Staying Sharp
University of Kentucky
June 2, 2012
THE DANA ALLIANCE FOR BRAIN INITIATIVES

BB: Hey, good morning, everybody. How is everybody today?

A: Good.

BB: Wonderful. Well, welcome to "Staying Sharp." My name is Barbara Best. I'm with the Dana Alliance for Brain Initiatives and that is an organization of more than 300 neuroscientists and clinicians throughout North America who are dedicated to educating the public about advances in brain research, to inform you about how to maintain a fit and healthy life as we all age, and to translating the science so it's accessible to a lay audience. I promise to be brief so we can get on with the program. You can find out more information about the Dana Alliance as well as AARP and Sanders-Brown Center on Aging in the materials that you picked up. If you didn't pick any up on your way in they will be there on your way out.

Before we start the program I must thank

MetLife Foundation who has graciously supported the Staying Sharp Programs throughout the United States. I'd like to thank AARP Kentucky and very, very special thanks to the Sanders-Brown Center on Aging for their help in organizing this session and also for providing our wonderful panelists today. I must say you are, indeed, very fortunate to have such an organization with a wealth of expertise right here in your community to take advantage of.

So now we'll move on with the program. I'd like to introduce the moderator for today's program, Dr. Linda Van Eldik. She is the Vernon Smith Endowed Chair in Alzheimer Research and the Director of the Sanders-Brown Center on Aging. She's also a valued member of the Dana Alliance. So without further ado, Dr. Van Eldik. (Applause)

LVE: Thank you, Barbara. So I'd like to add my welcome to Barbara's and thank all of you for coming today. What I'm going to do is just give you a little brief preview of what we're going to do today. First of all, we're going to have a brief introduction of the panelists and I'm going to act as moderator so I'm going to give them questions in the first part of the program.

We'll have a discussion in four different areas. One is a normal change in the brain as we age? Then we're going to cover certain disorders of memory and age related brain diseases. Then we'll talk about predictors of successful aging – how can we maintain a healthy brain as we age?

Then finally we'll have a brief discussion about clinical trials, what they are and why they're important. Then we'll open it up to a question and answer period from the audience and I'll give you more details about that when we get to that section. Then at the very end we'll have just a brief wrap-up by the panelists kind of looking forward and summarizing the field. I'd also like to request, in your programs you should have an evaluation sheet, so if you could please at the end turn it over to the volunteers they'll be collecting them as you go out. That helps us to see what we're doing right, what we're doing wrong and design better programs for you guys in the future.

So without further ado, we'll go to the panelists. What I'd like them to do is introduce themselves and just give you a very brief overview of who and what they are and their expertise. So let's start with you, Greg.

GC: I'm Greg Cooper. I'm a neurologist here in town. My background is primarily behavioral neurology, memory disorders, Alzheimer' Disease related conditions. If there is such a specialty as Geriatric Neurology that would probably fit me. That's it.

DW: So I'm Donna Wilcock. I have my own research lab here at Sanders-Brown Center on Aging and the focus of my lab is Alzheimer's therapies. So we study new therapies for Alzheimer's Disease primarily focusing on the role of inflammation in Alzheimer's Disease, also vascular dementia and how vascular dementia plays a role in Alzheimer's Disease as well as its own role in causing dementia in late life and how we might be able to treat that as its own disease.

FS: Some people in the audience know me because I've bene with the Aging Center here at Sanders-Brown before 1989. My name is Frederick Schmidt. It's used often as a curse word by some of our volunteers. (Laughter) Not pronounced quite the same either. I've heard. The reason I mention that is that I'm one of the people who put together the Normal Aging Program here in the Fayette County area with the

joys of having over 1,000 people in our effort to understanding brain aging. Those of you who are participants in the audience, I recognize some faces, thank you again.

Those of you who don't know me, the best description for what I do was actually coined about two decades ago. I was at a meeting in Washington and at the time I studied not just Alzheimer's Disease and related dementias, but I was also studying HIV associated dementia which was a big issue in the early Eighties and Nineties before we had treatment. I did a lot of treatment work and as a result somebody said, "Well, Fred, what do you do for a living?" And I told them, "I'm a neuropsychologist by training." And they looked at me and said, "No, but given what you do you're really," and listen very carefully, "a dementiaologist(SIC)." (Laughter) Sounds pretty scary. So we have a lab at the Aging Center. I collaborate with Dr. Cooper and I see patients. I collaborate with Dr. Wilcock and other researchers at the Aging Center looking at how the brain works. So that's my main focus – what comes out of the brain and what goes into the brain.

LVE: Okay, well, thank you. So I'll begin with

feeding the panelists some questions so they can have a discussion. The first area is on normal memory and normal changes in the brain. So Fred, why don't you tell us what is memory and what is normal memory as we age. What are normal changes that we can expect?

FS: So I'm going to try to remember all the literature on memory. (Laughter)

LVE: In a brief answer, please.

FS: Right. This is something that has been studied for centuries. The easiest thing to think of about memory is that there are two kinds. Memory researchers will always give you lots of labels. We call it all sorts of things. This is a good time to give a quick plug. Some of those definitions are in the lovely packets and booklets that you received or hopefully received from the Dana Foundation. They give some nice explanations about how memory works.

The long of the short of it is that there are two forms of memory. One we call "memory with awareness." Okay? Declarative memory. It's our ability to learn a phone number and remember it for as long as we need that phone number. On the

other hand, there's an automatic memory in the brain or procedural memory. Procedural memory and declarative memory, if you will, use different circuits to a great extent, but many people feel memory in and of itself is a whole brain phenomenon. So we develop associations over time. We learn how to do things. We learn what things are. We learn our language. All those things are based on our brains' unique ability to form associations. Those associations, we think, are related to brain chemistry and brain structure with they "sy-napse" or "syn-apse," depending on how you pronounce it, being the key element. There's lovely literature here, I won't go beyond that, other than to say that the impact of what happens at the synapse we believe is very crucial to how memories form and how memories are retained.

Now, what happens as we get older? It's normal to be forgetful. It happens all the time. You just probably don't think about it as much when you're younger. Right? I'm sure that everybody in this room can go back to elementary school, high school, college and realize that you forgot things during those days. Didn't you? But what was your emotional reaction to that? "Ah, you know, I'll do better on the next exam." "I remember that

woman's name after I date her the fifth or sixth time." (Laughter) Right? Isn't that how it works? I've been married forever and I sometimes get confused when I go home and call her by the wrong name and I get in trouble. (Laughter) That's normal.

It's normal to park your car, go into the store for several hours, come out, and not quite know where you parked your car. That's normal. Where memory isn't normal, that's the problem. When is memory not normal? It's when you forget that you parked the car. You forget what you were doing in the store. You forget to pay bills on a regular basis. When it interferes with day to day life significantly that's when memory is not normal. So normal aging of memory is, yes, it's harder to retrieve facts, sometimes it's harder to learn. The brain slows down a little bit, there's wear and tear, but there's a lot of information there. So normal is regular day to day forgetfulness. It comes back to you. Whereas abnormal, that's the key. When it doesn't come back to you and it makes life miserable for you.

LVE: (Inaudible) We heard the term "brain is plastic." The brain has plasticity. Tell us a little bit about what that means.

DW: So plasticity is really the brain's ability to form those new connections, to lay down new memories, to form new synapses, as Fred just described, to make new circuits and, essentially, to make those new memories. So when we say "plasticity" what we're really talking about is the brain's ability to create new connections, create new memories, and generate new experiences. So as you learn new things, as you read new books, as you sit here listening to us talk about all these wonderful things about the brain your brain is undergoing some form of plasticity and you're creating new connections and you are laying down some new memories. So the brain is being plastic right now. Plasticity as you age does decrease somewhat, but we all still maintain some ability to create these new connections.

LVE: (Inaudible) So we've heard this term from both of you, "synapse." Maybe what you should do is define what that is – for those of you who don't know what a synapse means.

M: You need to turn that mike up.

LVE: I know, it's green, but it's somehow not working. I can talk louder. (Laughter) So you heard Fred and Donna say synapse is very important in terms of memory. So can

you define what is a synapse?

DW: What is a synapse? So when two neurons or nerve cells meet they don't actually form a hard connection. So they're not joined like this, there's a gap. Between that gap the one neuron that is sending a message releases chemicals. What we call "neurotransmitters." So these chemicals will reach the next neuron that it's trying to send a message to and the receptors on that neuron will bind those neurotransmitters and then the signal starts again in the next neuron. So this gap between the two neurons is what we call a "sy-napse" or a "syn-apse." I'm English so I tend to say "sy-napse." So this area, this gap is the synapse. A lot happens in that area. So there are a lot of different neurotransmitters, there are a lot of different receptors, and there are a lot of imbalances that can happen in there. Not just in aging or in Alzheimer's, but in all kinds of neurological disorders and we'll get to that, I guess, later in the program. So this is where a lot of the drugs are targeted and a lot of those things. So yes, this is the "sy-napse." This is the "syn-apse."

