

## DIFFERENTIAL DIAGNOSIS VERSUS CAUSATION ASSESSMENT: WHY THEY ARE SEPARATE METHODOLOGIES AND HOW THEY RELATE TO DAUBERT

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In *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S.579; 113 S. Ct. 2786; 125L Ed 2d 469 1993) the U.S. Supreme Court enumerated the factors required to reach a well-founded causal conclusion. In that case, the concept of differential diagnosis was neither part of the decision, nor was it relevant. Rather, Daubert involved causation assessment: the methodology by which an external cause is linked to an internal disorder or disease process.

The distinction between "differential diagnosis" and "causation assessment" is critical, yet commonly misunderstood by the Courts. Differential diagnosis, the "methodology" of physicians, has been improperly broadened to include both: uncovering a diagnosis or clinical disorder and identifying the cause of that disorder. This assessment of the cause of a disorder is pertinent to liability determinations, but it differs substantially from differential diagnosis. Physicians have, in some cases, abetted the Courts' confusion by asserting that they performed a differential diagnosis, in the standard fashion, to determine causation. They may say: "After performing a standard differential diagnosis, I determined that mold caused the asthma," or, "In the course of standard differential diagnosis, I ruled out everything but the benzene in the well water as a cause of his leukemia." In actuality, in the first instance, the differential diagnostic process resulted only in a diagnosis of asthma. In the second instance, it led to a diagnosis of leukemia. In neither example does the exercise of differential diagnosis establish a cause of those disorders diagnosed by the physician.

This commingling of diagnosis and cause has been adjudicated by various trial and appellate Courts with mixed results, often leading to strange, medically-inaccurate decisions. A number of Courts have, erroneously, accepted the proposition that differential diagnosis leads to a causal assessment and that because differential diagnostic methodology is standard in clinical medicine so, too, is the resulting causation assessment. While the former is true, the latter is not.

The distinction between "differential diagnosis" and "causation assessment" is critical for the Courts to understand. If understood and implemented, it should define how conclusions are properly reached, the necessary factual bases for those conclusions, the recognized and appropriate methodologies for arriving at those conclusions and even, at times, who is qualified to testify.

"Differential diagnosis" and "causation assessment," both seek to uncover causes, but of very different things. An error, common to many decisions, is the Court's failure to ask, "Cause of what?" Differential diagnosis is the methodology which attempts to identify the internal disease or process which produces or causes the patient's symptoms or findings. Only rarely does it deal with the external cause of that disorder. That determination requires a separate causation assessment, an activity which utilizes an entirely different set of information.

The cases to be discussed illustrate how the Courts have confused diagnosis and differential diagnosis with cause and causation assessment and why better reasoned, more consistent decisions will emerge when these distinct endeavors are better understood. In *Daubert v. Dow Merrill*, differential diagnosis was not at issue. That case involved a congenital (birth) defect and its alleged causal connection to a drug, Bendectine, used to control morning sickness. The diagnosis was clear: the birth defect was unequivocal and unchallenged. Because the diagnosis was straightforward, a differential diagnosis was neither necessary, nor a part of the case. A birth defect was the diagnosed cause of the patient's deformity. At issue, however, was the cause of that defect and the methodology employed by experts to reach their conclusion that Bendectine was the responsible agent, that is the cause of the birth defect, or the reason that it occurred. How the experts decided that Bendectine caused the defect was the fatal methodological flaw of the case and the essence of the Daubert decision which focused attention on the causation methodology utilized.

The Federal Judicial Center's *Reference Manual on Scientific Evidence* (1994) defined the term "differential diagnosis" properly as:

The method by which a physician determines what disease process has caused a patient's symptoms. The physician considers all relevant potential causes of the symptoms and then eliminates alternative causes based on a physical examination, clinical tests and a thorough case history. (p. 214)

The critical component of this definition is that differential diagnosis is a quest for a diagnosis: what the patient has wrong internally. It is not, inherently, a search for the ultimate cause (critical to liability) of that disease process or disorder. In numerous decisions, however, the Courts use *cause of symptoms* and *ultimate cause of the disease process* interchangeably. By doing so, "differential diagnosis" becomes defined, incorrectly, as the methodology by which both a diagnosis and the cause of that diagnosis are assessed.

