

Federal Judicial Center  
Dementia and the Law: Scientific Medical Perspective Interview  
with Dr. James Noble  
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Jason Cantone, FJC: Thank you for joining us, Dr. Noble. The goal of this interview is to educate judges about the scientific and medical aspects of dementia. Now, as we know, dementia is an umbrella term that represents several diseases that affect cognition, memory, and thinking. Could you please define dementia? And also differentiate those diseases including Alzheimer's disease?

James Noble: Sure thing. So, dementia, as you said, is an umbrella term which really covers a wide range of diseases underneath it. But it's part of a spectrum of cognitive aging, with on the one hand being normal cognitive aging or expected memory changes over the course of aging. And on the other hand, it's dementia, whereby somebody has really serious problems with thinking or memory to the point they need help in accomplishing their normal day-to-day life activities.

In the middle of those two things is something called MCI or Mild Cognitive Impairment, which is often a transitional state where people may have some thinking and memory problems but not to the point that they need to change the way they lead their lives or rely upon others for help.

But within those umbrella terms, whether they be dementia or MCI, are a range of diseases. And we can think of them within one category, which are called these neurodegenerative diseases. The most common one within that group is Alzheimer's diseases. There are others within that category, including things like Lewy body dementia and frontotemporal dementia. We also think about vascular dementia, which is associated with strokes. And then there are other less common forms of dementia, which may relate to more medical problems or other inflammatory or other even infectious states. But the most common ones that we think about in my practice and the ones that often present in the public are those of the neurodegenerative process and vascular dementia.

So of those, we can think about Alzheimer's disease as a kind of a model for how we frame the term dementia. Alzheimer's disease is most often a disease that presents with a primary memory problem, forgetting. But it can also have problems with language or focus and attentional problems, visuospatial abilities. Or even behavioral symptoms where people may have more obvious or overt behavioral changes instead of cognitive impairment.

Other diseases that we just mentioned, Lewy body dementia and frontotemporal dementia, can have very similar features but may be a preponderance of one form or another. Maybe

frontotemporal dementia may have more executive or behavioral issues. Lewy body dementia may have more profound psychiatric symptoms or variability in thinking on a day-to-day basis. The thing that holds those things together is actually what happens biologically or microscopically. Where there's an accumulation of these proteins that we have in our brain that begin to become clumped together and toxic, and impact the way that normal neuronal circuits work within the brain.

Jason Cantone, FJC: You mentioned a spectrum from normal cognitive aging to severe dementia. Could you describe what's necessary for diagnoses across that spectrum?

James Noble: For sure. So, the spectrum of cognitive aging, as we mentioned before, ranges from normal cognitive aging or normal or expected aging on the one hand to dementia on the other hand with MCI in the middle. And then between normal cognitive aging and MCI or mild cognitive impairment is another transitional phase called subjective cognitive concerns or subjective cognitive impairment, where somebody may have a perception of thinking and memory problems without us being able to demonstrate those things.

And the way that we demonstrate problems with thinking and memory on that spectrum is through a combination of an engaged complex history that we take. Either in a neurologist's office or a primary care physician's office where we understand what is

the nature of somebody's cognitive problems, their difficulties with memory or language or executive abilities or visuospatial abilities. How does that relate to maybe behavioral problems that they're experiencing, including things like anxiety, depression, sleep disturbance or even changes in personality. In addition, how does that relate to maybe more physical problems that they're having, including things like mobility issues, tremors or balance concerns?

All of those things combined comprise a history that we take to understand not just the nature of the symptoms, how long have they been lasting, and how impactful are they on their day-to-day lives. So, in addition, we'll do a functional assessment to understand how badly affected may somebody be by all of these problems. In addition to asking the patient in our office who is experiencing these problems, we heavily rely upon others within their lives to provide that information. Often, it's an adult child or a spouse or a personal or a professional caregiver with a different relationship to the patient.

Taking all that together in conjunction with memory testing that we undertake in the office as well as a comprehensive neurological examination that begins to shape somebody's or our understanding of somebody's problems that they're experiencing when it comes to thinking and memory problems. That then helps us inform a diagnosis. Not just the stage on that spectrum but

the likelihood of it being tied to one or another biological problem.

Oftentimes, we will refer people to additional testing called neuropsychological testing, which is a more comprehensive, often several-hour-long assessment of all the thinking and memory domains that we just asked about in the office and assess through our screening evaluation. But it takes into account other factors, including things like educational abilities, prior attainments in life, and puts it on a normative scale relative to others with similar age and education and language backgrounds.

