THE COMMISSIONER: W can go on th record. This is the matter of in re: Estate of Alan Ardis and Estate of Alexandre Ozolins brought against the Olin Corporation.

This is a continuation of hearings that commenced on September 13, 1983, were continued to September 14, and then t September 15, then to October 26, and th n t November 4, then to November 16, and to this date.

MR. PROUT: I believe, Your Honor, the first November date was November 14, rather than November 4 --

THE COMMISSIONER: Did I say 4?

MR. PROUT: Yes, Your Honor.

THE COMMISSIONER: 14. Present today, attorneys are Attorney Robert Carter for th claimant, and for the respondent, William Prout from Wiggin & Dana and Barry David ff the Olin Corporation.

We left off on -- I believe Mr. Pr ut was cross-examining or present --

MR. PROUT: Presenting evidence, Your Honor.

THE COMMISSIONER: I think you began to

THE COMMISSIONER: We can g on the record. This is the matter of in re: Estate of Alan Ardis and Estate of Alexandre Ozolins brought against the Olin Corporation.

This is a continuation of hearings that commenced on September 13, 1983, were continued to September 14, and then to September 15, then to October 26, and then t November 4, then to November 16, and to this date.

MR. PROUT: I believe, Your Honor, the first November date was November 14, rather than November 4 --

THE COMMISSIONER: Did I say 4?

MR. PROUT: Yes, Your Honor.

THE COMMISSIONER: 14. Present today, attorneys are Attorney Robert Carter for the claimaht, and for the respondent, William Prout from Wiggin & Dana and Barry Davidoff the Olin Corporation.

We left off on -- I believe Mr. Prout was cross-examining or present --

MR. PROUT: Presenting evidence, Your Honor.

THE COMMISSIONER: I think you began to

present evidence on -- Do y u want to state for the record where you were when we left off on November 16?

MR. PROUT: Yes, Your Honor. We wer in the midst of presenting respondent's case. We had completed the testimony of Dr. Heying and Dr. Meigs, and we would like to begin today with the testimony of doctor Darryl Bigner --

THE COMMISSIONER: All right.

MR. PROUT: Dr. Bigner, will you take the stand, please?

D A R R Y L B I G N E R, called as a witness, having been first duly sworn by the Commissioner, was examined and testified as follows:

THE COMMISSIONER: You may be seated. Your full name and address, please.

THE WITNESS: I'm Darryl Bigner, and I live at 210 Longwood Drive in Chapel Hill, North Carolina.

MR. PROUT: May I proceed, Your Honor?

THE COMMISSIONER: Please.

MR. PROUT: Thank you.

DIRECT EXAMINATION.

BY MR. PROUT:

Q. Dr. Bigner, you're a neuropathologist, are y u

SANDERS, GALE & RUSSELL
Registered Professional Reporters
HARTFORD, CONNECTICUT 203-246-5563
STAMFORD, CONNECTICUT 203-329-9183
NEW HAVEN, CONNECTICUT 203-624-41[illegible]

not?

A. Yes.

Q. Let me show you a document which appears to b your curriculum vitae and ask you if the information se forth therein fairly and accurately sets forth your professional training and experience, professional activities and so forth?

A. Yes.

MR. PROUT: Your Honor, I would lik to mark that as the next respondent's xhibit which I believe is 13.

MR. CARTER: Let me just look at it. I me inquire the purpose of the offer.

MR. PROUT: The purpose of the offer i to provide -- to qualify Dr. Bigner as an expert witness. I offer it in this fashior the interest of saving time rather than ask the usual series of questions about each of the categories set forth in th CV.

MR. CARTER: I'll stipulate that he's expert and that he's qualified as a neuropathologist, but I would object to th offer. I stipulate that he's qualified a neuropathologist is enough.

THE COMMISSIONER: If he agrees to h

qualifications, I think that's sufficient.

MR. PROUT: Your Honor is going to be faced with serious issues of credibility in connection with testimony, only because there's testimony that's directly contrary t testimony presented by other witnesses, and I think part of the task of assessing that is to have the information as to what the individual has done.

THE COMMISSIONER: You have a right to present it.

MR. PROUT: All right, Your Hon r. I'll proceed in that fashion.

THE COMMISSIONER: As long as th re's objection to it --

MR. CARTER: He's qualified.

BY MR. PROUT:

Q. Dr. Bigner, would you outline briefly for us your current professional and academic activities insofar as they relate to the study of brain tumors?

A. I'm a professor of pathology and neuropathology at Duke University Medical Center, and I have my laboratories in the comprehensive cancer center there.

My entire professional career and all f my

publicati ns have been devoted to the study of malignant brain tumors, particularly glioblastoma multiforme.

Q. Dr. Bigner, let me interrupt you for a s cond and perhaps we can shortcut this a little bit. H w long has your professional career been?

A. The last 15 to 20 years. In this regard, I received my medical degree in 1965 --

THE COMMISSIONER: From where?

THE WITNESS: From Duke.

Q. Would you continue, please, with your current professional and academic activities as they relate to brain tumors?

A. Yes. I'm -- I spend the majority of my time in research on this problem, as I stated, in the cancer center, I'm in charge of the containment facility designed and built where we test hazardous chemicals and viruses in cancer research, and I'm leader of the nervous system neoplasia team in our cancer center leading a group of some 30-odd assistant associate professors and technicians in research on this pr blem.

In addition, I've just received the first major program project grant for research on brain tumors that the National Institute of Neurological Diseas s has awarded, which is a three-institution study with leven projects involving a large group of investigators there.

I participate -- There are only a small group of people in the world who have spent the majority of their time working on this problem, and we worked together world-wide in planning a series of conferences, and I participated on the advisory boards in the one that was held in California last fall, a recent ne in Switzerland last month.

We are planning two others with an English group this summer and a group this fall from the National Toxicology Program, and then finally another major international meeting we have every five years or so in London this fall.

Q. One additional area that I'd like you to comment on or to testify concerning is your current editorial board and reviewing activities, again limiting it insofar as it pertains to brain tumors.

A. Okay. I'm --

MR. CARTER: Objection. It's irrelevant.

MR. PROUT: Your Honor, I claim it.

THE COMMISSIONER: I'll allow it for the weight.

A. I'm --

THE COMMISSIONER: You may take an exception.

A. I'm a member of seven editorial boards,

editorial b ards in cancer, neuroscience j urnals and have the responsibility for editing largely relative to all aspects of brain tumor research there.

THE COMMISSIONER: What's the leading neuropathology?