*Troy Mattis, et al., vs. Carlton Electrical Products, et al.*, N. 98-4091, D.S.D.)

In this matter, the diagnosis of RADS (Reactive Airways Dysfunction Syndrome), the claimant's expert incorporated the cause of the RADS within the diagnosis of the RADS, asserting not only that the patient had RADS, but providing a causal attribution. "RADS due to toluene exposure," was the offered diagnosis. The Court agreed, incorrectly, that the determination of cause was part of that "differential diagnostic" activity. The appellate Court concurred. *Troy Mattis, et al., vs. Carlton Electrical Products, et al.*, N. 98-4091, D.S.D.)

The opinions of Dr. Hansen and Mr. Wabeke, and indeed the theory of RADS itself, are based upon a technique called differential diagnosis. "Differential diagnosis, or differential etiology, is a standard scientific technique of identifying the cause of a medical problem by eliminating the likely causes until the most probable one is isolated." (See *James C. Westberry vs. Gislaved Gummi A.B.*, 178F. 3d 257, 4<sup>th</sup> Cir. 1999.)

Comment: "Differential diagnosis" is not equivalent to "differential etiology." "Etiology" speaks more to the ultimate cause, that is, the cause of the disease process. Diagnosis speaks to the disease process: what is wrong with the patient. Thus, in this case, the differential

diagnosis would establish the existence of RADS (Reactive Airways Dysfunction Syndrome). This diagnosis is the disorder which patient has (not what caused it) and is the end of the differential diagnostic analysis.

Etiology or cause of the RADS is the next question. This involves a new process necessitating answers to other types of questions: whether the agent at issue is capable of producing RADS, i.e., whether it has irritant properties; approximately what level of exposure occurred (dose); what was the timing between symptom onset and exposure (clinical course); were there alternate potential causes of the RADS which have been considered and ruled out? The evaluation of these critical elements is not part of diagnosis, but is central to causation analysis methodology.

*Tina M. Glastetter, et al. v. Novartis Pharmaceuticals, et al, No. 00-3087, 00-3467, 8th Cir.; See July, 2000 p 12.)*

In *Glastetter v. Novartis Pharmaceuticals*, the trial Court dismissed the claimant's expert testimony that the drug Parlodel caused the claimant's intracranial hemorrhage (ICH). Affirming that decision, the appellate Court discussed properly certain elements of causation assessment, but they incorporated, improperly, cause in the concept of a differential diagnosis. They said:

Each of Glastetter's experts conducted a "differential diagnosis," which concluded that Parlodel caused her ICH. In performing a differential diagnosis, a physician begins by "ruling in" all scientifically plausible causes of the plaintiff's injury. The physician then "rules out" the least plausible causes of injury until the most likely cause remains. *The final result of a differential diagnosis is the expert's conclusion that a defendant's product caused (or did not cause) the plaintiff's injury.* (Sic, emphasis added.)

Comment: While the subsequent discussion delineated the elements of causation assessment, it is clear from that discussion and from the above statement that the Court failed to understand the definitional distinction between differential diagnosis and causation assessment. The suggestion that differential diagnosis has anything to do with a product is illustrative. Diagnoses do not involve products; they involve disorders or diseases. Here the differential diagnoses and the ultimate diagnosis which arose from that differential diagnostic process were clear: intracranial hemorrhage. That diagnosis was the end of the differential diagnostic exercise. The next question "What caused the ICH?" begins the new analytical exercise: the causation analysis.