There's no perfect test here, but putting all these things together gives us a comprehensive sense of how somebody's fairing in their current stage relative to where they were before these problems began. And all of that together begins to inform us on somebody's ultimate diagnosis of is this somebody who's facing dementia? Or are they facing mild cognitive impairment? Or are they just going through the normal process of aging concerns where nobody's memory is quite perfect as we get older? But it's a common concern that we face.

Jason Cantone, FJC: Now, you talked a little bit about the symptoms of dementia. But has science taught us about the potential causes of dementia?

James Noble: Yeah. So, within each symptom, we know that there is a specific area of the brain or a circuit within the brain that's associated with a thinking or memory problem. For instance, we know that there's a specific circuitry associated with establishing new memories or retrieving older ones. Equally, we know that there's a specific brain circuit that's associated with both understanding and expressing language. Or understanding one's place in an environment or assimilating all the kind of sensory information around us.

Taking all that into account, we know that there are specific regions of the brain that not only function well, but we can begin to detect them when they're not doing well. We also know that there are typical biological underlying problems that tend to affect certain circuits of the brain in certain conditions relative to others. So, for instance, Alzheimer's disease, while it can occur really in any place within the brain, it tends to begin within the areas involved with laying down new memories.

So, when somebody presents to us with specifically problems with forgetting new information that they just learned, that tells us there's a high likelihood that the circuits involved with establishing memories are affected. And just based upon the likelihood of the underlying pathology that we see we know

that most often that's going to be Alzheimer's disease although, there are other explanations for it.

Now, the ones that I've talked about mostly so far are diseases that are neurodegenerative diseases and they progress over time. But people can present with vascular dementia where suddenly, there's a specific part of the brain that is injured as a consequence of an ischemic or hemorrhagic stroke. And when that part of the brain is affected or really functionally knocked out, the symptoms that are evident in that patient reflect the fact that a part of the brain is no longer functioning well.

So, in that regard, we can understand that the clinical symptoms that a patient presents with gives us a suspicion or a high likelihood that the underlying part of the brain that's affected is specifically affected by a certain pathology or a cause. That leads us from that whole course that we just talked about, with establishing history, taking in examination, leading us into the underlying syndrome as well as likely biological diagnosis of disease.

Jason Cantone, FJC: Now I understand that dementia can't be prevented. But are there things people can do to reduce their likelihood of getting dementia?

James Noble: We know through a multitude of large epidemiologic studies, including studies that have followed

people over adulthood as well as ones that have started following people in their later years, have given us a lot of understanding about different risk factors that make somebody more or less likely to develop dementia. We know that people who have had problems with vascular disease or vascular risk factors like high blood pressure, high cholesterol, or diabetes are more likely to have vascular issues like stroke. But they may also be likely to have problems like Alzheimer's disease as they age.

We know also that there are complex genetic reasons for why people may express Alzheimer's disease or really the dementias. But we also understand that aside from age alone, about 50 to 60 percent of people have no identifiable risk factor for dementia. That is just age is the primary risk factor for developing dementia. However, based upon what we know about those modifiable risk factors like diabetes, high blood pressure, cholesterol, we think that things that are generally good for one's health are also generally good for brain health. So, we usually advise people to keep themselves physically active, socially engaged, eating a healthy diet, and keeping their brains kind of cognitively active in all the things that they do in their day-to-day life.

Those pieces of advice are probably valuable over the course of one's adulthood. But once somebody begins to develop



dementia, the value of those things is not so clear and may actually make no big difference. But we still advise them. Because what's ultimately the downside of being more active or eating a healthy diet, right? Those things are generally good for all of us and may be just as good for the heart.

Jason Cantone, FJC: Now, there's been a lot of news recently about different pharmaceuticals seeking to improve the lives of people with dementia, mostly Alzheimer's disease. Could you discuss how those pharmaceuticals work and whether they've been proven effective?

James Noble: So, for several decades, we've had medications that are pill-based therapies that are really focused on treating or targeting some of the symptoms associated with dementia. So, for instance, we've had medications that provide a very modest benefit when it comes to supporting somebody's memory. But ultimately, they don't affect somebody's course of disease or the biological underpinnings of disease. More and more, and really since that time of those first medications, there has been an understanding that we really need to get to the biology of disease. Begin to affect how the disease begins to process over time as well as the findings that we have microscopically. If we can impact those, maybe we could impact the course of disease.