THE WITNESS: There's a Journal f the Association of American Neuropathologists, which is a journal of neuropathology and experimental neurology, and I've just been elected to the editorial board of that. It doesn't show on this copy of the CV.

The other international, Europe j urnal is Acta Neuropathologica, and I'm a m mber of the editorial board of that journal. Th ir articles in this field, of course, are published in the general cancer literature and clinical neurology and neurosurgery journals as well.

Q. You stated, Dr. Bigner, that all of your articles and publications were related to the subject of brain tumors in one aspect or another. Appr ximately how many have there been?

A. About 130, 140.

Q. Now, you were present when Dr. Krigman testified in connection with this case?

A. Yes.

Q. Dr. Krigman testified that he had r viewed certain categories of materials, and what I would like to do is -- ask you is to recite what those categories were and ask you if you've reviewed the same materials in the interest of saving time.

MR. CARTER: Let me just voir dire with respect to the scope of this testimony. We've had for the respondent one neuropath l gist testify from the neuropathological point of view, and I'd like to, if we can, limit by agreement, just to prevent redundant testimony or merely cumulative testimony, the scope of this witness' evidence.

MR. PROUT: We intend to do that, Your Honor, not go over areas that I asked previous witnesses about, but it's not a Proper subject for voir dire.

What counsel is trying to do is cross-examine at this point.

THE COMMISSIONER: I think it's a well taken point, and we won't name the point, we won't call it voir dire, but how long does your presentation -- your direct-examination do you plan on taking?

MR. PROUT: Twenty minutes, perhaps, Your Honor, thirty minutes at most.

THE COMMISSIONER: Will it be new material or --

MR. PROUT: It will relate specifically to the matter of the animal studies, and as Your Honor may recall, Dr. Krigman did not testify concerning that on direct-examination, in the face of counsel's objection, Dr. Meigs certainly didn't testify concerning that, nor did Dr. Heying.

MR. CARTER: Dr. Krigman did testify about animal studies, pages 550 to 554. He said he reviewed the animal studies himself and found nothing useful in the animal studies with respect to the causation in this case.

MR. PROUT: Now, anything regarding animal studies is claimed to be redundant.

MR. CARTER: I claimed that at the end of the last hearing. More -- I would ask that more testimony by neuropathologists on animal studies not be allowed because there was testimony on that before.

THE COMMISSIONER: Why don't you ask the direct question, if that's agreeable, and th

we can move on? I think the point is well taken that we should accelerate where w can.

MR. PROUT: Clearly, Your Honor, and I don't intend to ask him anything that's been asked before by me.

THE COMMISSIONER: I want to give you every opportunity. We're already in Volume 6.

MR. PROUT: Or 7.

THE COMMISSIONER: And for new material or for -- I think you can lead your witness if there's no objection.

MR. CARTER: Let me see how much leading he does.

THE COMMISSIONER: You may take an objection, but let's have counsel speed it where we can.

MR, PROUT: Yes, Your Honor.

BY MR. PROUT:

Q. The question that I intend to ask you, Dr. Bigner, is whether you have reviewed in connection with this case, these claims, the following categories f materials: The medical records of Dr. Ardis and Mr. Ozolins, employment data concerning these individuals, medical literature dealing with the subject of brain

tumors, the pathology slides of each of these individuals and of Dr. Karabinos, the exhibits which were marked, I believe, Respondents Exhibits 2 through 8, which were the materials prepared under the direction of Dr. Heying, the transcript of these proceedings and the exhibits that -- the documents that have gone into evidence.

Did you review each of those categories of materials?

A. Yes, I reviewed all those things.

Q. Did you review any additional materials in connection with the formulation of your opinions in this case again by category?

A. Well, as I think I've indicated, I spent all of my time working on brain tumors, so I review data, literature, and my entire professional time is d voted toward considering current state of the art in this area.

Q. Have you -- Approximately how many experimentally-induced animal tumors have you pers nally examined?

A. Well over 10,000.

MR. CARTER: Objection, without clarification. Is he talking about chemical carcinogenesis?

Q. Of those more than 10,000, can y u tell us approximately how many of those were chemically-induced brain tumors?

A. At least a third of them were chemically-induced. There were virally and spontaneous brain tumors in the group as well.

Q. Have you also reviewed series of spontaneous animal brain tumors?

A. Yes. I'm currently working with a group fr m the National Toxicology Program to try to establish a meaningful classification for spontaneous rat brain tumors that are seen in the controlled animals f r all the chemical carcinogen studies in that program.

Q. One additional preliminary question, Dr. Bigner: Have you also had opportunity to examine human brain tumors?

A. Yes. I had seven years of training in neurology and neurosurgery and neuropathology, and in our research work we used human tumors extensively in transplanting athymic mice, and we review in my laboratory, receive tissue from every malignant brain tumor removed at Duke or the University of N rth Carolina and have for the last ten years.

Q. There has been testimony previously in this course of these proceedings regarding the animal

studies, the experimental work, and their relevance to the question of chemical causation of human brain tumors generally and specifically their relevance to the question of causation with respect to the cases of Dr. Ardis and Mr. Ozolins.

Are there certain principles of carcin genesis which are established by the animal studies which you believe bear upon each of those issues?

A. Yes.

Q. Would you tell us what those principl s ar , please?

A. Well, the first general principle is that brain tumors are very difficult to induce experimentally, and historically, it has taken us a long time to develop the tools to induce them and study them in the laboratory.

There are a number of factors that I think may be relevant to the human brain tumors that we found over the years.

For example, the species that we test is very important in determining the ability to induce the tumors or not. It is much more easy to induce brain tumors experimentally in mice and rats than it is in larger animals, and particularly in primates.

The genetic susceptibility is very important

even within the speci s that we work on.

For example, there are several strains of rats, particularly the BD-9 strain and the Fisher 344 strain who differ markedly in their genetic susceptibility to chemical carcinogens.

The age of the animals is extremely important. In general, we find that young animals or neonatal animals, animals during fetal time are more susceptible to all of the agents than are adult animals.

It's quite difficult to induce brain tumors in adult animals. The dose of the agents used is important.

In general, the best results that we obtain are with high -- very high doses of agents or large cumulative doses of agents.

There's a special property of the brain that we think makes it resistant to this tumor in deduction called the blood brain barrier, and with many of the inducing agents, it's necessary to use highly artificial means of introducing the cancer-causing agent into the brain to make it work.

For example, with the polycyclic hydrocarbons, it's necessary to take a pellet about the size of your little fingernail and permanently implant it in the brain of an animal to make it induce cancer.

