the court concluded, this evidence “does not preclude a finding by the jury that the polio contracted by plaintiffs was vaccine induced” so long as none of the other evidence rules out causation, such as the disease occurring outside the latency window of four to thirty days post-vaccination, the period when the vaccine could cause disease. So much for evidence that connects the study results to the individual plaintiff’s disease, which later came to be termed “specific causation.”

Let’s fast forward to the Agent Orange and Bendectin litigations. In Agent Orange, Judge Weinstein, with the assistance of his Special Master, Ken Feinberg, managed to craft a $180 million settlement, which was not a lot of money given the number of veterans and the seriousness of their conditions. Not unexpectedly, there were opt-outs from the class, and Judge Weinstein was faced with 281 claims by veterans who opted out of the class. His opinion dismissing those claims on causation—a foregone conclusion, as if they were able to pursue individual claims, Judge Weinstein’s class action pennies-on-the-dollar settlement would lose credibility with all of the ailing veterans who remained in the class—developed two critical points. One was the identification of epidemiology and its statistical basis as critical for causation in toxic cases, contrary to most prior courts’ reluctance to accept statistical evidence to prove the particular, and Judge Weinstein’s careful parsing of the studies submitted by the parties. The second was the introduction of Frye to civil cases. Judge Weinstein employed it to rule the two plaintiffs experts’ favorable opinion testimony was inadmissible after expressing skepticism about expert testimony, which required “robust screening” of experts, as “insufficiently grounded in any reliable evidence.” Note the two-pronged approach of Judge Weinstein: one was to examine the scientific evidence proffered by the plaintiffs in support of causation, and the second was critically to examine the opinions of the plaintiffs’ expert witnesses and rule them inadmissible.

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20. Id. at 375.
21. Id. at 375-76.
25. Id. at 1242.
26. Id. at 1250, 1260.
27. Id. at 1243-45. While these two approaches are not as discrete as I present them, these categorizations are useful for understanding the future course of judicial confrontation with science and where we have landed today.
The Bendectin litigation generally followed one or the other of the two strands set out by Judge Weinstein. Thus, for example, Judge Thomas Penfield Jackson who sat on the federal district court in the District of Columbia, examined the scientific evidence bearing on whether Bendectin caused limb reduction birth defects. Ruling on a motion for judgment as a matter of law, he addressed whether the scientific evidence was sufficient to permit the jury reasonably to draw an inference of causation\textsuperscript{28} and concluded it was not and thus, granted the defendant’s motion\textsuperscript{29}

The sufficiency-of-the-evidence strand played out in another Bendectin case, \textit{Brock v. Merrell Dow Pharmaceuticals, Inc.}\textsuperscript{30} This case is not a showcase for judicial competence in the field of bioscience. Indeed, it starkly revealed the necessity of better judicial education and understanding of the sciences that were increasingly employed in toxic tort cases. In \textit{Brock}, the court did three things: 1) it acknowledged the days of no review of the substance of an expert’s opinion, but announced that a new day had arrived;\textsuperscript{31} 2) it identified the three potential sources of error in an observational epidemiologic study;\textsuperscript{32} and 3) it announced the magic potion of confidence intervals, which could account for all of these sources of error.\textsuperscript{33} This explanation of confidence intervals was a stunning error—there is simply no way to wiggle around the fact that confidence intervals, which reflect the results of significance testing, are only about random error and say nothing whatsoever about the effects of biases and confounders in producing erroneous study outcomes. The irony could not be thicker—more so than naming the drinking water system Hemlock in \textit{Stubbs}, given the \textit{Brock} court’s introductory expression of the goal it hoped to accomplish:

\begin{quote}
Ultimately, the “correctness” of our decision that there was insufficient evidence presented by plaintiff on the issue of whether Bendectin caused Rachel Brock’s limb reduction defect to enable a jury to draw a reasonable inference may be just a matter of opinion, but hopefully the reasoning below will persuade others of the insights of our perspective.\textsuperscript{34}
\end{quote}


\textsuperscript{29} \textit{Id.} at 803-04.