M: (Inaudible)

DW: I'm sorry?

M: How do you spell it?

DW: Spell synapse?

M: S-I-N?

DW: S-Y-N-A-P-S-E, synapse.

M: Thank you.

DW: You're welcome.

LVE: Okay. Well, that can lead into then that's normal memory and how it changes as we age. Well, what about dementia? That's actually a disease of memory and not normal aging. Greg, can you tell us what dementia is?

GC: Yes. Dementia, there are different potential definitions, but the simplest way to look at dementia is a chronic disorder of impaired cognition. Now cognition can mean a lot of things. You may have impairments of memory. You may have impairments of language or ability to communicate with words. We may have problems with jugement, decision making, sense of direction, orientation. So a number of things like that. So this is typically an acquired chronic condition that impairs cognition. We would usually say it impairs multiple areas of cognition – memory and thinking – to the degree that it prevents us from doing our

normal day to day activities. I may no longer be able to handle my own finances or medications. I need assistance at that point.

LVE: Are dementias reversible?

GC: There are a lot of causes of dementia. Dementia is a broad term and there are many individual causes of dementia. So in many cases when we think of dementia we're thinking of Alzheimer's Disease or we may be thinking or a vascular dementia or a dementia related to stroke or any number of other conditions that may be partially treatable, but they're not really reversible. On the other hand, some people will develop, at the very least, symptoms that are similar to a dementia that are related to medications or perhaps other chronic medical illnesses or toxic exposures, other situations like that. Depression would be another one. In that case it may be considered a dementia or it may be considered a mimic of dementia. If we treat the underlying cause then we may be able to reverse the symptoms in those cases.

LVE: Okay. Any other comments from the panelists?

FS: So I can't resist making a comment. Dr.

Cooper obviously has a wonderful wife and family since he's allowed to manage his finances still. I must be demented. (Laughter)

GC: Actually, no. (Laughter)

FS: No? Okay. Because I don't get to manage my finances. With that aside, I have to mention that the key elements are what we see as treatable dementias. That's one of the reasons that I personally believe that it's important to know about your memory, know about your thinking and have it checked from time to time. Because you can have a condition, let's say, low B-12, that is treatable. It's very treatable and the sooner you treat it, the happier your brain and thinking abilities are as a result.

Dr. Cooper mentioned depression. Twenty or thirty years ago when I started my training we couldn't treat depression very well, but we know depression involves changes in brain chemistry. The brain signals change. One of the key chemicals in the brain that is associated with depression is serotonin. Serotonin levels go down and so many of the drugs, the most familiar potentially to you folks is Prozac, if you remember when that drug came out, they boost serotonin levels. But what's

important from the standpoint of memory and thinking is, is not only does it treat the depression, but the neurochemical boost of serotonin boosts the memory chemistry of the brain as well downstream. It allows the memory circuits, we believe, to actually release more acetylcholine which is one of the key memory neurotransmitters.

So when people are depressed we used to think that they didn't remember very well because they were busy thinking about how depressed they were. So you would give them a memory test and they wouldn't do well. But then research began to show that if you asked a depressed person to remember and you organized the information that they had to remember they did better. They almost looked normal. That's what lead to research into that brain chemistry that shows that if you treat the serotonin deficiency, if you will – that's oversimplification – you actually boost the thinking not because the person is worried about and thinking about their depression, but because the brain chemistry is pushed back into a normal balance.

Those are the important things that Dr. Cooper alluded to and Dr. Wilcock alluded to where our research is

giving us those answers of what happens at that synaptic junction. Think of it as two wires with sparks going in-between to give you signal. What's happening there, what's happening to the brain structure? So those are the important aspects that both Donna and Greg mentioned. That's where the research is important. The research Dr. Van Eldik does is also important. What are the mechanisms? Is it inflammation? Is it changes in blood vessels, as Dr. Wilcock does. All of these things are tied in. The brain, as you know, is a very complex organ.

GC: I'd like to pick up on a thread there. As sort of realization of some of these things, there is a movement in medicine now for primary care physicians to start doing memory screening. I don't think this is in place yet, but hopefully soon they'll actually get reimbursed for taking the time to screen for disorders. Then if we find a memory disorder perhaps if we can identify it and treat it earlier we'll be much more successful.

LVE: So we've also heard the term "mild cognitive impairment" and the "stages of memory loss." Fred, can you tell us what is mild cognitive impairment and is it always a precursor to Alzheimer's Disease?

FS: Okay. That's a double question. So real quick, what is mild cognitive impairment? Mild cognitive impairment as a concept has been around for decades. We used to call it "benign senescent forgetfulness." Right? First off, what's benign about being forgetful? I don't know. (Laughter) So over the years as we studied the changes linked to Alzheimer's Disease and related disorders we discovered that long before people have real trouble day to day – so you have memory thinking changes that start somewhere, they start some point in time. Eventually they get to the point where you have trouble doing day to day things. At the point where you have trouble doing day to day activities you have a dementia.

So what do we call that interval, that time where memory is becoming less efficient, thinking is becoming less efficient? The answer is the concept of mild cognitive impairment. You have mild thinking problems that don't just yet affect day to day living, but why is this important? It's important because the nature of the mild cognitive impairment we think can tell us where you're headed. Okay?

So if you have primarily amnestic mild

cognitive impairment or what some people call “hippocampal based MCI,” and we can talk about that later, memory is starting to go. Many people think that that’s the first sign that you’re headed towards Alzheimer's Disease. Other people have said that if you have trouble with organization – your memory is okay, but you’re a little bit disorganized, you’re not paying a lot of attention, they call that “dysexecutive or executive mild cognitive impairment” and some people believe that that presages diseases like frontotemporal dementia or that there is a vascular process behind it. That there are mini strokes, if you will. So the mild cognitive impairment is the stage between normal and dementia. So you’re in-between. You have mild impairments in thinking. The question is what causes that, can we treat that before you move further down the road.

LVE: So Donna, tell us a little bit about various risk factors for getting dementia, particularly Alzheimer's Disease. Are there risk factors that would enhance our chances?

DW: I think right now the way the field is going is pretty much what’s good for the body is good for the mind. So as far as a consensus goes, there really has not been a lot of defined

risk factors that we can hang our hats on and say, “Yes, this is a risk factor for Alzheimer's Disease.” We know, for example, if you have a high level of cardiovascular risk factors, high blood pressure, you have a history of heart attack, you have a history of stroke – all of these stack up against you as far as your risk for developing Alzheimer's later in life. Type II Diabetes is kind of coming to the forefront as a risk factor for Alzheimer's Disease. Education level seems to kind of take you the other way. So the higher your education, the lower your risk for Alzheimer's Disease. Maybe Greg you can add to this as a clinician with what you see?

GC: The first thing you said is what I think is really spot on. What’s good the body is probably good for the brain. In particular, I believe this and I think there’s evidence for it, that vascular health is particular important. So the same risk factors that we might have for stroke or heart attack largely would correlate with risk factors for Alzheimer's Disease. Whether that’s related to our overall vascular health or some other factor is probably debatable, but I think paying close attention to risk factors like high blood pressure, high cholesterol, diabetes, those sorts of things I think really do play a role.

FS: Just to comment. Again, I feel like I'm pitching Sanders-Brown Center on Aging when I say this, but there are genetic risk factors as well. One well identified genetic risk is based on the apolipoprotein E gene. There are, essentially, several combinations of this gene, but if you happen to have what's known as the 4 allele, this one particular mutation, your risk tends to go up. The question is why? And that's an area of research that is currently ongoing.

What is it about this gene that increases your risk? Is it because of the vascular factors? It's related to that. In fact, it's been shown that people who have had bypass surgery who have this apolipoprotein 4 allele, they tend to age more rapidly in their cognition. They lose cognitive capacity more readily than people who don't have this gene. We see that if you have this gene your risk for Alzheimer's compared to a person who doesn't have it is four to eight times greater. So something about this gene actually promotes this.

The question is how does this gene promote dementia and how does it interact with other health conditions? One of the things I should mention, and I'll mention a few

colleagues here – Dick Crissio(?), Pete Nelson, and others – we've just received funding to study these clinical variables using new statistical methods and compare it to the findings that we have from brain tissue across about six different studies across the country. So we're going to be able to study over 9,000 brains in terms of what was found in the brain tissue and link it back to those risk factors. So we're hoping that by using these methods in this study, it will take about five years to do this, we'll be able to say more definitively this is how these risk factors lead to brain injury or brain change.