If you give that -- those agents systemically, they don't work. The same is true with many of th viruses with which we induce brain tumors in the lab. If you give them intravenously, they don't work. You have to inject it directly into the brain in a very high dose to make it work.

Most of the chemicals that work systemically, if you give them by intravenous injection, hav t have special properties to work, such as high degrees f lipid solubility so that they can cross the bl od brain barrier.

So there are many special features that we think, or I think are protective of the brain that account for its relative resistance to tumor in deduction.

THE COMMISSIONER: You spoke of inducin brain cancer by injecting viruses directly into the brain tissue.

THE WITNESS: Yes.

THE COMMISSIONER: Are those viruses -- obviously they're identifiable?

THE WITNESS: Yes, yes.

THE COMMISSIONER: What success has There been in -- from that concluding what viruses might produce brain cancer in huma

THE WITNESS: Well, the maj rity f my first ten years of work was really addr ssed at the question of whether viruses were involved in human brain tumors, and although we fully published very little of that, because the data was all negative, we have not been able to show that retro viruses, which are in the class that are most successful in terms of the experimental brain tumor induction, are associated at all with human brain tumors.

THE COMMISSIONER: Excuse me. I just want to be sure I understand. You can induce a viral-induced in mice?

THE WITNESS: Mice, rats, dogs, cats, many different species.

THE COMMISSIONER: And you have not been able to duplicate this in a human?

THE WITNESS: Well, we can't do the human experiments --

THE COMMISSIONER: I wanted to see if you were listening.

THE WITNESS: You can do it in primates with the virus --

THE COMMISSIONER: You can?

THE WITNESS: Yes, ma'am. It's n t glioblastoma.

THE COMMISSIONER: I didn't talk about the instant one. I was just interested in your answer.

So, what is your deduction on that from the animal studies on viruses not dealing with the instant cancer but in general?

THE WITNESS: Well, we either -- either viruses are not associated with human brain tumors or we haven't found the way to look f r them and the right ones. You know, we haven't found many viruses in many human cancers.

The recent success with the human T-cell leukemia virus is the only success in finding that class of viruses associated with any human cancer, and it took some very sp cial tools to do that with.

So, I think recently, there is another class of viruses that most of us haven't worked with that extensively that there's som clues it may be associated with human brain tumors. These are called the papova viruses, and they have recently been shown to induce glioblastoma like tum r in

monkeys, and the fingerprints of that virus in the meeting I was just at in Switzerland, a very respected virology group in West Germany were reported to be involved in them, and I think that needs to be explored, but the data is all negative in toto now relative to virus involvement.

THE COMMISSIONER: Are there more cases of glioblastomas being diagnosed with the level of knowledge increasing?

THE WITNESS: The incidence overall is increasing somewhat, but I think the only real Influence of CAT-scanning and these sort of things is how some of these patients would die in nursing homes in the past, and be signed out on death certificates as having strokes; whereas, we would have some warning now with CAT scan and non-invasive kinds of diagnostic methods to suspect it, but there's been n real major shift in the diagnoses or incidence.

THE COMMISSIONER: All right. Go ahead.

MR. PROUT: Thank you.

BY MR. PROUT:

Q. Dr. Bigner, in response to my question

directed to principles of carcin genesis, y u listed a number of factors, and I won't reiterate them at this point.

Will you tell us in your opinion what the significance of those factors is when applied to the question of causation with respect to the claims of Dr. Ardis and Mr. Ozolins in these proceedings?

A. Well, the fundamental thing that I believe, and most of us as cancer biologists believe, is that the principles are the same in animals as pertain to man, and we use those principles as one of the factors to look at cases of -- and causation of human canc r, and these were the questions that led me, when I was first approached by Olin, to think about what was going n here.

The immediate questions that went through my mind were to determine if there had been a -- common agents worked with, and any evidence for exposure to agents that would have the properties that we know work in animal systems, such as lipid solubility, and the ability to cause -- cross the blood brain barrier, these sorts of things, and particularly if there was any evidence of any prolonged and high dose contact that had taken place.

Q. When you applied these factors, what

conclusion did y u come to with respect to the issue f causation as to these two claims?

MR. CARTER: Objection without clarification. Is he testifying just from the review of the materials that you suggested and his animal work?

MR. PROUT: Yes.

MR. CARTER: Is this based also, then, upon his review of human epidemiol gical studies?

MR. PROUT: No, at this point the only thing I'm asking him about is --

Q. -- are the conclusions which you draw from the principles of carcinogenesis which emerge from the animal studies. Did you understand my question t be directed to that?

A. Yes. No, based on applying those -- Well, you're asking me -- Let me just elaborate.

As a physician and a pathologist and as a cancer biologist, I am trained and do look at the total situation. I have to evaluate all of the evidence that I have, and I would not make a limited conclusion base on one set of data, or apply one narrow set of principles to reach a conclusion.

Q. All right. Well, let me ask you, then, what

additional materials are you relying upon with respect to the conclusions that you draw from the animal studies and these principles of carcinogenesis that emerge from the animal studies?

A. Putting all of those principles together with a comparison of the morphology of the tumors in these particular cases, which I personally reviewed in great detail and had some of my other colleagues review as well, together with the epidemiological data, I don't believe that either is there any evidence or conclusion I can put together about the cause of the brain tumors in these three cases or -- nor could I find anything to pointed me towards in my research, which was my real interest here.

I have not come away enriched or knowing any better how to approach the problem from the study of these three cases, what chemicals to look at or what mechanisms to consider for cause of glioblastoma multiforme.

Q. You indicated in your response just now, Dr Bigner, that one of the factors that you took into account and found significant was the morphology of the tissue samples that you reviewed.

What significance did you draw from the review of the tissue samples?

A. Well, first of all, our institution has been the pathology referee institution for all the treatment trials on glioblastoma that are conducted throughout the country, and we've come to recognize that diagnostic errors are not infrequent, even from other pathologists, about the tissues.

So my first instinct was to be absolutely sure in my own mind by re-examination that we were dealing with glioblastoma here and we were -- all three cases are what I would describe as garden variety glioblast ma multiforme cases with all of the more logical hallmarks of the disease.

This is a well-described disease, Verchow found the same findings and described them in G rman in 1865. It hasn't changed for we will over one hundred years.

So this told me that there was nothing morphologically, or for that matter clinically or otherwise, distinctive or unusual about these cases.

The possible importance of this is vi wed in light really of some questions we're asking in the laboratory, and that is I think it's fundamentally important to be able to associate cause in individual cases of human cancer where we can, and we're studying this question of is there morphological distinctiveness

r lative to inducing agents.