\textsuperscript{30} Brock v. Merrell Dow Pharm., Inc., 874 F.2d 307 (5th Cir.), \textit{modified on reh’g}, 884 F.2d 166 (5th Cir. 1989).

\textsuperscript{31} \textit{Id.} at 309-11.

\textsuperscript{32} \textit{Id.} at 311-12. These three sources of error are random error, bias, and confounding.

\textsuperscript{33} \textit{Id.} at 312 (“Again, it is important to remember that the confidence interval attempts to express mathematically the magnitude of possible error, due to the above mentioned sources as well as others, and therefore a study with a relative risk of greater than 1.0 must always be considered in light of its confidence interval before one can draw conclusions from it.”).

\textsuperscript{34} \textit{Id.} at 309.
In a number of other Bendectin cases, courts took a different road. These courts focused on the plaintiffs' expert witnesses' opinions on causation and employed Frye. What Judge Weinstein had done in Agent Orange in this regard, many courts in the Bendectin litigation followed.35

By the late 1980s, most courts had become skeptical about Bendectin suits, as epidemiology study after study that emerged after the litigation began36 found little or no association between the use of Bendectin and an elevated risk of birth defects. Yet plaintiffs' lawyers had invested heavily in the litigation and found a bevy of experts who reanalyzed those studies, proffered in vitro and in vivo animal studies, as well as chemical structural similarities to other known teratogens in support of their testimony about causation. One of those late Bendectin cases was brought in Los Angeles and involved two children, Eric Schuller and Jason Daubert, both born with limb reduction birth defects.

The trial judge in Daubert dismissed the case, concluding that the plaintiffs could not meet their burden of production on causation.37 Had that been the rationale for affirming, Daubert would never have made it to the Supreme Court.38 But, the court of appeals took the road not taken by the district court and, employing Frye, concluded that the plaintiffs' experts had not complied with generally accepted scientific methodology.39 By relying on Frye to affirm, the Ninth Circuit enabled the case to reach the Supreme Court on an issue that had played virtually no role in previous toxic tort causation disputes. The Supreme Court agreed to review the issue of whether Frye survived the adoption of the Federal Rules of Evidence. We all know what the Court said there. The road going forward would be expert witness reasoning and methodology, not sufficiency of the evidence, and Justice Blackmun provided four factors to assist courts in examining experts' methodology and reliability.40

One year after Daubert, the Federal Judicial Center published its Reference Manual on Scientific Evidence, a single volume designed to

36. The state of reproductive toxicity testing of Bendectin from the period when it was first formulated as a combination of three existing drugs in the 1950s through to when suits began to be brought in the 1970s was woefully inadequate, especially given the lessons of thalidomide in the early 1960s, which convincingly and tragically revealed that drugs could cross the placental barrier.
38. When the case did reach the Supreme Court, the Court showed no interest in the causation dispute or the scientific evidence that bore on that question.
40. See Daubert, 509 U.S. at 593-95.
educate generalist judges in the sciences with which they were confronted (and maybe prevent embarrassing revelations of the lack of judicial scientific savvy as Brock had demonstrated). Now in its third edition, with the National Academies of Science as an institutional co-sponsor, the Manual has chapters on many of the sciences that experts bring into court, including most notably, for our purposes, epidemiology, toxicology, and exposure science. It has been provided to more than 3,000 federal judges and even more state court judges and others and has been cited in over 1,700 opinions. It can be downloaded for free from the NAS website, and I can’t imagine a lawyer practicing in this area who doesn’t have a copy on her desk.