More importantly, up until now we knew that if you have depression during life your risk is almost doubled for dementia. Why is that? We don't know. If you had high blood pressure it's almost doubled, and so on, but nobody knows how these risk factors combine and that's one of the biggest issues for us. What is the combination? Is it additive? So you were depressed and you had high blood pressure so your risk is four time? Or is it multiplicative? We don't know. So these are the tough questions. But that's the key, what's good for the body is good for the brain. No surprise because the brain needs the body

to survive. Or as some people have said, “What’s good for the heart is good for the head.” So that includes things like relationships. Not just the physical heart, right? So those are important aspects.

LVE: Okay, well, let’s talk about stroke. We talked about cardiovascular risk factors. Greg, why don’t you tell us what is a stroke? What are the early signs of stroke?

GC: Well, stroke most broadly defined is just a sudden vascular event. That can mean a hemorrhage or a bleeding in or around the brain. Most of the time though what we’re talking about is what we term an “ischemic stroke.” Meaning there’s a blockage and blood flow to part of the brain. So typically a blood clot will form in one of the arteries in the brain or travel to the brain and it will block blood flow to part of the brain. When you don’t get oxygen nutrients the brain stops working in that particular area. Depending on where that is you’ll get very specific symptoms.

So for example, if I have a stroke I might have difficulty with my speech. It might be very slurred or it might be perfectly clear, but not make any sense at all. I may say words

that don't really make sense or I may not be able to understand when people are speaking to me. So some problem with my speech. I may develop a weakness on one side or the other of my body or loss of feeling on one side or the other, a loss of coordination, clumsiness. There may be vision problems. I may lose vision off to one side or I may develop double vision. It's usually going to be a fairly specific symptom so it's not going to be a situation where I'm just weak all over or feel bad. It's going to be a situation where part of my body is not working and other parts of the body are working. It's typically going to be a fairly sudden onset. It's going to hit us pretty quickly.

LVE: Is there anything that you can do when you think someone is having a stroke?

GC: The most important thing you can do is, really, I would call 911. Get them to the hospital. If this is an ischemic stroke or blockage of blood flow to the brain the term that's often used is "time is brain." And that's really true. If I develop a stroke right now and I make it to the hospital six or seven hours from now there may not be a heck of a lot that anybody can do. It's over. If somebody gets me to the hospital

within 30 minutes or an hour we may be able to give medications or do some kind of procedure to open up that blood flow. To restore blood flow before there's been any lasting or permanent damage. So it's critical to get medical attention, get to an Emergency Room as quickly as possible.

LVE: Can we wait for the questions until the question and answer?

M: (Inaudible)

GC: Sure.

M: (Inaudible)

GC: (Laughter) Just remember, 911, write it on your palm. So vascular means having to do with the blood vessels. So from a stroke standpoint that usually means there's going to be a rupture. The blood vessel breaks open and we have bleeding. That's going to be a relatively small percentage. Or there's loss of blood flow. There's a blockage in one of those blood vessels. So that's why we mean vascular.

LVE: So one of the other major brain disorders in the elderly is Parkinson's Disease. Greg, can you tell us a little bit about Parkinson's Disease and whether there are any medications

for it?

GC: Sure. It's a bit of a complicated issue. As neurologists, we often think of a broad category called Parkinsonism. Parkinson's Disease is the most common aspect of that, but there are a number of conditions that will cause similar symptoms. Now, when we think of Parkinson's Disease we're usually thinking of a degenerative brain condition where people will develop a tremor. We call it a "resting tremor." So it's not if I'm holding my hand out it's going to shake. It's where it's resting in my wrap and it's going to kind of shake like this. Some people call it a "pill rolling tremor." It's almost as if I'm rolling a pill like the old pharmacists used to in their hand.

So I'll often develop a tremor. It's more often going to be worse on one side than the other. I'll develop slowness or stiffness of my movement. So it's as if everything has slowed down. There's less facial expression. I may not blink as well. I may have trouble getting out of a chair not really because I'm weak, but because I can't coordinate my muscular activity. Things are just much slower. Now, there can be any combination of those symptoms and there can be additional symptoms that go along

with that. Most of the time we really don't know what causes that. In rare cases there can be toxins. In rare cases there can be a very strong genetic or inherited component. But most of the time it's idiopathic which is just a fancy way of saying we don't know, it just happens.

There are medications that treat the symptoms. So we don't have medications that will reverse or stop this condition, but we do have a lot of treatments that, depending on the individual, can do a nice job of treating that. The most common ones are a medicine called Sinemet, a couple of medicines called Mirapex, Requip. The idea behind these medications are to replace a neurotransmitter. You heard us talking about neurotransmitters, chemicals that help neurons or brain cells communicate one with another. In Parkinson's Disease there's a deficiency of dopamine. So really almost all the medications that we use for Parkinson's Disease are aimed at restoring or at least replacing dopamine. So we're trying to help restore some of that normal communication, some of that normal functioning in the brain.

LVE: Okay. So let's move onto predictors of

successful aging. Let's be positive now. So we all know the kind of four pillars of successful aging which are increases in physical activity, mental activity, social engagement, and as you heard, controlling your vascular risks. So Fred, tell us a little bit about what kinds of mental exercises would be useful to us.

FS: Okay. I don't recommend the Jimmy Carter approach. Anybody remember? What was Jimmy Carter during his election campaign raked over the coals with? He was being honest with us. Anybody recall? Something about his heart?

F: (Inaudible)

FS: Lusting in his heart. Yes, I don't recommend that. (Laughter) But see? People remembered. This is good. This is good. See? Who would have thought you'd remember those things? So that's a nice healthy sign. So let me mention one thing before I get into the healthy activities because this is the most preventable. This just came to mind and it shows that sometimes I'm a little slow too. Sleep, sleep, sleep. One of the most treatable aspects of aging, even young age is obstructive sleep apnea or Sleep Apnea syndrome. It's where when we're asleep we don't breathe well, brain oxygen levels drop, and brain

injury can be the result. It's very important. It's important because as we get older our muscles become a little less toned. Hence, one of the four pillars of successful aging is exercise. Keep your muscles toned.

As sleep disordered breathing goes on over time the wear and tear on the brain and the rest of the body is significant. It can lead to rhythm changes in the heart, but the main aspect is oxygen loss in the brain. We were talking before about risks for dementia. There was a study late last year and this was done by some sleep researchers that looked at women, older women who had Sleep Apnea Syndrome. Their risk for developing a dementia was five times that of women without a sleep disorder. Five times. That's how important restful sleep, but good breathing during sleep is.

When I used to see older patients that was one of the first things I did. What are the risks? Snoring, high blood pressure. Okay? Sometimes it's made worse by smoking before bedtime, alcohol before bedtime because it relaxes the muscles. What it requires is an overnight sleep study. They measure how you breath and if you have breathing problems it's

treated with a machine CPAP, continuous positive airway pressure, and the studies that we've done here at UK, Dr. Phillips, Dr. Barry(?), part of the team show that you can arrest cognitive changes due to that oxygen deprivation by getting it treated. What's more important is that there is evidence that suggests that if you have Sleep Apnea Syndrome your risk for dementia goes up and there's evidence, there are several studies show that if you have dementia and Sleep Apnea Syndrome your dementia gets worse faster. So it's very clear how important oxygen is to the brain.

Now back to good things you can do for your brain. Some of the research that we've done here at the Aging Center, Sanders-Brown Center, some of Dr. Sheff's(?) work shows that those synapses, those junctions where the brain cells communicate, even in Alzheimer's Disease they change shape. They try to adjust to the fact that there's a disease there to maintain the connection and maintain communication. That's what Donna was talking about when she was talking about plasticity. So how do we promote plasticity? How do we make more connections in the brain? One of those is learn something new like

you're doing today. It's even more important because the evidence from both studies of animals and, to an extent, people shows that brain activity and brain connections change as we learn.

There's an old, old study, Dr. Diamond did this with rats. She took rats, put them in a regular rat cage, put the other rats in a fancy rat cage where they had all sorts of stimulation and the rats could learn new things. Then when they died she looked at their brains. Guess what? The rats in the fancy cage had better brains. More connections. We used to think that the brain doesn't remodel itself. We know better. So learning new things. If you've never played an instrument tackle a new instrument. Learn a new language. Try something different. In addition to the four pillars that Linda mentioned – exercise, healthy eating, maintain your health – learn something new. That's the best thing that you can do.