For example, will ethyl nitrosoureas-induc d brain tumors or acrylonitrile brain tumors be distinguishable from glioblastoma multiforme, and although a formal and full-length study has not been completed, my opinion, based on studies of spontaneous tumors in a large number of these induced tumors now, is that a significant number of them can be distinguished; that is, that the different inducing agents perhaps as much as 60 to 80 percent of the time do have morphologically distinctive features and can be separated from one another on that basis.

THE COMMISSIONER: Could you separate any of these three cases or were they identical --

THE WITNESS: Well --

THE COMMISSIONER: -- in the tissue? You said a garden variety, and I'm not sure I comprehend your garden variety and mine.

THE WITNESS: The World Health Organization has published straightforward criteria that we look for in establishing the diagnoses of glioblastoma multiforme in these cases possessed -- each of them possessed all of those criteria.

Now, there's some differences among the

individual ones. One group of cells would be in one tumor that were not in another, and that sort of thing, but pseudopallisading necrosis in endothelial proliferation, multiple cellular forms, and no plastic cells were present in all three of these cases, and not only did I -- I showed these blindly and independently to three or four of my other colleagues who were among the most respected tumor pathologists. We all independently came up with the same thing.

THE COMMISSIONER: In lay language, would it be fair to say that substantially they were very similar, had the components of very similar brain tissue, leading to a diagnosis of glioblastoma multiforme?

THE WITNESS: Yes. They'd be like all other eight to ten thousand glioblastomas th occur in the U.S. every year. Nothing unusu to set them apart, which is what I was l oki for.

THE COMMISSIONER: When you said you're the treatment center -- Duke is the treatme center for all glioblastoma cases, I was curious as to who designates that. Is that

the NIH r who designates you?

THE WITNESS: Let me clarify that. W 're not the treatment center. There are two -- There's a large multi-institutional trial sponsored by NIH that 15 institutions participate in.

Duke is the diagnostic center, the pathology diagnostic center. All the slides from all 15 institutions from patients that are entered into that cooperative tr atment trial are sent to Duke.

THE COMMISSIONER: Aren't they sent to the other 14, too?

THE WITNESS: No. Well, they go to their hospital pathologist, but then he sends the slides to us, and we make the official study Diagnosis so that there's a common set of criteria applied for study purposes there.

THE COMMISSIONER: That's of all brain tumors?

THE WITNESS: Yes, all malignant. This trial is limited to malignant brain tumors.

THE COMMISSIONER: Now, for malignant lung tumors, are there other centers designated?

THE WITNESS: There are other trials of that nature where there would be an ther pathology center designated for that.

THE COMMISSIONER: You're designated for the broad category of all malignant brain tumors?

THE WITNESS: Yes, for that study. That's the National Brain Tumor Study Group. We also -- Or one of our pathologists reviews for the Southwestern Oncology Study Group. My program project grant has the same pathologists.

THE COMMISSIONER: I understand that. But you said for all throughout the whole country in --

THE WITNESS: Only for the Brain Tumor Study Group. That's the largest and ldest treatment trials.

THE COMMISSIONER: That's comprised of 14 --

THE WITNESS: Fourteen to fifteen institutions. The center of it is at Memorial Sloan-Kettering in New York, Dr. Shapiro was the principal investigator, but Duke was one of the founding members.

BY MR. PROUT:

Q. Dr. Bigner, in your testimony a few moments ago in talking about the principles of carcinogenesis, you indicated that the particular substance that was involved in a particular animal experiment was significant with respect to one's ability to induce brain tumors in animals.

Did you look at the question in connection with these cases of whether the tumor -- whether the chemicals which have been successfully used in the experimental studies were chemicals to which either of these individuals had a significant exposure?

A. Yes. That was my initial question in discussing this case, was that Olin compile -- take the known list of published human carcinogens first by the international agencies and then give me a contact list from each of these workers, paying particular attention to any agents in that list that might have ever induced experimental brain tumors in animals.

Q. What did you find?

A. We found, first of all, that there was no common agent of any kind in the carcinogenic group, and secondly, the one chemical that I am presently investigating in some detail as an experimental brain tumor agent, acrylonitrile or vinyl cyanide had been an

agent that had been used by -- I don't remember the details. You may want to give me the list to look at of actually the amounts that -- Yes.

Both Ardis and Ozolins worked with acrylonitrile, but on questioning this, and th conditions and the amounts, I am presently running a study with acrylonitrile where the brain tumors in that study are induced only with large doses, 500 parts per million or one hundred parts per million of acrylonitrile in the drinking water through a continuous lifetime exposure of the animals.

Acrylonitrile is cyanide, it's vinyl cyanide, and any organic chemist knows, or should know, that vinyl cyanide or cyanide is an acute toxic agent and would handle it with care, and the amounts and conditions under which this was handled did not convince me that any significant contact with the agents, any significant doses occurred.

MR. PROUT: May I have a moment, Your Honor?

THE COMMISSIONER: Yes.

(Pause in the proceedings.)

BY MR. PROUT:

Q. Dr. Bigner, on approximately how many occasions did these two individuals work with that

particular substance you've identifi d as vinyl cyanide or acrylonitrile?

A. It looks like there are about ten listings here for Ardis and four or five for Ozolins.

Q. All right. And do the notations there indicate that the amounts were on the order of grams?

A. Yes. These are all gram quantities of the agent.

Q. And that the substances were used under closed system conditions?

A. Yes.

MR. CARTER: Objection. I think that's without any foundation except for this characterization of the list. I don't think there's any review of the actual evidence which is in -- --

THE COMMISSIONER: I'll sustain the objection.

MR. PROUT: I'll withdraw the question, Your Honor, but that is part of something that's already in evidence. It's redundant, if nothing else. I'll withdraw the question.

BY MR. PROUT:

Q. This is part of one of the Exhibits 2 thr ugh 8 that were introduced through Dr. Heying.

Dr. Bigner, do you have an opinion that you can state with reasonable medical probability with respect to the issue of whether the glioblastoma multiforme of each of these individuals, that is, Dr. Ardis and Mr. Ozolins, arose out of or were caused by exposure to chemicals in the course of their employment at Olin Corporation?

A. Yes.

Q. What is that opinion?

A. Well, I've stated part of my opinion as we've gone through this. My opinion is that it is not possible to determine with all of the evidence and evaluation of this situation what the cause of these individuals' glioblastoma multiforme is.