We are now entering into an era where we have the capacity of taking out of the brain some of the central pieces that we see microscopically for people who have things like Alzheimer's disease. And for many years, even though those drugs have been developed and seemed to be effective at pulling out those problems, these clumped proteins out of the brain; it wasn't entirely clear that they actually helped people.

But the most recent phase of discovery and some of the new medications becoming available seemed to not only be able to biologically change the course of disease, but actually clinically, change the course of disease. That is, they look to be helpful in slowing down the course of somebody's progression. But they don't seem to be able to really fully arrest or recover that is there's no real cure for these diseases as yet.

These medications also come with some risks. They have complications associated with them, and is a very individualized decision about whether or not somebody wishes to take these medications. That said, it's an exciting time for us, where we have new therapies coming about in a disease that was previously really functionally untreatable.

Jason Cantone, FJC: Now let's focus on the courts a little bit. As people are able to live longer, the prevalence of individuals with dementia is expected to increase. What should

courts know about that increased prevalence to better prepare for it?

James Noble: I think just starting with simple numbers. So, how common are these diseases? It gives us some, I think, a real perception of how important this is to the courts. So, starting with just generally speaking, we know that about 15 percent of all people over the age of 65 will either have or develop dementia at some point over the course of their aging into their later years. More specifically, we know through large epidemiologic studies that roughly 3 to 5 percent of all people, not just people presenting to an office but just generally people in the community, 3 to 5 percent of all people aged 65 to 74 have dementia. Those numbers go up to about 15 percent for those aged 75 to 84. And over the age of 85, nearly half of all people will have dementia. So, that is not just that will develop it but may even have it when you meet them.

So, just thinking about those numbers, we know that overall, there are probably about 6 million Americans who have Alzheimer's disease, the most common form of dementia. There are probably 1 million to 2 million more individuals who have some of the lesser common forms of dementia, like Lewy body dementia, vascular dementia, and frontotemporal dementia.

So, that's millions of individuals in our population that have dementia right now. Moreover, there are probably millions

more that are at risk or will eventually develop dementia who are living right now. So, there's a big problem when it comes to evaluating somebody who hasn't yet been assessed for thinking and memory problems. These problems are exceptionally common. But, one of the big issues we face in our practice is that it often takes a long time for these people to come to our attention.

I Jason Cantone, FJC: When judges learn about issues related to litigants having dementia, they often receive that information in evidentiary reports. What should judges be looking for in those reports?

James Noble: So much like I discuss the process of establishing a diagnosis of dementia, we document all of these things in our notes. So, a primary care physician and a neurologist will document the course of illness as well as the primary symptoms that have led to the diagnosis. Or maybe lack of diagnosis of something like MCI or dementia. So, neurologists' notes, primary care physicians' notes, other specialists including the geriatric psychiatrist, psychiatrists and geriatricians are often a resource to look to, to see if there any evidence to have a concern for a diagnosis like dementia.

In addition, a neuropsychologist note will often have a much more in-depth review of thinking and memory problems. As I

mentioned before, a neuropsychologist will be several hours long evaluation which takes into account somebody's educational background, their professional abilities, their likely pre-morbid intelligence, as well as assessments of thinking and memory including verbal and non-verbal memory, executive abilities, language abilities, visuospatial abilities. In addition, we'll take into account behavioral assessments done in the course of those evaluations, including whether or not there may be something about anxiety or depression that influences things.

In some cases, although not often, there may be actually assessments of whether or not the answers are being given in a genuine manner. So, there are concerns for some individuals, not often in the dementia population but perhaps in younger individuals maybe not giving truthful answers. So, there are actually assessments of malingering that can be done. So, those may not be included in every report, but that's information that people can look to for more substantive information about the validity of the assessment that was just done.

Jason Cantone, FJC: Now you've described both neurologist and neuropsychologist. Can you describe the difference between the two roles?

James Noble: So, a neurologist is a physician that's gone through a training including internal medicine and neurology.

And individuals like myself may have had additional specialty training focusing on dementia and behavioral neurology or neuropsychiatry.

A neuropsychologist on the other hand is not a physician but is a doctor, a PhD, who is a psychologist with specialty training in assessment and interpretation of complex evaluations of thinking and memory called a neuropsychological report.

Jason Cantone, FJC: And recent evidence has examined the use of biomarkers as surrogate evidence of dementia. Can you describe how biomarkers work and how they might be used?

James Noble: Sure. So just starting with the definition of biomarkers themselves, independent of whatever medical or disease entity we're thinking about, they're really simply a way to better understand the biology of disease. They're really biological indicators of a disease.