Try something that is really novel for you because that forces your brain to make new connections. Let's say you played the piano all your life and you switched to the accordion – there's not a lot of new learning that goes on there. Because you know the music through the keyboards. But maybe

you switch to playing pool. (Laughter) I knew I'd get a reaction. It engages a new aspect of the brain. They eye/hand coordination and the motor movements are very different than piano playing. So those are the kinds of challenges. Always something novel. Think of novel, read a novel, but think of novelty. Learn something new.

LVE: So Greg, tell us about some kinds of activities that we can do to stay socially engaged. What would you recommend?

GC: This is going to sound overly simplistic. I think people should do what they enjoy doing because in that way we know that they're going to keep with it. They're going to get engaged. So if someone would enjoy being part of a book club that's fantastic. If somebody wants to be part of a church organization, a civic organization, if they want to volunteer. I think any of those things are good. What I would like to see them do, primarily, is just be around other people. I don't want folks volunteering in a room by themselves isolated. The key is to be part of a larger group that forces some interaction there. And I think it's okay to even go outside of the comfort zone a little bit. I

tend to be a bit shy. Well, that's alright. Maybe I should force myself to be around other people that I don't know.

So I think the important thing is to try to pick something that you think you would reasonably enjoy so it won't be a one time deal so you'll continue to do that. Find a people with similar interests. I say a book club. This, arguably, is not social quite in the same way, but I would encourage people to become a Donovan Scholar, a program which is fantastic through the university where folks take classes. Sometimes it's in a classroom, sometimes they take a trip to Shaker Town and learn about the Shakers, an historian teaches that. Things like that, I think. I have a hard time giving any real specifics. Maybe you all will have a better idea.

FS: I think those are excellent examples. Part of the reason Donovan Scholars work and going back to classes is a good idea is because not only do, I look around the room and there's not anybody under 18, right, so I won't insult them? (Laughter) We all know, everybody in this room knows that there is a lot of experience and knowledge that can be shared with people who are 18 and under. Those are perfect examples. The

Donovan Scholar Program, you can actually interact with younger students and share ideas. There is a learning that goes on. We all know that different generations have different social interaction styles. You may discover that you become a fanatic for Facebook. (Laughter) And in so doing you learn something new. You learn how to operate the equipment, whatever you choose to do Facebook, but then you're now interacting with people in terms of ideas and sharing ideas. That happens both in the classroom and after the classroom.

Many of you probably remember having discussions after your philosophy class, if you ever took a philosophy class, or sitting as a group trying to solve that awful calculus problem. Right? The social interaction stimulates the mind and the reverse and one of the interesting things is that it also stimulates other positive aspects of brain. As you feel good about yourself you tend to release endorphins. That happens when you exercise. Endorphins are good for the brain. They make you feel good. So you're remodeling your brain structurally as you do social activities such as taking a class or playing a round of golf with buddies or bridge club. Those things all add the social aspect,

but there's a mental aspect as well because you have to keep your mind sharp in order to be successful in those activities.

LVE: So I'd like to be able to have just a little bit of time before the Q&A to talk about clinical trials because we want to give you guys chances to ask questions. So Greg, tell us a little bit about clinical trials and why they're important.

GC: Clinical trials, first thinking broadly, are any kind of trial involving human beings. That may simply involve seeing and observing people over time or it may involve some type of intervention and that may be medication or otherwise. For example, you could be in a clinical trial where we're studying exercise and its effect on memory. Most of the time what we're thinking about are medication trials. So for example, what I've been most involved in are stroke and Alzheimer's Disease where folks will get a medication, it's an experimental medication, but the goal is to see if that medication can improve the condition that we're trying to treat.

Now, most trials are largely the same. Most trials will involve folks who are already being treated in some fashion with the treatments that we know or think are effective.

Then they enter into the trial and they'll be randomized to one of multiple arms, we'll call them. So for example, let's say everyone gets a pill to take. Let's say they're taking a pill once a day. In some cases that pill may be a placebo like a sugar pill. In other cases it may be a particular dosage of the medication that we're studying. We're usually blinded so that I'm not going to know what a person is taking and they're not going to know. That's important because at the end of the trial we want to compare how people did on the treatment versus not on the treatment.

It may or may not surprise you to know that many people who are even on the placebo show some improvement during the trail which is great, I'd like everyone to improve, but we need to really be able to compare and find out are people doing better on the treatment. Of course, the hope always is that the folks on the active medication will improve, unfortunately, in many cases we don't see an improvement. That's still important knowledge for us to have. Unfortunately in only one case, so far for me, the people that are on the active medication don't do as well as the people that are on placebo. Sometimes it's actually good to be on the placebo.

Typically, we've got enough background information to know that we think a medication is going to be promising, but it is important to understand that these are experimental studies. So if we already knew the answer we wouldn't have to do the study. We don't know for sure if the medication is going to work. These studies, I think, are of critical importance. Just put very simply, there's no way we can move forward from a clinician's standpoint without these trials.

If we don't do clinical trials we are never going to develop better treatments than we have right now. We just can't move the field forward clinically. We can't translate all of the things we're learning in the lab to the clinic without doing these trials. Even the trials that turn out to be negative, that don't show a benefit, those are still important because that helps direct us toward what directions we need to pursue in the future. So not to get overboard or get on my soapbox too much, but I think it's very important that we do these trials in order to move forward. We all know that we need to have better treatments for all of these conditions.

LVE: Okay. Well, I'd like to thank the panelists.

We're going to move onto the question and answer period to give you guys a chance to ask questions of the panelists. The way we're going to work this is there are microphones there and there. You guys can line up behind the microphone. If you can't get to the microphone we have some volunteers who will bring the microphone to you. Just to keep us on schedule we ask just one question per person please. We'll try to keep our answers brief so we can get as many questions answered as possible. Then we'll do this for about a half an hour or so before the wrap up.

FS: While Dr. Van Eldik gives up her microphone to the crowd, it's about to be stolen from you. (Laughter) Let me mention a few things about clinical trials that people always ask. Dr. Cooper and I have worked together with clinical trials for several years. The key element is if a person has a disorder a clinical trial gives them a new and possibly better chance at treating their disease. That's a lot of the motivation. But what's important about is, as Dr. Cooper said, we need to know if the medicine works or not. And what often happens is we have a good idea. We say here's the mechanism that leads to this disease or this symptom. Here's a treatment and we test that treatment in

animals. In mice, in rats, cats and dogs, whatever model is the best and we see that, gee, the medicine works here.

Then we go out and we give the medicine to people who don't have an illness. It gives us information about how the medicine moves through the body, what are the side effects and so on, and then we give it to the people with the disease. It's usually a small group to start with because we want to know several things. Can we tolerate the medicine? In other words, when you give somebody that pill or that infusion can they tolerate it?

The second thing is is it safe? Are there side effects that we didn't think about or didn't know about that jump out? Something as simple as a rash. You know, a lot of folks in this room probably have an allergy to something, some medicine. So we're looking at safety. Safety, safety, safety, safety is the big push early in clinical studies.

Then we do a larger study to see if the medicine works. The bad news is, because no matter how smart we think we are, no matter how good science has been up to this point, and no matter how many animals got better it doesn't always

work in people. So some scientists walk around and we jokingly talk about Alzheimer's Disease and what we call Mouse-heimer's Disease. (Laughter) We used to say there's no animal model for Alzheimer's Disease. I think that's still the case. We're closer, but it's not a perfect model. We can change the genetics of a mouse so that mouse produces the proteins that we see in the brain of people with Alzheimer's Disease.

So you'd naturally say that's Alzheimer's Disease in the mouse. That's Mouse-heimer's. They have the same abnormal proteins so we can test all sorts of treatments on those mice and make the mice better and we do. The problem is, it's like the old novel, "Of Mice and Men." People are an awful mess compared to mice. We're much more complex and we do unexpected things so the medicines don't always work. That's where the clinical trials are important. As Dr. Cooper pointed out, sometimes people don't do well on the new medicine and sometimes they do.

I'll give an example that he and I both shared. It's rare. We haven't seen a lot of this, but it's rare and it's exciting when it happens. We did a study combining two medicines and

one lady whose daughter was going to place her in a nursing home, she had Alzheimer's Disease, this is what, now, ten years ago would you say?

GC: Probably eight or ten years.

FS: Eight to ten years ago. This lady was lucky. She got on the active medicine and the active medicine worked to some extent. It didn't cure her, but the combination of the medicines she was on kept her at home for close to four years. She still lived by herself for close to four years. The bad news is she developed a case of pneumonia and that was the tipping point. The medicines could no longer protect her and the disease, of course, overtook the benefit of the medicine.

So now we're looking at what kinds of clinical studies do we do? And I think this is important and you should all know this. One, we've been targeting the diseases that we talked about. We target Parkinson's. We give a medicine, boost some brain signal, people get a little bit better. We target Alzheimer's. We give a medicine, we boost the brain signals, they get a little bit better. We're treating the symptoms.