I can find nothing that sets them apart from all of the others that occur at a significant r te, significant numbers throughout the country, and I don't think we can establish the cause of the glioblastomas in these individuals.

Q. All right. Is it your opinion -- Do you have -- Withdrawn.

In your opinion, is it reasonably probable that their cancers were caused by exposure to chemicals in the course of their employment at Olin?

A. No, I find no reason to involve or implicate

their employment r work at Olin any more than anything else that may have happened in their lives. I don't know what the cause is.

MR. PROUT: I have no further questions for Dr. Bigner at this time, Your Honor.

CROSS EXAMINATION

BY MR. CARTER:

Q. Dr. Bigner --

THE COMMISSIONER: You may.

Q. You did diagnose all of the glioblastomas multiformes, the three?

A. Yes. One of the tumors, that is a variant of glioblastoma multiforme, which is gliosarcoma, but they're within World Health Organization criteria as glioblastomas.

Q. Now, you said it was important to you that there was nothing distinctive or unusual about these pathological slides that you reviewed; that is, that these glioblastomas looked like every other glioblastoma multiforme, more or less. Is that correct?

A. Yes. I said I looked at them particularly trying to determine if there was anything special or distinctive about them and could find no such distinctiveness.

Q. Does a lung cancer that's caused by asbestos

look any different from lung cancer caused solely by cigarettes?

A. I'm a neuropathologist, not a lung pathologist.

Q. You were trained as a pathologist, weren't you?

A. No. I received one year of training in anatomic pathology, and I haven't looked at any lung tumors in ten years, and I'd rather not comment on the morphology of lung tumors.

Q. So, based upon your analysis, would you expect that a lung tumor from -- lung cancer from asbestos would look different from a lung cancer caused by another substance, arising spontaneously?

MR. PROUT: Objection, Your Honor --

THE COMMISSIONER: Let the doctor answer.

MR. CARTER: He may know the answer.

THE COMMISSIONER: Yes.

A. I -- You know, I'd rather not comment about lung tumors. I haven't studied lung tumors --

THE COMMISSIONER: If you kn w, Doctor.

Q. If you know, answer it.

THE COMMISSIONER: If you don't know, just say "I don't know."

THE WITNESS: I don't know.

THE COMMISSIONER: All right.

THE WITNESS: He's asking me to speculate.

THE COMMISSIONER: Don't speculate. Just say "I don't know."

BY MR. CARTER:

Q. Do you know anything about whether bladder cancers caused by aniline dyes look any different from bladder cancers arising in the background populati n?

A. No, I don't know anything about bladd r cancer, either.

Q. Would it surprise you that they all look exactly the same?

A. I don't know --

MR. PROUT: Objection. If they looked exactly the same? Objection, Your Honor. I think there's no foundation for the question.

Q. Do you know whether leukemia caused by benzene looks on the pathological slide any different from leukemia caused by something else or arising spontaneously?

A. No, I don't know about benzene leukemias, either.

Q. Do you know about any other end organ tumors caused by chemicals except for brain tumors or central

nervous system tumors?

MR. PROUT: Are you limiting that to the specific issue of morphological appearance? Otherwise your question is too broad.

MR. CARTER: I'll limit it.

Q. Do you know any tumor -- any human tumor that has a different appearance when caused by a chemical exposure from that tumor, a garden variety of that tumor?

A. I can tell you the tumor that I think would be best to study in that regard.

Q. No, that's not what I'm asking. I'm asking if you know of anywhere the appearance is different.

A. I don't think it's been studied well enough to draw much conclusion --

THE COMMISSIONER: What hasn't been studied?

THE WITNESS: There are only a handful of human tumors where we know the cause, and y u have to have the background tumor, on that's been around for a long time, and then known specific causes to do the comparison.

THE COMMISSIONER: What are the handful?

THE WITNESS: The angiosarcoma of the liver would be the ideal one to study where we

have known about the tumor and where we know about vinyl chloride and where we had the old data from Thorotress, for example, s we've got the basic same kind of tumor so that the study could be carried out properly.

THE COMMISSIONER: What is the other -- What others do you know about? You said there's a handful.

THE WITNESS: Of human tumors?

THE COMMISSIONER: Yes.

THE WITNESS: Well, the asbestos-related mesotheliomas, the problem there is that tumor hasn't been recognized clearly for 20 or 30 years, and it may very well be that all mesotheliomas are associated with asbestos, so you don't have the background to compare with it in those cases.

The bladder carcinomas would be another one where there are at least a handful of human cases where the study could b carried out critically.

THE COMMISSIONER: What's the causation there that's been established for the bladder cancer?

THE WITNESS: There are some of the dyes

and some of the dye industry, particularly in old -- in the older coal, tar industry exposures.

The leukemia situation is opening up now where with HTLB and our very sensitive markers, where we can precisely classify leukemia, where you could do those sorts of studies, and I think they need to be done.

THE COMMISSIONER: What is pointing as to causative agents there? What are the causative agents leading to the leukemias?

THE WITNESS: The human T-cell leukemia virus now has enabled us to -- They know that the virus is associated with those tumor cells and we have antibodies to the virus proteins and can very precisely identify and separate that kind of leukemia relative to its cause and look at it in background of all the other leukemias where we don't know the cause.

BY MR. CARTER:

Q. Isn't it true that for -- that for chemically-induced tumors, as far as you know, that the morphology really is no help at all in determining whether or not those are chemically-induced?

A. No, I just testified to the contrary. I think

that I can distinguish acrylonitrile-induced brain tumors across the room. They're very distinctive, they stand out.

Q. In rats and mice?

A. Yes, in rats, not in mice. It's not been studied in mice.

Q. Now, do other people working in your area feel that the animal glioblastomas that are chemically-induced have different morphological appearances from spontaneously-appearing glioblast mas?

A. Let me be very precise about how to answer that. When I'm -- The statements I've made are referring to malignant glio brain tumors. Ther ar not very many animal glioblastomas, and you -- if you limit your comparison to animal, experimentally-induced glioblastomas in animals, you're only talking about a very narrow spectrum of cases.

Q. So that if Harry Zimmerman -- Who is Harry Zimmerman?

A. A very well-regarded friend and colleague in this business who is the neuropathologist at Montefiore at Einstein in New York.

Q. Would you disagree with him that over 40 percent of experimental gliomas produced with carcinogens are glioblastoma multiformes?