This Fourth Circuit case, is frequently cited to support the use of differential diagnosis as the methodologically-proper way of assessing causation. In the underlying case, the claim was that the inhalation of talc from workplace exposure caused a sinus disorder in the claimant. A verdict was delivered for the claimant. The appeal argued, among other things, that the claimant's physician's methodology in arriving at a causal conclusion was defective. The appeals Court disagreed with this argument saying:

GGAB contends that Dr. Isenhower's testimony was inadmissible because it was not based on reliable scientific methodology. This is

so, it argues, because Dr. Isenhower had no epidemiological studies, no peer-reviewed published studies, no animal studies and laboratory data to support a conclusion that the inhalation of talc caused Westberry's sinus disease. Further, GGAB continues, Dr. Isenhower did not have any tissue samples indicating that talc was found in Westberry's sinuses, nor did he have studies showing that talc, at any threshold level, causes sinus disease. Instead, Dr. Isenhower merely relied on differential diagnosis - supported in part by the temporal relationship between Westberry's exposure to talc and the problems he experienced with his sinuses.....GGAB maintains that neither a differential diagnosis nor a temporal relationship between exposure and onset or worsening of symptoms is sufficient to establish the reliability of Dr. Isenhower's opinion. We disagree.

Comment: Here the Court noted some of the necessary elements of causation when it repeated the defense's arguments. While rejecting those, it accepted the identification of a temporal relationship as a component of "differential diagnosis." It rarely is (except in acute poisoning matters). Rather, temporal relationships are a regular component of "causation assessment." Finally, the Court ruled that differential diagnosis is the proper methodology for assessing causation. In fact, assessing causation requires knowledge of those elements enumerated in the defense's arguments and, sometimes, others as well.

Rodney Cutlip v Norfolk Southern, et al. , No. 02-1051, Ohio App. , 6th Dist. 2003 Ohio App LEXIS 1785)

In *Rodney Cutlip v Norfolk Southern, et al.*, No. 02-1051, Ohio App., 6th Dist. 2003 Ohio App LEXIS 1785, the claimant's medical experts testified that the claimant's respiratory disorders arose from exposure to diesel fumes in his worksite. In doing so, they used "differential diagnosis" as their methodological argument which was accepted by the trial Court. In its Appellate decision, the Court agreed, stating the following:

In this case both physicians testified that they personally examined appellee, they reviewed his medical records, they took a history, they ordered tests and they reviewed the results of those tests. They both also considered other possible causes (such as the chest wound and smoking) and ruled those out as possible causes of appellee's asthma. Based on the law discussed above, we conclude that Drs. Khan and Kelly arrived at their conclusions following a thorough differential diagnosis, and their testimony is therefore reliable under Daubert and Evid R. 702.

Comment: The first sentence of the above statement correct delineates the process of differential diagnosis. The second sentence, including ruling out other causes of the disease, is not. Once again, the Court intermingled "differential diagnosis" with "causation assessment."

*Gary Hardyman v Norfolk & Western Railway, et al.*, No. 99-4218, 6th Cir.

The Hardyman case involved a claimant with carpal tunnel syndrome (CTS), the alleged

cause of which was a specific set of occupational activities. In a Sixth Circuit decision overturning the trial Court's exclusion of the claimant's expert, there was extensive discussion of both differential diagnosis and of cause. At the trial level, the claimant's expert himself, clearly separated the elements of each, but the Appellate Court merged them. Dr. Linz, the claimant's medical expert said:

Once we go beyond the issue of general causation and get away from evaluating and criticizing the literature whose only purpose really is to establish how well-established this work is (sic) causation in general, then we get to specific causation. And the approach to specific causation is really quite difficult. We are looking at: 1) whether or not the person had carpal tunnel syndrome. It is absolutely clear in this case that he did; and 2) does he have documented medical conditions which might be significant contributors to his condition. That was evaluated by me and I felt that he did not. The third is whether his work activities are significantly more hand intensive than his nonwork activities, and in addition are his work activities significantly more hand intensive than other jobs (sic).....