Now science is starting to look at prevention.

Okay? So when people have mild cognitive impairment do the drugs we use to treat Alzheimer's Disease help them? Well, not in the long run. They get a little bit better for a while, but in the long run it doesn't seem to help because it's not treating the disease. But then there are people such as Dr. Brightner(?) and others who have said let's treat the mechanism. Dr. Brightner put together a study to look at NSAIDS, non-steroidal inflammatory agents to see if it could prevent Alzheimer's. We're doing a study based here at Sanders-Brown that's looking at antioxidant vitamins to see if it can prevent or reduce the occurrence of dementia. There are other studies that are being planned looking at prevention from different angles. That's the exciting part. When I started in 1981 at Duke, which Dr. Van Eldik and I share in common, Duke, right?

LVE: We won't say that. (Laughter)

FS: Okay, it's safe. Wildcats. Thank you. (Laughter) Well, you just get rid of two letters. It's the same thing. (Laughter) Blue and white? I can't tell the difference.

LVE: Okay, Fred, move on.

FS: Sorry. (Laughter) I just had Wildcats waved at me. The key is prevention. What works? What mechanism is

involved? Can it be through treating diabetes? Can it be through treating heart disease? Can it be through treating inflammation? Can it be through directly treating the protein we see in the disease? Those are the important studies. So you'll see more and more about prevention because people believe that once the disease is present the horse is out of the barn. So that will be the thing about clinical trials.

Without volunteers, and we have volunteers in this room, I won't point any of them out, who are willing to get poked and prodded by people like me and Dr. Cooper and Dr. Wilcock to an extent, they provide that information. They provide us with information about what's normal or what's usual about aging that we can then use that information to test ways to prevent disease. That's the exciting part. So you actually deserve the credit. The folks out here, your interest alone deserves that. I see microphones so I'm going to be quiet.

LVE: Okay. Does anyone have a question? Over here?

W: (Inaudible) the Donovan Scholar's Program. I expect that people are not aware of what that is. So if you could

explain what the Donovan Scholar's Program is and who it effects?

GC: I'm not sure I know entirely. It's a program through the university that offers classes for senior citizens. There's a wide range of them. Sometimes they're involved just in the classroom. Sometimes they involve field trips. My father is an historian. He taught a class at Shaker Village, for example. I don't believe that it's aimed toward any particular degree. It's just aimed at people who have an interest in taking courses. I don't know any other details about it.

FS: Well, it's run in part by Mike Smith at the university. There's a website. Some people will take courses and some will then continue to take courses and get degrees.

W: That's right.

FS: So you have both options. You can be as involved or less involved as you would like.

W: It's for folks over 65. Donovan was President at Eastern and Donovan was President at UK. Whether these are the only two institutions, I don't know, but you can take a course for $5 if you show that you're 65 or older and you do that with a driver's license.

GC: At one time it was relatively unique to this area. I don't know if other schools have picked up on it.

FS: They have. There's a Lifelong Learning Institute that's kind of national. Other schools have picked up on it, but the Donovan program is one of the oldest.

M: How are you differentiating Alzheimer's Disease with dementia? Are they the same or are you differentiating them?

GC: Sort of yes and yes. Alzheimer's Disease is a cause of dementia. It's the cause, depending on how you look at it, from 50 to 80 percent of the time. So dementia would be a broad term just describing the whole syndrome. Alzheimer's Disease is the cause of that much of time. We try to come up with the cause of the dementia. So for example, I might see someone next week and determine, yes, they have a dementia, but it's not because of Alzheimer's Disease. It's related to stroke or it's related to frontotemporal dementia or Lewy Body Disease or some other cause. So I guess the bottom-line is Alzheimer's Disease is the most common type or cause of dementia. Does that answer your question? I don't even know where you are. (Laughter) I can't

quite see very well.

W: Following up on that. I do have two questions. One is clarification and one is a little bit more detailed. So you've mentioned frontal lobe dementia, vascular dementia, Alzheimer's – can someone just kind of distinguish between those in terms of the meaningful differences and behavior treatment? That's my clarification question. The other is genetically my father has been diagnosed with both vascular dementia and Alzheimer's and his two brothers died of Alzheimer's related things so half of me is heading in that direction, I assume. My life is quite different than my father's and my uncle's so I'm wondering about how much does genetics determine things? I exercise. I am a professor, etcetera, so can you speak a little bit about that? Thank you.

FS: I can try and I'll do it briefly. If we're thinking about different types. So Alzheimer's Disease, for example, is most often going to affect recent or short term memory, cause a kind of forgetfulness. I'll repeat myself, I won't remember things that happened recently. Commonly that may also affect language, my ability to come up with words, express my thoughts, it may affect my sense of direction. Those are the things that we're

thinking about most commonly, at least early on with Alzheimer's Disease.

Then there's frontotemporal dementia and that can be about as complicated as we want it to be. When I look at that I think of folks that may have fairly marked difficulties with language and perhaps not with memory or other aspects – now all of these things are relative. Then we also often think of those folks as having very prominent personality changes. So for example, someone who had previously been very shy and retired, now they're at the grocery store making lewd gestures to people. They're spending their life savings. They're doing things that are just out of character for them. You might say they've lost their filter. They're just disinhibited. So you would often think of that.

Now vascular dementia I think opens up quite a can of worms. I think the truth is, as smart as we like to pretend we are in medicine, our understanding is relatively poor here. It would be easy to say and this is what we used to say that vascular dementia meant that someone had a stroke and related to that stroke they developed problems with language, memory or cognition in some way. I think it turns out that's really a minority of

the cases. Very often vascular dementia is there and we're perfectly unaware of it. Very often when we say someone had vascular dementia the real answer was Alzheimer's Disease or when we say Alzheimer's Disease the real answer was vascular dementia or maybe it was both. I would have to admit that I don't think we're smart enough to separate that out. There are other people who are more competent than I am.

Often we would think with vascular dementia that there would be almost a slowing down. That if you ask me to remember something I would remember it, but it may take me much longer than it did before or if you give me some cues I might be able to pull it up better than I could before. So I have clear impairments in my memory and thinking, but it's almost as if just the wheels are grinding a little bit slower. Now that's an oversimplification, but I think that might be true.

Now if we think about the genetic component in my mind that's even worse. I think that we do clearly inherit a greater or lesser risk for dementia in the same way, in my little mind, that we inherit a greater or lesser risk for stroke, heart disease, high cholesterol, high blood pressure or anything like that.

I have a very difficult time putting a number on that. I do think, I can't support this as well as I'd like, but I do think very often that may indeed be related to our vascular health. So if we have relatives – all my relatives grew up on farms eating cornbread, beans, and terrible food probably for them with no exercise, smoking, everything they shouldn't be doing. So I think by having a healthier lifestyle – eating better, not smoking, not doing all of those bad things – I think it's very reasonable to think that we are lessening, we are ameliorating that risk. But to put a number on it, I'm not smart enough to do that.

DW: And with respect to the genetic issues, I think we know now there are some clear genes that are inherited. They're on from birth, they're your genes and you have them. There's also this vast pool of genes that you inherit, but whether they get turned on or not is determined by your lifestyle. If you have an inflammatory response in your life that may turn on some genes that you inherited, but if you don't have that happen in your lifetime then those genes stay turned off. So you know, this is getting down to a level of genetics that we haven't really considered before and a level of inheritance that isn't just you

inherit this so you have it. You inherit it, but it's up to you whether it gets turned on or not. It sounds like, you know, you exercise, you eat well, you're doing the right things. You know, you may have inherited potentially a chance to turn it on, but it's up to you whether you turn it on or not. So that's kind of our understanding at this point.

LVE: Let's go on to the next questioner.

W: Well, my question was very similar. I had a mother who had dementia and she died about five years later after being diagnosed with it, but I'd like to go onto the next step of that where you were talking about apolipo(SIC) 4 little thing gene. (Laughter)

LVE: Just call it ApoE.

W: Thank you. But is that something that has a parent, some close relative that has been diagnosed with this. Of course, we've lived with it as caregivers and know what's going to be happening. To get a feel from this particular test, can you get a test like this and know something that might be going on?

DW: So everybody has what we call an ApoE genotype. So you can have a two, a three or a four. And you

inherit one from each parent so we'll say you're a two/two, you're three/three, you're a three/four, you're a four/four. You get two numbers. If you carry a four you have a slightly increased risk of Alzheimer's Disease. If you have two fours, so you're a four/four, you have a greater risk of Alzheimer's Disease. Even a four/four doesn't guarantee you will get Alzheimer's Disease. Okay? But it does increase your risk.

W: And is there testing for this now that's available to people who have family members like this and are very worried about it?