A. Well, could I see what you're quoting from, please?

Q. This is Dr. Zimmerman's 1969 Annals of the New York Academy.

A. What Dr. Zimmerman was talking about were some experiments he did in the early 1940's that he -- It's a cumulative data, and what he's referring to there are these highly artificial inductions with pellets of metal cholanthrene that he put in the brain of rats and mice, and, yes, he was speaking about his own work in that very limited set of experiments.

Q. He found that they resembled human glioblastoma multiformes almost identically, didn't he?

A. Yes. With metal cholanthrene pellets put in the brain of rats and mice, he was not talking from 1984 about all the agents in the broader scope of agents we've studied since, and that paper was published in 1969, I think.

Q. He also cites dibenzothiazine and dibenzopyridine, so he was at least reviewing experimental glioblastoma multiformes produced by those other chemicals?

A. Which are all polycyclic hydrocarbons which all have to be put into the brain in big pellets to induce the tumors and which is regarded now as a highly

artificial model and induction method.

Q. Now, do you believe that any human glioblastomas are induced by chemicals?

A. I believe we do not know the cause of human glioblastoma multiforme in any case except for the handful of cases associated with radiation exposures.

I think it is possible and likely that the same thing will turn out with glioblastoma multiforme a it has -- as it is with other things. A small number may be caused by viruses, a small number of other cancers we know are caused by chemicals. The majority of all human cancer we don't have the foggiest idea about the cause end now.

Q. You've written with Dr. Swenberg; isn't that correct?

A. Yes.

Q. You would disagree with the statement state by Dr. Swenberg, "It's been estimated that 80 to 90 percent of all human cancers" --

MR. PROUT: May I have a clarification Are you representing that he's a co-author?

THE COMMISSIONER: He said if he agre with Dr. Swenberg.

Q. If you disagree with Dr. Swenberg's citati

A. Dr. Swenberg said -- He's quoting. He sa

"It has been estimated by some people." He's not saying "I believe that," or have evidence that 80 percent of human cancers are used by chemicals.

And, you know, let's put that in its proper perspective. The cancer research has waves of enthusiasm. Fifteen years ago, we thought everything was caused by viruses.

Now there's a big trend toward environmental agents, and it will cause a great deal of study, but we don't know, we cannot prove, and I don't think anyone in the scientific community believes that we know the cause of most human cancers, especially in individual cas s.

Q. So, do you still feel that it's -- there's a strong possibility that viruses cause some human brain cancer, or have you abandoned that?

A. I think it's a possibility that needs to be explored. I'm not personally exploring it any longer.

Q. Now, in some human -- Sorry. Strike that.

In some experimental glioblastomas or animal brain cancer, which has been induced by chemical exposure, virus particles are released, aren't they?

A. Yes. Dr. Zimmerman reported that and there are other instances in which that's been reported.

Q. Now, has there been further work on that mechanism?

A. Yes. There's been a great deal of work on that mechanism. What we believe most of those viruses are, are indiginous retro viruses whose replication or multiplication is stimulated or turned on by the chemical or the tumor, and that in most cases, that doesn't have anything to do with causing the transformation of the malignant process.

Q. But these virus particles or virus-like particles that are released from a brain tumor that is clearly caused by chemicals, when those are transplanted into another animal's brain, those virus particl s themselves will induce cancer; isn't that true?

A. There is one, I believe, Dr. Zimmerman's work, he published one or two -- unconfirmed by other people -- situations in which those virus particles wer shown to induce sarcomas, a different kind of tumor, when they were injected into other hosts.

THE COMMISSIONER: It wasn't the same as glioblastoma?

THE WITNESS: No, it wasn't the same ki of tumor at all.

THE COMMISSIONER: Isn't it true in hum cancer that one kind of cancer often produce or the body produces another type of cancer? I don't know how to put it into technical

terms, but if you have one cancer, you often find a host and then you get another type of cell cancer.

THE WITNESS: Yes. Again, you can take one of the brain tumor-causing chemicals. If you want to look at that ethyl nitrosoureas causes glioblastomas in rats, if you give it to gerbils, it causes melanomas, and if you give it to mice, it causes lung tumors.

So, the organ site is often not predictive.

BY MR. CARTER:

Q. In connection with that same truth of different organ sites, did you investigate in these cases what other known human or suspected carcinogens these people were exposed to?

A. Yes. I asked that, and went over the data that all known or suspected human carcinogen contact histories in amounts, duration and so forth, had b en compiled and analyzed, and --

Q. What did you find there? I mean, what were these other human carcinogens or other suspected carcinogens to which these two men were exposed?

A. I'd have to go back to Dr. Heying's testimony, I believe is where that was entered into evidence, and

look at that. I haven't reviewed that.

Q. You don't have a present recollection?

A. No. I was not impressed with anything particularly striking in there, and I don't remember the details.

Q. Do you recall that they were exposed to a number of known and/or suspected carcinogens?

A. The most striking memory I have is there was no common contact with known carcinogens. If you took all three of them, I asked that a checkerboard b prepared so we could look across and identify very simply any consistent or common contact with known or suspected human carcinogens, and that's my most striking memory that that was not present.

Q. So you were looking for common exposures to known or suspected carcinogens?

A. No. All exposure, but particularly for -- I shouldn't say "exposure." I think contact or working with something. We do it every day in the laboratory under safe conditions, and that doesn't mean you're exposed to it because you work with it.

Q. Was there concern -- If you know, in the '50's, was there concern in laboratory work as to carcinogenicity of low dose substance? If y u kn w.

MR. PROUT: Objection at this point. I'm

not sure conc rn where -- and I don't think there's any foundation for this with respect to --

THE COMMISSIONER: I'll allow it for the weight. Let the doctor answer, if he knows. I think he understands the question. If he knows.

MR. PROUT: I'll withdraw the objection, Your Honor.

A. Well, I don't think there's any questi n that our general societal awareness of safety and danger of chemicals and other agents is increasing all the time, and I'm sure what was done in the '50's wasn't at the same level of awareness we have today about it.

Q. I got you off the track there. You were -- You were particularly looking for common exposures to known or suspected carcinogens. Why would they be particularly significant?

A. Well, really, in a sense because you didn't have any other thing to look for. I mean, you very quickly exhaust what you can do in a situation like this when you're trying to find out what the cause is.

Q. That is, you were trying to get a clue as to what particular chemical might have been the cause?

A. Yes, as I say, my compelling interest, as

tragic as it would have been and is, in the case of these individuals, it would have helped our research t find something to work on here.

Q. But many chemicals might, and, in fact, d cause brain cancer in animals; isn't that true?

A. Well, it depends on what you mean by "many." Not many out of the total human carcinogens, only a handful among the known human carcinogens.