Now, some biomarkers are not just used in the context of establishing a disease but maybe in anticipation of a disease. We know that there are many different things that we all go through as far as screening evaluations to say, well, this may be an indicator of a future risk for something like breast cancer or prostate cancer or a cardiac disease, these kind of things. Those assessments that we undertake whether they be blood-based assessments or X-rays, these are all biological indicators of either current or future disease.

In our practice, we have had really an explosion of understanding, an increasing ability to make a biological basis of a diagnosis either at the time of a clinical diagnosis and sometimes in advance of establishing a clinical diagnosis. So that is for a patient who comes to see me. And I've done a comprehensive evaluation including history and examination. Maybe I've referred them to a neuropsychologist. We've come up with a likely assessment or we've come up with an assessment of a likely diagnosis that causes somebody's problems, their thinking and memory problems that came to me in the first place.

But that doesn't give us an answer as to exactly why. And this information is becoming more and more important in my clinical practice as we've moved towards biologically-based treatment options. So, that is that we have medications that can help out with symptoms, these pill-based therapies I mentioned a moment ago. But we also have medications that are infusion-based therapies or other medications that are coming down the line that really focus on the biological basis of disease. If somebody doesn't have that biological reason even if we think clinically, they look like they have something like Alzheimer's disease, if they lack a biological indicator of disease then they have something else that explains their memory problems even though it looks like Alzheimer's disease.

So, in my practice, we've been using these tools. These biological indicators whether they be imaging modalities, brain imaging modalities, fluid-based biomarkers, including blood and spinal fluid, to help us better understand and more exactly diagnose somebody's problems before us.

There is a temptation but we're not there yet scientifically to use biomarkers to diagnose somebody before those symptoms become apparent. We use these as a tool for research right now to say, well, maybe if we can help somebody in the clinical stage where they're obviously having memory problems, maybe if we move back that timeline towards an even earlier basis of diagnosis, maybe that would help even more.

So, in a research framework, we are using biological indicators. But it's really not appropriate for us to use those indicators right now unless somebody has an established thinking or memory problem. We use those biological indicators right now to differentiate the reasons why, but they're really not used as a diagnostic tool in advance of the thinking and memory problem right now.

So as much as we have this kind of a new environment in which we work where we have a clinical diagnosis, a biological basis of disease, we're hopeful to move up that timeline, but we're not there yet. So, we're not at a point yet where we can use biological indicators to say somebody has dementia. But we



can use biological indicators to say, well, this person seems to be at risk for developing problems down the line. But they have no obvious or overt problems with thinking or memory at this point.

Jason Cantone, FJC: Now you mentioned that we're not there yet in using biomarkers as surrogate evidence of dementia. What are the concerns?

James Noble: So, we've known for years that through large autopsy studies, we have some in our center and many others, that if you look at people who have biological evidence of Alzheimer's disease microscopically, that is, they come to the point of death. We've examined their brains. And it looks like if you were to look at this brain versus somebody who had obvious dementia, about 30 percent of people who come to the point of death, who have had recent memory and neuropsychological assessments, had no evidence of thinking or memory problems and yet they had evidence of Alzheimer's disease microscopically.

So, we know just from that information that a biological diagnosis is not enough, right? So, 30 percent of all people have pathologically indistinguishable problems from somebody who clearly had an overt problem, which presents an issue in making sure we're not prematurely diagnosing somebody based upon a biomarker alone.

Now, we're not doing obviously brain autopsies on living individuals. We've now gotten to the point where we can confidently say that what we see microscopically through an autopsy tissue can be identified through brain imaging and can be identified through biological indicators like through fluid indicators. But, because we know that many individuals have no clinical symptomatology despite having an indicator, we see those individuals as somebody being at risk, but we cannot make a diagnosis clinically at this time on those individuals.

Jason Cantone, FJC: What are some of the legal issues that dementia presents for the courts?

James Noble: Sure. So, the primary legal issues presented to the courts may regard somebody who has developed dementia and commits a crime in the context of that and has really no criminal background. This is a signal for the courts to pay attention to maybe a symptom of dementia rather than an indicator of somebody's longstanding or even their personality or criminal activity. But this is maybe something that reflects a change in this individual that's beyond their control.

In addition, I know there's great concern about an aging population of incarcerated individuals and how punishments may be carried out on those individuals. I think I'll defer to Dr. Denno about that.