GC: There is genetic testing. It's commercially available.

W: Affordable and insurance paid? (Laughter)

GC: No, it will not pay.

W: Okay.

GC: And the sort of governing bodies that issue opinions about this clinically say that we should not be testing people for this. Really because we don't know what to do with it. So I would be opposed to testing. Other people may not feel that way.

FS: But I think it's safe to say that if you have the disease in your family your risk is above that of somebody who doesn't.

W: What's normal risk thought? You've always talked about it's higher than, like if you're in your fifties or normal across the board. I'm sorry.

FS: Excellent question.

W: I'll walk away.

FS: No, that's important information. Everybody is going to need to hear that. So what is the incidence of this disease? Before the age of 62 or 63 it's near zero. You have to have a very specific genetic mutation on specific genes to get Alzheimer's before you're in your sixties. If you're in your sixties it's about one percent. That's the average risk averaged across everybody. If you're in your seventies, depending on who you believe, three percent, eleven percent, and it goes up when you're in your eighties. Some people argue 40 percent in your eighties. There are other diseases, obviously, that make these numbers loose. So that's your average risk. You turn 62 or 63, your risk goes from near zero to about one percent and then continues to go

up as time goes on. If you have Alzheimer's in your family your risk is higher than that average.

W: (Inaudible)

FS: We don't know for sure, but yes. You can do the math. You can say there's an additive risk. That's what these epidemiologic studies have done, these studies of large groups of people. They try to estimate the risk.

LVE: Okay, let's move on. The next question?

W: First of all, thank you all so much. This has really been fascinating. You might have already touched on the answer to this with talking about something being turned on genetically. You mentioned that if you at some point in your life had had depression, and I'm assuming, of course, clinical depression, that your risk would go up. Are you talking about untreated depression? Or what if you got treatment? That's my question.

FS: Treatment makes no difference.

W: That's what I thought. (Laughter)

FS: That's the bad news.

LVE: Next question over here?

W: Hi. Thank you all for the great discussion. It was really informative. My question is involving this apolipoprotein again. Is there any current evidence where a person has the gene and even the gene is turned on presenting with increased levels of the protein itself, but still exhibiting no symptoms? If that occurs can you theorize why? Is that lifestyle related as like with prevention of having the gene turned on at all?

DW: Well, you know, ApoE is just a risk factor. It's like high cholesterol for risk for heart attack. Even if you have high cholesterol doesn't mean that you are going to get a heart attack. Same thing with ApoE 4. If you have the ApoE 4 gene, even two of them, it doesn't mean you're going to get Alzheimer's Disease. It just means you have a higher risk. So, yes, there are people who we've had, we've looked at the brains of these individuals who do not have Alzheimer's Disease. They are ApoE 4. So it isn't a guarantee of anything. It's just the risk factor.

W: Even after they present with high levels of the protein being expressed?

DW: Yes.

FS: The important question I think you're asking

is because you have an E4 gene when you get Alzheimer's is it worse or more progressive? The answer is no. Whether you have that gene or not does not affect your disease course. It affects your risk of getting the disease, but not the course once you have it. Does that answer the question?

W: Yes, mostly. I just wondered, let's say once you've already presented and you're producing a lot of the protein, the gene is turned on.

FS: Well, the gene is always on.

DW: This gene is always on.

W: Oh, the gene is always on.

FS: Always on.

W: Oh, I see. Okay, okay. Thank you.

LVE: Question over here?

W: Hi, yes. I have a question that's two-pronged, but both prongs concern the rate at which oxygen is absorbed into the brain. Is there any evidence that suggests that strong fragrances, perfumes inhibit the rate at which oxygen is absorbed by the brain? And also if oxygen is so good for the brain should we all go out and buy oxygen machines to sleep with at night?

(Laughter)

LVE: Okay, Fred, you opened that can of worms.

(Laughter)

FS: Let me answer the second part of your question first. So maintaining homeostasis is the body's job. Maintaining the appropriate oxygen levels at any given level of activity is key. The brain uses a lot of oxygen. The problem with just going out and getting an oxygen ten and sleeping in it is that you still may not absorb the oxygen if you have respiratory issues that block your body's ability to do that. The other problem is that oxygen may be a two-edged sword. Oxygen is necessary for energy in the body. It's necessary for lots of activities, but at the same time one of the biggest mechanisms, one of the biggest chemical processes that is part of aging is reactive oxygen species. Our body chemistry makes mistakes, chemistry then creates a free radical, a very hyperactive oxygen molecule that becomes like superglue in the body.

Some of the research done here at UK by Dr. Butterfield shows that the abnormal proteins that we see in Alzheimer's – the beta amyloid that lead to the senile plaque that

we see in the Alzheimer's brain – those proteins stick together because of reactive oxygen species. So oxygen enrichment is probably not going to make a difference. In fact, we've tried to treat diseases through oxygen enrichment. We've put people into chambers, boosted the oxygen level, it didn't do much. Now that's different if you try to treat carbon monoxide poisoning. Now the question of absorption. I know that there are people who do research, I've not read any of it so I'm going to turf that question. (Laughter) That's why it's good to start sometimes.

DW: And now I'm going to turf the question. (Laughter)

GC: The wonderful thing in medicine, it shouldn't be shared, but we learn early in medicine if you don't know the answer be really confident. (Laughter)

DW: I'm sorry, I'm mean scientifically based on my knowledge of the olfactory system I don't think that absorption of oxygen would change with that.

W: I'll Google it. (Laughter)

DW: Yes, you may want to do that. I don't know.

W: Thank you.

FS: Pull out the smart phone.

LVE: Go ahead. You can ask the question.

GP: My name is Gloria Parker and these questions are for Dr. Gregory and Dr ...?

LVE: Fredericks.

W: Fredericks.

GP: I have a sister that's had a stroke and she's been very independent all of her life. We've tried to get her to go to a speech therapist. She doesn't want to go. I want to know what I can do to help her? She does her own showers, she takes care of the house. She knows words. She recognizes people's voices. She knows them and she can answer "Yes," "No," and things like that, but she can't do sentences. I want to know what I can do to help her to make up her to go and have these things done? And also, I want to know how I can get into the program to have myself checked?

GC: I'm not sure I have the answer. Can you say why she is unwilling to go get help?

GP: She's been independent all of her life.

GC: That's just her personality?

GP: Yes.

GC: Okay.

GP: She's been independent all her life and she thinks she can do this herself. And you know, you need help sometimes.

GC: You do. And I don't really have the answer. What I would try to do is impress upon her how much improvement she could potentially have. It sounds like from what you're telling me she could benefit potentially greatly from working with a speech therapist. Perhaps her language won't get perfect, but she can improve her ability to communicate – to express her ideas, her needs, her wants, to interact with people. I guess that's what I would try to do. Impress upon her that things can get a lot better if she will do that. Now, unfortunately, just the opposite is true if she refuses to get help. There is at least some risk that things could get worse over time. Now, I wouldn't overstate that, but I think that's possible.

GP: I told her that I would go with her to the therapist and she nods her head and says yes.

GC: If you just made the appointment and you

said, “We’re going,” would she go?

GP: She probably would.

GC: That’s what I would do.

GP: What gets me. This is a time that she should be enjoying life.

GC: Yes.

GP: Because she’s put two sons through college and it just hurts me to see it.

GC: Well, that’s what I would try now.

GP: Okay.

GC: Fred’s interpersonal skills are far superior to mine. (Laughter) He might have a better ploy.

FS: So two suggestions related to that. And not having met your sister and spent time with her I can’t say. This is all conjecture. First off, stroke often affects how we feel and it’s not uncommon to have low levels of mood changes related to that. Also, depending on where the stroke was it affects our ability to understand ourselves, our insight. So these are hard to overcome. I think if what you say that if you make an appointment she’ll go, start out with her doctor. The first thing a speech therapist will do

is do an evaluation so that they can say, “Here’s what we think you’ll gain or you won’t gain.” If she would go to that step and develop that relationship with your assistance and her doctor’s assistance that’s the first step. The other way to do it is there are home services and sometimes the rehab hospitals will do a home service which makes it easier and more acceptable. But I’d start with her doctor. Go ahead and see if she would agree with you if he sets up an evaluation. That’s the first step in either regard.

GP: How can I get into this program?

FS: There are lovely people in back that volunteer with the Aging Center. Chat with them. There’s the table out there. You can chat with any of them and they’ll give you all the information that you need to hook up.

GP: Thank you.

FS: Well, thank you.

LVE: Question here?

W: Having your memory tested. Hi, Dr. Cooper.

GC: Hello. (Laughter) Wait a minute. What’s going on here?