The Appellate Court misconstrued this correct analytical approach as a "differential diagnosis" when it commented upon that testimony:

Although the district Court acknowledged that differential diagnosis is an acceptable method of determining causation, it not only failed to recognize that Dr. Linz applied a method of differential diagnosis in reaching his conclusion, it seemed actually to reject this method saying....

The statement by Dr. Linz noted above and cited by the appeals Court actually incorporated both methodologies: differential diagnosis and causation assessment. The end of the differential diagnostic exercise was the diagnosis (carpal tunnel syndrome). Whether or not that diagnosis was accurate could be a matter of dispute between medical experts, but the method of arriving at that diagnosis, history, physical examination, laboratory testing, is not. In contrast to the misunderstanding of the Appellate Court, however, the diagnosis - and only the diagnosis - was the outcome of the differential diagnosis. All of the other components (which the claimant's expert acknowledged as difficult) were elements of causation analysis. This included the general causation question: Can such activities cause this disorder, CTS? The causation analysis also included the specific causation questions: have other causes been considered and ruled out? Was the work activity sufficient? Was it more significantly intensive than non work-related activities?

*Paul and Linda Lawrence v Synthes, et al.*, No. 1623 EDA 2003, Pa. Super

A recent case involving orthopedic spinal screws, was dismissed by the trial Court for a number reasons. Among them was the lack of reliability of plaintiff expert physician's testimony.

That *motion in limine* and summary judgment were reviewed in this Appellate decision and upheld. This Appellate Court noted, in citing Gots et al. (2004): (Gots, R. E., Clark G. L., Franklin, D. E. "Differential diagnosis vs. causal assessment: relevance to Daubert." *Metropolitan Corporate Council*. (2003) October 11:10.29.

[Http://www.ictrm.com/pdf/Vol2no6.pdf](http://www.ictrm.com/pdf/Vol2no6.pdf)

Differential diagnosis is the determination of which of two or more diseases with similar symptoms is the one from which the patient is suffering, by a systematic comparison and a contrasting of the clinical findings...

In other words, differential diagnosis is used to determine what the condition is and how to treat it. Causal assessment, on the other hand, is the methodology used to determine how the condition arose and to determine responsibility or liability. .... The differential diagnosis methodology does not lead to a causal determination.

Comment: In this decision, the Court accurately distinguished the separate activities of differential diagnosis and causal assessment.

The differential diagnostic process, then, is methodologically-designed to uncover a physical disorder or a disease state. It asks, for example, "Why is this person having a headache" Is it a brain tumor, a sinus infection, poor reading glasses, neck strain, or a migraine?" The methodology employed to answer this differential diagnostic question is the standard methodology of medicine: history taking, physical examination and diagnostic studies. Assume it is learned (through CT or MRI scanning) that the patient has a brain tumor. The diagnosis determined by the physician, brain tumor, explains the headaches (likely caused by the tumor), but the cause of the brain tumor has not been elucidated. Assume further that occupational exposures to chemicals at a petrochemical facility are the alleged cause of the tumor. This causal attribution: the central medical/scientific exercise, as well as the proper subject of Daubert challenges in toxic tort claims, requires causation assessment (not differential diagnostic) methodology. Both general causation and specific causation elements need to be satisfied before such an attribution can be established.

Thus, the differential diagnosis came first, the diagnosis was made; now, the ultimate claimed cause of the disease requires a separate step. It is that causal assessment step which is not the standard methodology of clinical medical practice. In actuality, it is generally foreign to medical evaluation and to a physician's expertise. It is a methodology more common to public health, epidemiology, toxicology and other sciences. Because of those differences and because physicians are not, in general, expert in causation assessment, the validity and reliability of that causation testimony is not established by an expert's statement, "Differential diagnosis is what I did and it is the standard methodology of medicine."