The Reference Manual deserves a great deal of credit for the improved science IQ of the judiciary—nothing resembling Brock has surfaced since it was published in 1994. Today courts reflect a much more sophisticated understanding of epidemiology and toxicology than was found previously, revealed in opinions expressing these and other propositions:

1. An association, by itself, is not equivalent to causation;41
2. The use of Sir Austin Bradford Hill’s factors for assessing whether a study’s association is causal or spurious and that the factors are not requirements that must be met for an inference of causation;42
3. The relationship between statistical significance and a confidence interval;43
4. The proper and improper use of epidemiology for addressing specific causation;44

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41. FEDERAL JUDICIAL CENTER, REFERENCE MANUAL ON SCIENTIFIC EVIDENCE (1st ed. 1994).
42. See generally FEDERAL JUDICIAL CENTER & NATIONAL ACADEMIES OF SCIENCE, REFERENCE MANUAL ON SCIENTIFIC EVIDENCE (3d ed. 2011).
43. A Westlaw search (((Reference w/1 Manual) w/2 scientific) or Reference w/1 Guide) on November 4, 2020 found 1,777 cases and 10,000 secondary sources that cited the Manual.
5. The scientific principle of a weight-of-the-evidence approach to inferring causation.\(^48\)

6. The role of dose in determining causation and appreciation that dose-response is not necessarily linear;\(^49\)

7. The proper and improper uses of a differential etiology for determining specific causation and the critical role of unknown causes;\(^50\)

8. Recognition of the relative probity of an ecological study as compared to other types of studies;\(^51\)

9. The healthy worker bias inherent in occupational studies;\(^52\)

10. The role of power in determining whether a study’s failure to find a statistically significant association is negative evidence or evidence of nothing;\(^53\); and

Many more that, if time permitted, I could catalog.

The fact is that the judiciary has come a long way in its understanding of epidemiology and toxicology and a great deal of that understanding should be credited to Joe Cecil, the Director of Research at the Federal Judicial Center for many years, who, with others, had the inspired insight to appreciate how badly needed the Reference Manual was.

One final note: Why, you may be wondering, are courts delving into the depths of scientific evidence when \textit{Daubert} took the expert admissibility approach rather than the sufficiency of the scientific evidence fork? Good question, and one I will briefly reply to by saying, bless his soul, but Justice Blackmun in \textit{Daubert} adopted factors that just don’t fit experts who come to court with scientific evidence to support their opinions and so the reality is, courts pay lip service to the factors but, in fact, employ a sufficiency of the scientific evidence approach.\(^54\) More details on this will have to await another day or the sources cited in the previous footnote.


Thank you.

Slide 1

A MODEL FOR CAUSATION

Stubbs' Typhoid

Holly/Hemlock
Intermingling
(A's Negligence)

Slide 2

STUBBS' STATISTICS

1) 223 Typhoid cases in 1910; excess of 58 over prior years
2) 180 of those cases occurred in the 3 months (Aug., Sept & Oct.) following intermingling
3) 59 others drank intermingled water and contracted typhoid
4) One-third of typhoid cases were in Stubbs' water district
**SLIDE 3**

![Diagram: Multiple Competing Causes]

**SLIDE 4**

**The Development of Epidemiology (Statistical Investigation of the Cause of Disease)**

- Forerunners in 19th century: most famously John Snow’s study of Cholera in London
- Development of principles guiding study design and interpretation of data not until post-World War II.
- “Framingham Study” of heart disease begun in 1949
- Salk polio vaccine largest study ever involving over one million school children
- Salk study makes an appearance in an early case that employed epidemiology.
The Laissez Faire Approach to Expert Testimony

- Cigarettes: [P]laintiff’s expert stated that causation existed in his opinion, and that is not only sufficient, it also requires no further examination.

- MER/29: P’s expert, a doctor, testified: “with a reasonable amount of medical certainty that [P’s] cataracts and other adverse events were caused by the taking of MER/29; he relied on ‘medical literature’ and conversations’ that many persons who developed skin and hair changes like Roginsky’s after taking MER/29 also developed cataracts.” That, declared, Judge Friendly was sufficient for leaving the issue to the jury.

- Salk Vaccine: “it was impossible to prove that any individual case was caused by vaccine” Nevertheless, this evidence “does not preclude a finding by the jury that the polio contracted by plaintiffs was vaccine induced.”