W: I’m a patient of his of sleep apnea. It’s

working great. Anyway, you mentioned having your memory tested. Where would one go to have this done?

FS: Come see me.

W: Okay. I'll come see you.

LVE: They'll have all the information out at the Sanders-Brown table and we do regular memory testing.

W: Great. Wonderful. I'm sure it's in my packet then. Thank you.

LVE: It probably is. Over here? A question?

W: Oh, goodie. Thank you so much for being here and I hope this will become a regular event for those who are listening. It would be fabulous. I have a question about coconut oil for Alzheimer's. It's in the news. So I realize I checked Snopes(?) and this doesn't meet the criteria for good research. It's anecdotal. It's just one person. So is there any interest in the scientific community to do good research on coconut oil? If not, how could the public encourage the scientific community to test this?

DW: So usually what happens with these things is they do get picked up.

W: Okay.

DW: You just don't hear about it.

W: Oh, I want to hear about it. (Laughter)

DW: So I can almost guarantee you that there are scientists out there who are testing this in mouse models trying to get mechanism of action, trying to get whether this is really something that's going to work or not.

W: Sure.

DW: Trying to find out what in the coconut is causing this to happen. Can we make it a capsule instead of coconut oil? Can we identify what the compound is? The trouble is what happens the media gets a hold of these initial reports and they put it out there and then you never hear about it again.

W: Right.

DW: Right? And so then you never hear about the ten or fifteen studies that come out either proving it or disproving it or anything else. So yes, everybody does follow up.

W: Okay.

DW: There's a conference that the scientists go to every November called The Society for Neuroscience Conference. There will be posters there I can almost guarantee you where

people are showing some preliminary data on the coconut oil that will either prove or disprove that, and will be looking at the effects that it's had on Alzheimer's pathology in the mouse models.

W: Great.

DW: And whether it's working or not. So people do follow up on those things.

LVE: And actually, it's interesting that you should bring up coconut oil because that is in our Sanders-Brown newsletter. The next issue that's coming out that I was just proofreading, there's an article about coconut oil.

W: Oh!

LVE: So you will be able to read all about it in our next newsletter.

W: Thank you.

LVE: Over there?

W: Dr. Wilcock, you mentioned early that in your lab you were doing work on inflammation as it relates to Alzheimer's. My question is how does the inflammation of rheumatoid arthritis play into this or not have any role to play?

DW: That's a very good question and actually both

myself and Linda, we both work on inflammation in Alzheimer's Disease. So there's a lot of kind of anecdotal reports out there about rheumatoid arthritis, whether it increases or decreases your risk of Alzheimer's Disease. There are not that many people out there that have arthritis that haven't been treated with something. So everybody has usually taken drugs for their arthritis. You've treated the arthritis. So most of the reports out there are related to the drugs that people have taken for the arthritis long term and the effects that those drugs have had on risks of Alzheimer's Disease. So there have been a lot of studies done on the use of NSAIDS, non-steroidal anti-inflammatory drugs, and whether they prevent the onset of Alzheimer's Disease. So NSAIDS would be drugs like your Advil and ibuprofen. I don't know what the trade name is.

LVE: Tylenol.

DW: Well, Tylenol.

FS: Yes, any of the NSAIDS.

DW: Any of the NSAIDS.

FS: Even aspirin.

DW: Aspirin. So all of these are classed as NSAIDS. There were a lot of epidemiology studies that looked

back at people who had taken NSAIDS for a long period of time for conditions like arthritis and found that it looked like they had a decreased incidence of Alzheimer's Disease later in life. When a study was designed to addressed this issue where they designed a study to put people on NSAIDS with the goal of studying whether it did preven their Alzheimer's Disease the results were a little more grey, let's say. So instead of finding that it prevented Alzheimer's Disease, in some cases it slowed down the way that people developed Alzheimer's, but in some cases people actually got worse quicker. So that study was stopped prematurely in some cases for side effects, but in other cases the results weren't showing what people wanted them to show. So that study is being continued to be analyzed. I'm kind of waffling.

The bottom line is inflammation is emerging to be a very complicated issue. So that's one of the things we're studying in the lab – how different types of inflammation can be targeted for Alzheimer's Disease. So there may be a subset of people that can be targeted with NSAIDS, but a subset of people may not necessarily benefit from them. So really as far as arthritis goes it's probably the drugs you're taking for the arthritis that may

impact Alzheimer's Disease rather than the arthritis itself.

LVE: Okay. Over here, a question.

W: Can you hear me?

LVE: Yes.

W: I hope I can remember. I've been here so long. (Laughter)

FS: That's part of the test. (Laughter)

W: My husband developed mild dementia in his seventies. He's 85 now. It followed an injury to his frontal lobe – considering jugement and so forth. He's now 85 and we've just been to see Dr. Cooper recently. He's very pleased with his IQ, his answers, and all, but now that I've learned some things I have questions. One is about vascular dementia. I just realized is that why he's beginning to need me more and more for his daily activities like getting dressed, I shave him, sometimes I help with his bath. Of course, I've always served his meals and everything. Is that what you call vascular dementia? With that in mind and the fact that it happened after an injury, do my children, and we have young adults in their thirties and forties, do they have to worry about having dementia or Alzheimer's?

GC: I'm going to speak sort of in generalities and then if we need to speak in more detail separately we can. In general, if someone is needing more help with their activities and daily living that you can't always give the same answer for everybody. So it could be related to vascular disease, it could be related to some other degenerative condition like Alzheimer's Disease or otherwise. Very often these conditions coexist. So I don't think it's going to be possible in a general to give a more specific answer. We can always talk separately and in more detail if we need to.

In terms of risk to children, I think that's also a difficult one and it's often going to depend on the individual. So let's say if one of my parents had dementia related to a head injury I'm not sure that that would necessarily have a big impact on my risk of dementia. Alternative, if they had stroke and that led to dementia, well, that may affect me because I also had an increased risk of stroke as well. If they had a combination of head injury and they developed a progressive dementing illness on top of that like Alzheimer's Disease that would put me at increased risk. Now, I don't think I can put a better number on that. So it

really depends on the mechanism, I think, as a general rule. In most cases if we have a first degree relative, a sibling or a parent with dementia, that is going to increase our risk, but it's hard to take it much father than that. Do you all agree?

W: Thank you.

LVE: I'd like to just have these last three questions so we have time for the final comments.

W: Thank you. I had read one of Dr. Perricone's books that suggested that acetyl L carnitine with alpha lipoic acid affected the workings of the brain. And I asked two neurologists before I started to take it and I was just amazed in less than two weeks I could tell my brain was working faster. I was just wondering what supplements and over the counter things that you all are working with? I know research takes money, but what are you all finding out besides something like that that can really help us nutrition wise or supplement wise that would be available?

FS: So I'll start and I'm sure everybody will answer with their opinions. So we've studied supplements for quite a while. Based on those studies that suggest increased risk, no risk, you know, based on that. So far the supplements haven't

done much at all in careful controlled studies. That's probably due to the fact that each individual is unique. They have unique needs nutritionally.

So I'm going to mention a couple of general things that scientific community seems to agree on. One of those is if you're worried about reducing your Alzheimer's risk you want to do the best you can from a dietary standpoint you follow a Mediterranean diet. The evidence suggests that a Mediterranean diet reduces your risk. How does that work? We're not sure, but we think it has to do with the type of fats that you ingest.

In terms of over the counter supplements, I'll give you an example of one that failed. Ginkgo biloba was big and hot and everybody was taking it. It was over a $2 billion industry in this country alone. Then a little study came out, it wasn't very well done. It said ginkgo makes people with Alzheimer's better and so the large study was done. About $70 million later we discovered two things. One, it did not prevent Alzheimer's Disease. Two, if you took it you actually had an increased risk of small strokes. Okay? Not a good outcome. But people still take ginkgo and it's still a big business.

So the issue of supplements, and this goes back to coconut oil, there are theories behind why the supplement might work, but for each person it's unique. You need to talk to your doctor if you're going to take supplements. If you see your doctor and you're taking supplements talk to them about the supplements. Those can interact with prescription meds and based on your health situation can cause problems.

Even Vitamin E which for a long time was the Alzheimer's treatment. Vitamin E showed that you could slow Alzheimer's from the moderate to severe stages over two years. So everybody said take Vitamin E. It makes sense. Stop oxidative stress. Maybe it will prevent Alzheimer's Disease. What they neglected to say from that one study that it showed it slowed progression was the risks. Greater risk of vascular events in the brain, small strokes, because of the oils that are used to provide the E. Greater risk of infection for reasons we don't know, and so on. There's recent data from a prostate cancer study that suggests that Vitamin E actually increases the risk of prostate cancer. Not a lot, five percent.