Q. Are there at least 28?

A. You know, it depends on what kind of points you want to make. If you break them down by classes f compounds and related compounds, there are only a few classes of compounds that induce experimental brain tumors.

If you want to list all of them that have minor ring differences from one another, you can link them on either of the lists. There are quite a number of chemicals and viruses and radiation that will induce brain tumors. It's very difficult to do and requires special situations to make it work in general.

Q. So, what we're testifying to, then, is that you couldn't locate a specific exposure that you thought -- a specific chemical exposure that you thought was fruitful for your research here, and analysis?

A. No.

Q. Now, the issue here -- Let me -- I'll withdraw that.

Did you entertain the possibility that there may be multiple chemical causes of brain cancer?

A. Yes, in fact, another area that's just funded for research in this new grant that we have is the business of promotion. Promotion has never been demonstrated relative to nervous system tumors.

There are no known promoters that increase the instance of the experimental brain tumors in animals, and that's a potential mechanism to think about, about multiple action, but again, we're very ignorant in this area. We don't know that promoters work at all, and yes, any combination would have been -- --

THE COMMISSIONER: Can you explain your use of the word "promoter."

THE WITNESS: A promoter is an agent which acts on so-called initiated cells that aids in completing the transformation pr cess to full cancer, if you will. And it can act in concert with other agents to speed up or help the process.

BY MR. CARTER:

Q. So, do you understand, then, that the issue here is not whether we can locate a particular chemical

cause, but whether it's more probabl than not that these brain cancers arose from the occupational exposure?

A. You know, the issue seems to be broader than that to me. It's whether you can establish a probable cause for the glioblastomas in these individuals, and --

Q. What do you mean when you say "a probable cause"?

A. Anything that would contribute toward causing the glioblastoma multiforme in these individuals, and I was able to come up with nothing.

Q. And, I mean -- Would you call -- ever call a particular occupation a cause of cancer without kn wing the particular substance that was the pathophysi l gical agent of causation?

A. Well, perhaps it's easier with a nonoccupational situation with cigarette smoking. This has come up before in this trial. We don't kn w, and what Dr. Krigman was saying and said badly was we don't know the mechanism by which cigarette smoking causes cancer. We know that it does.

Q. Dr. Krigman didn't say he thought it caused cancer, did he?

A. You --

Q. Strike that.

MR. PROUT: I don't know that it's appropriate for counsel and the witness to argue over what another witness' testimony might have been. It was what it was.

Q. What -- Maybe you could just answer the question. Now, would you ever call a particular occupation a cause of cancer?

MR. PROUT: Objection. There's no foundation. On what facts and circumstances?

MR. CARTER: I'll try to analyze the basis of his response to your question. That is, what standard is he using.

Q. If you can't a find a particular cause, a particular chemical cause, does that put an end t the inquiry of whether there's an occupational cause? And I think the question is proper.

MR. PROUT: I don't have any probl m with the question as explained.

THE COMMISSIONER: Let him answer. It's cross-examination.

MR. PROUT: Withdraw the objecti n, Your Honor.

A. Yes. We could find a situation that had -- where the association was strong enough that we w uld say there's a link here.

Now, h w far we can go in determining what the specifics in that link and association are varies all the time, and what we -- we hope to do and study out mechanisms is to further refine and refine all the time and identify more specifically what it is, but certainly, you could start with an association with an occupation.

Q. And that's true at this stage for hematite mining, or do you know that?

A. No, I don't know that.

Q. Or top side coke oven workers, do you know that?

A. No, the only industrial things I would comment on would be vinyl chloride, for example, or something of that nature, and there the association was with repetitive exposures. Largely the people that went in and cleaned the vents out, and a clear-cut link, but --

Q. How high was the relative risk in those initial vinyl chloride studies, that is, the relative risk of angiosarcoma?

A. I can't comment on the specifics of that. I can make a general comment as a cancer biologist about this, if you'd like.

As these stories emerge, they fit, and ther 's a common theme to them. One of the things that we learn

in psych logy and medicine is that things that are true in nature occur separately in space and time, and the truth emerges with time, and it doesn't happen usually just once and in one situation. The story fits together and --

THE COMMISSIONER: How many cases f glioblastoma percentage-wise are ther compared to other brain cancers? Bec use you say that Duke is the treatment center of all glioblastoma cases, so you must have these statistics. What are they?

THE WITNESS: It varies. The numbers vary somewhat depending on whether you're looking at an autopsy series or a surgical series where we're just looking at biopsies, whether we're looking at patients that come from major referral centers or out, but overall, the incidence of glioblastomas of all brain tumors is from 40 to 60 percent, and the reason, of course, that we focus on them is that this is the most malignant one, th on that we can't treat, can't prevent. It runs such a rapid uniformly fatal course.

THE COMMISSIONER: So glioblastomas multiforme comprise about 40 to 60 percent f

all brain cancers?

THE WITNESS: Yes.

BY MR. CARTER:

Q. Now --

THE WITNESS: Excluding metastatic tumors to the brain.

THE COMMISSIONER: I'm excluding that. Primary brain tumors.

THE WITNESS: Yes, primary brain tumors.

Q. Now, isn't it true, for example, with vinyl chloride, you have some familiarity with vinyl chloride production of angiosarcoma?

A. Yes.

Q. Isn't it true that the relative increase in angiosarcoma in those initial studies, and even in the defined studies, was only about tenfold relative risk? Do you recall that?

A. No. You know, I don't even -- The details of individual studies from where I view these things are less important than how many of them showed the same thing, whether you can then go in and remove the agent and affect the incidence of the disease, stop cigarette smoking, decrease lung cancer.

There's another whole loop in determining cause and effect, and bacterial diseases and others w

talk about Koch's postulates. You don't conclude cause and effect on the basis of individual case clust rs, individual studies. You have to put the whole thing together.

Q. In asbestos -- You don't know about asbest s, is that right?

A. I don't know enough other than a first-year medical student would.

Q. In angiosarcomas from vinyl chloride, at what stage would you have said in the investigation pr c ss that you thought there was a reasonable medical probability that vinyl chloride caused angiosarcoma?

A. Well, I would have -- Let's review a little bit of the data in the situation. What you had and what emerged very quickly was a common agent, and --

Q. How did that emerge, if you can just explain?

A. By taking this very rare tumor, which is a different situation than we have here, this is a v ry rare, very outstanding tumor where the background incidence is extremely low --

THE COMMISSIONER: The angiosarcoma?

THE WITNESS: Yes.