But the more common thing that I face in my office are more simple matters around things like more family matters and family legal issues around advanced care planning. So, advanced care planning includes things like do not resuscitate, do not intubate orders as more of a kind of a finite anticipatory plan around the time of death, or really kind of a dire circumstance around near death. But, more common issues that go along with advanced care planning, including designating an individual through a health care proxy document. Include more financial planning and living wills as well.

There are many different resources that are out there that have been made available to the public without necessarily needing to engage legal assistance. Those resources have become really essential for making sure that somebody with dementia can have their wishes expressed and followed by their families.

I think it's also important to realize that although somebody may have thinking or memory problems, they often still have the capacity to engage in meaningful conversations. And this is something we talk about in my office all the time. To make sure that any decisions or any advanced care planning and wishes about how they wished they want the future to occur, those conversations take place with families at an early time. So that the families have confidence that when it's their turn to enact changes or enact plans on behalf of an individual who

can no longer express those concerns for themselves that they've had those conversations. And they have the confidence that they're doing things in line with the advance care plans and expressed wishes of the individual.

So, all of that comprises an advance care plan. Some of these matters do require some legal understanding and legal engagement. Especially if there may be some conflict within families. We try to avoid those things to the extent possible by having clear plans in the earliest phases of disease whenever possible.

Jason Cantone, FJC: Now, in the presentation with Professor Denno, we talked about competency, and how in the traditional competency process, someone is ordered to treatment to restore competency. But that doesn't really work in cases of dementia, does it?

James Noble: That's right. For most individuals, the expectation in dementia is that things will progress. That is nearly the uniform process that happens in individuals with neurodegenerative diseases and in many forms of dementia. But maybe the one exception may be somebody who has vascular dementia where a specific sudden insult to a part of the brain has left a fixed deficit that really generally does not recover or has a very slow amount of recovery but often leads to a new normal for that individual.

Nonetheless, those individuals, even though they have a fixed deficit from a vascular basis, they may also have another pathology or a second problem happening in the brain. So that is somebody who has a history of stroke may also develop Alzheimer's disease. It's actually the norm for individuals to actually have several pathologies that develop in their brains as they age over time when expressing dementia. Individuals who don't have thinking or memory problems like MCI or dementia tend to have fewer or no pathological changes within the brain.

So, the competency restoration is really not something that one can expect among individuals who have dementia simply because there's a progressive nature to the disease itself in most persons who are affected by it. And even as we step into this new era of therapies and biological therapies, we are not yet at a point of restoring somebody's cognitive abilities. We are simply slowing the course of illness over time. Certainly, we would love to be at a point of being able to restore some of these cognitive abilities, whether there are legal implications or not. We are far from that at least at this point in our field. It's something that we aspire to all the while.

Jason Cantone, FJC: Is there anything else that you believe judges in the court should know about the science of dementia?

James Noble: We are in the middle of a truly transformative period in our field where we have for years

worked to understand the biological underpinnings, have established these biomarkers that I described including biofluids and imaging biomarkers. We're also transitioning to a phase of not just being able to biologically diagnose somebody very well but even treat that biological problem.

As is the case in any disease, it's rarely that the first medication that becomes available to the public ends up being the one that endures. It often becomes something that becomes part of a treatment strategy for many. I think the other thing to know is that we've come to realize that Alzheimer's disease, or frontotemporal dementia, or Lewy body dementia, none of these diseases, even though they have singular names. likely represent singular diseases.

We know that there's very complex genetics about these diseases, many different risk factors, a very long procession of changes that occur over years and even decades before the first symptoms emerge. And we know that if we can affect the later stages of disease, and this is from really any other disease entity, if we know that we treat somebody at the later stages of diseases, the treatment response is never as good as where we are at the beginning of the stage of disease.

So, we are really in this transformative period of new approaches to diagnosis, new biological therapies to help treat the disease. But it may be that we're entering into another

phase of our field where we're actually treating people for longer periods of time. So, it's a tradeoff, right? We know that we have a very common, very prevalent disease among an aging population. And we now have available to us therapies that prolong the disease. So, there's a chance that we actually may increase the overall burden of these diseases on our population as it comes to the total number of people affected by these diseases because they're going to live longer with these therapies.

Until such time that we have medications that really stop or cure these diseases, that may be the new reality that we face. And in that regard, these issues that we've just talked about become even more important to the courts simply by sheer numbers of how many people that may be affected.

Jason Cantone, FJC: Well, thank you for your time, Dr. Noble.

James Noble: Thank you for having me.

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