So there are pluses and minuses to every

supplement. So it's very important. We don't have all the information. Talk to your doctor. I think it's neat that you decided to take those and they worked for you, but they might not work for the next person. And I could not tell you the side effects of doing that because there are no studies to inform us.

LVE: Okay, over here, please?

M: Yes, I'd like to hear a few words about the possible therapeutic effects of humor and laughter in all of this?

LVE: Of what?

DW: Of what?

FS: Of humor and laughter.

GC: The therapeutic effects of humor and laughter. (Laughter)

LVE: Wonderful.

GC: This is really pathetic. I think it's great, but I have no idea. I can't support that. I don't know how it would be beneficial even though I'm a strong believer.

DW: Endorphins.

FS: So there are studies on humor and laughter, as well as prayer in medical settings. Controlled studies. I haven't

seen the outcome of those involving prayer, but the humor and laughter actually seems to help some. It helps with recovery. Nobody to my knowledge has studied humor and laughter for dementia risk because it's hard to measure. How funny are you? (Laughter) I can tell you that I think I'm a riot and I should go on tour. My wife thinks every one of my jokes stink. (Laughter) How funny am I? Not very funny. But it's an area that's important. It does affect the brain. The creativity and humor, making a joke, finding the associations – that's important. That may make brain links. Those are the important aspects, but nobody has studied it to my knowledge very, very carefully. But yes, there is potential from what I've seen.

LVE: Yes, last question over here.

M: I finally made it. (Laughter)

LVE: Saved the best for last.

M: It appears the ladies have all the problems and men don't. (Laughter)

LVE: That's because you have humor.

FS: That's an inflammatory statement. (Laughter)

GW: My name is George White. I'm 85 years old

and a lot of people think I'm about 70, but they don't know what's going on in my body. I've had high blood pressure for 30 or 40 years. It's stays fairly close to what it should be. I don't have a cholesterol problem. I have essential tremor. Now you all haven't touched on that. I'm diagnosed in my right hand and I take primidone for that. Well, this lady ahead of me answered one of my questions. It was over the counter things to help your memory and there's really nothing from what I understand it is going to do it. But I have moderate neuropathy in my legs and feet and I take medicine for that. All these prescription drugs have 20 or 30 things that might happen to you and scares you to death to even take it. I know they're protecting themselves insurance wise I'm sure, but it makes you wonder whether you're just buying a pig at a poke. (Laughter)

FS: Do you have relatives that are lawyers by chance? (Laughter) You know about this, huh?

GW: No, but I would be a volunteer if you need one. (Laughter) But I keep plugging along with medicines and everything. My mother died at 97 ½ with Alzheimer's, but I don't think it was really Alzheimer's. She had fallen when she was in her

early nineties and it turned out she had some blood between her skull or brain or something. So the day we had her scheduled to come to St. Joseph's Hospital she wouldn't go. She just flat out wouldn't go and I was willing to have her knocked out, but my two sisters wouldn't let me do it. (Laughter) I was going to bring her over anyhow. But I really think that's what caused her to be diagnosed with Alzheimer's.

FS: Well, you point out a very important thing that we have not yet talked about yet in terms of risk. And that is head injury.

DW: Yes.

FS: Head injury is a very important risk at any age and it's been in the news lately for football players, as you know, because of multiple concussions. Think of Muhammad Ali who took many blows to the head. Every time you get hit in the head, every time you get a concussion or get knocked out that means that your brain is addled, to use the old term. Something is affecting your brain. And even though we're learning about this it turns on different brain repair mechanisms that may or may not work or go wrong.

One of the things that we know is that a significant head injury even without a subdural hematoma, from you say it sounded like, can increase your risk. Part of that is related to brain chemistry and brain proteins. Because the beta amyloid, the amyloid precursor proteins that are in the brain tend to up regulate after a head injury. It's part of the repair process. So it's not unusual to hear that a person has had surgery and has had a fall and suddenly you see memory problems. Is that because it's throwing the switch, so to speak, or it's been there? You've been teetering on the edge and the health injury or the brain injury pushes you over. That's a very important point. The good news for you is longevity. You've already exceeded that.

GW: I'm on borrowed time. (Laughter)

FS: Oh, I don't think so. I don't think so. It sounds like you've got at least another two decades.

GW: I'm hanging in there. You did answer my question and the other lady too. That there's nothing really on the market that's going to help you remember things better. I just need to get more exercise. I'll get off of here and we can go home. (Laughter) (Applause)

LVE: Okay. So we're going to wrap up now by having each of us give a very, very, very brief summary so that you guys can go home. And I'll start. I just wanted to really say thank you guys for coming. This has been very fun. It's been fun for me not having to answer all the questions and just being able to shoot questions at the panelists. I'm very pleased to have moved here to Kentucky a couple of years ago and to be the Director of the Sanders-Brown Center on Aging and the Alzheimer's Disease Center at UK. I would encourage all of your who are interested in volunteering or even just to find out more information about what we're doing to take some of the materials or look on our brand new website that is finally looking good. It's centeronaging.uky.edu. I think there's a lot of hope on the horizon. I think that we all know, at least now I've learned a lot about how to stay sharp as we get older.

GC: I'll be very short too. Kind of building on that, I certainly want to thank you all for coming here. I want to thank the Dana Alliance for helping organize this whole thing. From my perspective as a clinician, until the real scientists are able to provide us with the cure for some of these diseases prevention is

obviously our dream. And I think the most realistic aspects we have are to become better educated and do some of these lifestyle changes that, at least in my mind, will help prevent folks from developing dementia down the road. This is where it starts, I think. Becoming informed and educated. I think we owe folks that are organizing things like this some real gratitude. (Applause)

DW: So I just want to say thank you all for coming out and listening to us. I hope you all go away with something from this. As a scientist it's great for me to come out and meet you guys and talk to you, and tell you all that we're trying to work on this problem. We're trying to learn about not only Alzheimer's Disease, but aging and how we can promote healthy aging, how we can prevent some of these diseases and how we can treat them. Without our research volunteers, without all of your help we can't do what we do in the lab without being able to come back to our research volunteers and take what we learn in the lab, and be able to put that into practice, go to our clinicians, and use that. So thank you to all of our volunteers. Thank you all for making me feel so welcome. I've been in Kentucky for 18 months and it's really been great. Everybody in Kentucky makes me feel so welcome.

So thank you. (Applause)

FS: You get the final word though, right?

LVE: No, you get it.

FS: Oh, I get it.

LVE: Only if it's brief then I'll have to cut you off.

FS: Uh oh, I'm in trouble now. (Laughter) So I can only reiterate what my colleagues have said so far. Everybody here is great. I think that the key element is to retain your curiosity. Keep learning. Those are the keys. Take advantage of the knowledge that is unique in many ways to what we have here in Lexington. It's an under advertised resource. The Sanders-Brown Center on Aging has been around since 1979 and has done unique things related to brain aging. It's one of those gems, just like Kentucky is in the national scene, that is under recognized and underappreciated.

The best example came from a meeting I went to in Washington involving some scientists years ago and they had just discovered Blanton Bourbon. They were all excited about it. (Laughter) And they were paying like $50 a bottle. They told me about this. I said, "At the next meeting I'll bring some if

you'll give me the difference in price." They said, "What do you mean?" I said, "Well, where is Blanton made?" They go, "Well, somewhere. Tennessee or somewhere like that." And I said, "No, no, it's made in Kentucky and I can get it for 20 bucks a bottle," at that time. So I probably got a ticket for bringing all that. But the key is there are under recognized resources here and nationally.

Keep curious. Read the websites, but we critical. Always be critical. I'll pick on coconut oil, I apologize. So coconut oil made one person better, we think, but how many people are advertising coconut oil in different variations? No, no, it's not just plain coconut oil. It's virginal coconut oil only from the Island of ... that did it. Why? They can charge you more. Be cynical. Talk to your doctor, talk to the experts. That's why you're here, I hope. Always, always, always keep active, keep your body active and keep your heart and soul active. Those are the key elements. They've always worked.

The diseases may just be a bump in the roadway that come along with aging. We all, as we get older, will deal with something. Our hearing may get worse, our vision may get worse, our phone may never shut up. (Laughter) I have young

graduate students who can't live without electronic devices. They're going off in meetings and they're paying attention to them so I carry a hammer in the meetings. (Laughter) Anyway, enough. You see what my colleagues have to put up with? And Dr. Van Eldik has to put up with this on a daily basis so be sympathetic. But anyway, thank you again. Don't forget Sanders-Brown represents a great resource on aging. There are a lot more experts there than you see here on the stage. Brilliant people. Take advantage. Thanks again.

LVE: Come and see us anytime. You're welcome.

(Applause)

(END OF TAPE)