THE COMMISSIONER: What is angiosarcoma for the record?

THE WITNESS: It is a malignant tumor of

the blood vessels. In this case, the blood vessels in the liver that has sarcoma implies a malignant transformation of fibroblastic cells.

So, you had a common agent, you had it happening at more than one place in this country. There were a number of plants in which very quickly one could look at figures and incidences.

BY MR. CARTER:

Q. And what did they find?

A. Again, as the story emerged, there wer mor than one place in which an association between vinyl chloride and angiosarcoma of the liver emerged. I can't and won't go into the details of the studies. I don't know --

Q. Didn't they find three or four cases h re and three or four cases there in different worker populations?

A. But there was a common thread. The common thread is vinyl chloride.

Q. First the common thread was the occupation, wasn't it?

MR. PROUT: May I object, Your Hon r? The witness had not finished his respons .

A. And high dose exposure over a prol nged period of time to the agent stratified even among a particular class of the workers.

Q. What they found at first, didn't they, were clusters of three or four workers in different worker populations?

A. I don't know. I have not reviewed this literature in detail, and --

Q. Do you remember enough to say whether the increasing risk of getting angiosarcoma from this particular occupation was only about tenfold?

A. No, I don't know. You asked me earlier ab ut at what point you could determine this. I don't believe -- I'm not aware of any given instance wher you can go back to a single cluster, random cluster or single first cluster even of something that ultimately became proven and be sure or have -- have general consensus and acceptance about cause at that point. That's the beginning point.

Q. How long did it take OSHA to reduce vinyl chloride exposure to one part per million after those initial few clusters were identified of angiosarcoma?

A. You're making a difference between ne cluster and few clusters.

Q. Few clusters then.

SANDERS, GALE & RUSSELL
Registered Professional Reporters
HARTFORD, CONNECTICUT 203-246-5363
STAMFORD, CONNECTICUT 203-329-9183
NEW HAVEN, CONNECTICUT 203-624-4157

A. I'm sure it didn't take long at all. I don't know specifically.

Q. It took about two months, didn't it?

A. I wouldn't be a bit surprised if they acted very rapidly on that.

Q. How many clusters of brain cancer did you review, that is, positive studies among worker populations working with short chain and small aromatic and especially halogenated hydrocarbons in connection with this case?

MR. PROUT: Objection, Your Honor. It goes into an area that we didn't go int with this with --

THE COMMISSIONER: I'll sustain the objection. Rephrase your question. I'm not sure I understand.

MR. CARTER: I'll strike that.

Q. Dr. Bigner, you said that in expressing your opinion as to causation, you relied upon analysis of epidemiological literature, that is, clusters in different industries of brain cancer. Is that true?

A. Yes.

Q. Now, my question was: How many of these clusters of brain cancer in the chemical industry did you review through studies?

MR. PROUT: Your Honor, may I just renew my objection for the record, for this reas n, that this is not an area that we went into n direct-examination, that what's going to happen here, I believe is, that Mr. Carter --

THE COMMISSIONER: I don't think you should foresee what's going to happen. I'm going to allow it for the weight. I think the witness can handle the question. We'll pursue it as we go along.

MR. PROUT: May I state my concern?

THE COMMISSIONER: No, I think w should let the witness answer the question.

MR. PROUT: I'll withdraw the objection, Your Honor.

THE COMMISSIONER: All right. It's cross-examination. You may -- Do y u remember the question?

BY MR. CARTER:

Q. I'm just asking -- You were saying vinyl chloride -- it took a long time before there was a consensus -- at least, I think was your word -- about causation from vinyl chloride monomer, and I'm looking for that point in the appearance of, you know, various clusters, various investigations of the epidemiol gy at

SANDERS, GALE & RUSSELL
Registered Professional Reporters
HARTFORD, CONNECTICUT 203-246-3563
STAMFORD, CONNECTICUT 203-329-9183
NEW HAVEN, CONNECTICUT 203-624-41[illegible]

which it's r asonable to say there's s me reasonable medical probability of an association.

Now, I'm looking for that same analysis with respect to chemical industry workers and brain cancer, and I'm just asking for what you did review with respect to this case -- these cases.

A. I reviewed -- There are 15 to 20 published papers in addition to this proceeding, there ar a number of clusters that I've been called about r have reviewed papers that I've even rejected -- had rejected for publication about clusters of brain tumors.

In looking at this, and my conclusion is that the data is contradictory, and that we are not at a point where one can make a statement about cause and effect or what would you regulate.

If I were an OSHA man, what would I come in and tell them to stop doing?

Q. We're not asking about regulations. That wasn't the question. This is a question of compensation, not regulation.

Now, in those studies, you said the data was contradictory. What do you mean?

A. I mean some studies will claim an ass ciation, and others do not.

Q. Wasn't that true in the beginning of the

studies about asbestos lung cancer, if you know?

A. I don't know about asbestos lung cancer.

Q. Isn't it true that consistently in the brain cancer clusters, the brain cancer industrial studies, if a latency period of 10 to 20 years is accounted for, there's been a consistent increase in relative risk of brain cancer in working in the petrochemical industry and specifically with short chain halogenated and aromatic compounds?

A. Those studies are riddled with problems. Well over half of them are uncontrolled pathologically. There is not -- in my opinion or a consensus opinion of the serious people that work in neurooncology with this problem that we can establish cause and effect yet.

Q. Now, when you say "cause and effect," you're talking about a particular association with it --

A. I'm not talking about anything. We don't know what causes or what associations exist with glioblastoma that are consistent and that would help us.

Q. Do you know who Dr. William Lloyd was?

A. No, never heard of him.

MR. CARTER: I guess I have no further questions.

THE COMMISSIONER: Do you have anything?

MR. PROUT: Just one, Your Honor, I

believe.

REDIRECT EXAMINATION

BY MR. PROUT:

Q. You were asked a question concerning the percentage of -- the percentage of brain tumors which is made up of glioblastoma multiforme. Does that percentage change as you go from one age group to another?

A. Yes. That's an extremely important thing that always should be qualified when you're asking that question, because there's a clear-cut, age-relat d instance of glioblastomas.

It's very uncommon in children, for xample, and peaks in middle -- to middle adult life, and th relative percentage of that type is different at that -- if you're comparing that age group of people than if you were looking at children.

MR. PROUT: Nothing further, Your Honor.

THE COMMISSIONER: Thank you very much. We'll take a five-minute break here.

(Recess taken.))

MR. PROUT: Your Honor, at this time, I would like to call Dr. Irving Kessler to the stand. Doctor Kessler.