Why is this important? It is important, frankly, because failing to probe causation methodology undermines the intended purpose of Daubert's emphasis on accepted and proper methodology. Confusing the methodology of clinical practice with the methodology of

causal assessment permits physicians to opine about causal conclusions absent a proper analysis. The clinician can ignore temporal relationships, dose, duration of exposure, alternate causes, latency periods and even general causation (*Is the agent at issue known to cause this disease?*) and other factors, simply averring to causation, while ignoring contradictory facts.

Differential diagnosis is, in fact, the standard methodology of clinical practice. In general, however, it rarely uncovers the ultimate cause of the disorder; in a few instances it may. For infectious diseases, such as influenza or tuberculosis, the diagnosis of the disease, implies a cause as well: *Tuberculosis bacillus*, or the influenza virus. Similarly, certain acute poisonings bring diagnosis and cause together. If a child has all of the typical manifestations of aspirin toxicity, was found with an empty bottle of aspirin and has high blood salicylate levels, the diagnosis incorporates the cause: aspirin toxicity. The same is true for other acute poisonings such as a rattlesnake bite.

In most instances in clinical medicine, however, that is not the case. The diagnosis of a brain cancer, an autoimmune disease such as lupus, a neurological disorder such as MS, is the end of the differential diagnostic process, leads to no causal attribution. Moreover, assessment of causal attributions is unrelated to most clinical practice. Oncologists diagnose and treat cancers: they do not commonly sleuth out the potential causes. The same is so for the rheumatologist, who manages patients with scleroderma or lupus and the neurologist who deals with Parkinson's disease or MS. Consider a more common example: a patient sees a physician complaining of pain in the leg. The differential diagnoses might include: soft tissue trauma, a pulled muscle, a fractured bone, arthritis of the joint, a tumor, an autoimmune process, etc. The differential diagnostic process considers these entities, works the patient up appropriately and concludes with the diagnosis.

If the patient does have a fracture, for example, that diagnosis does not establish the cause of that fracture, merely the cause of the patient's pain. Whether the patient was in an automobile accident, fell out of a tree, or was hit by a baseball bat is not relevant to the diagnosis. It is, however, the essence of a causal assessment, i.e., the reason that the patient's leg is broken is what causation is all about. For the broken leg, that causal determination may be easy to make by simply asking the patient, but if that injured person won't or cannot tell the physician what happened, the cause may remain undetermined. In this case, a differential diagnosis was conducted and completed. Causation assessment was not.

It is far more complicated when exposures, rather than recent trauma, are at issue. A medical evaluation for "trouble breathing" may lead to the diagnosis of asthma. This diagnosis ends the differential diagnostic process. Determining the cause, or even or exacerbator or aggravator, is a new exercise. The physician cannot, for example, identify an indoor mold exposure as the cause, if the asthma predated the exposure, or if the patient has not undergone testing to establish allergy to the molds at issue.

While both "differential diagnosis" and "causation assessment" use similar inductive reasoning processes, they use different information and data. The former involves only the patient and data from various types of testing; the latter requires scientific support for general causation and all of the specific causation elements: exposure data, additional patient test data, a detailed historical review of medical records, and a close scrutiny for other potential

causes. In the case of chronic pain which the patient associates with an automobile accident, the forces of the accident, the immediate post accident findings, the temporal relationship and other factors are crucial in assessing causation. They are not, however, important to the differential diagnosis. Properly-trained physicians are quite capable of conducting thorough differential diagnoses and arriving, thereby, at diagnostic conclusions. They are not, by contrast, well-trained in causation assessment. The treatment of a broken wrist does not depend upon how it was broken; nor does cancer treatment depend upon the cause of the cancer.

Whenever a physician says "I conducted a differential diagnosis, ruled out everything else and that's how I arrived at my causal conclusion," the antennae of \*counsel should be fully deployed. Perhaps, the physician did perform a competent causal assessment but, more likely, that statement is a ploy to end questioning and prevent exclusion. Also, it is incumbent upon counsel to point out the very real and important distinctions between differential diagnosis and causation assessment to the Courts.