SUPERIOR COURT OF THE STATE OF CALIFORNIA

FOR THE COUNTY OF LOS ANGELES - COMPLEX

NC, A MINOR,

PLAINTIFF,

VS.

CASE NO. 21STCV22822

CERTIFIED COPY

HAIN CELESTIAL GROUP, INC.; BEECH-NUT NUTRITION COMPANY; NURTURE, INC., PLUM, PBC, DBA PLUM ORGANICS; GERBER PRODUCTS COMPANY; WALMART, INC.; SPROUT FOODS, INC.; RALPHS GROCERY COMPANY; AND DOES 1 THROUGH 100, INCLUSIVE,

DEFENDANTS.

REPORTER'S TRANSCRIPT OF PROCEEDINGS

FEBRUARY 4, 2022

(DAY 4)

STENOGRAPHICALLY REPORTED BY:
JEANESE JOHNSON, CSR NO. 11635
OFFICIAL PRO TEMPORE

HELD BEFORE:

THE HONORABLE AMY D. HOGUE

A P P E A R A N C E S

(ALL APPEARANCES VIA REMOTE)

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ALSO PRESENT:

CHRISTOPHER CLEE, TECHNICIAN

IAN ANDRYSZAK, TECHNICIAN

I N D E X

WITNESS: MICHAEL ASCHNER, PH.D.

DIRECT	CROSS	REDIRECT
7	71	139

WITNESS: BEATE RITZ, PH.D.

CROSS (RESUMED)	REDIRECT	RECROSS
145	167	197

E X H I B I T S

EXHIBIT NUMBER/REFERENCED		EXHIBIT NUMBER/REFERENCED	
1	9	627	160
148	22	629	163
28	45	32	165
74	66	678	166
713	124	119	175
26	129	92	181
712	130	24	184
140	145	682	196
677	147		
4	148		
7	152		
703	153		
704	154		
706	157		
705	158		

LOS ANGELES, CALIFORNIA;

FRIDAY, FEBRUARY 4, 2022; 8:59 A.M.

BEFORE: HON. AMY D. HOGUE DEPARTMENT 7;

SUPERIOR COURT OF THE STATE OF CALIFORNIA

--OOO--

THE COURT: ALL RIGHT. ALFREDO, WILL YOU SWEAR IN -- IS IT DR. ASCHNER?

MR. ESFANDIARY: YES.

THE WITNESS: GOOD MORNING, YOUR HONOR.

THE COURT: GOOD MORNING. HOW ARE YOU?

THE WITNESS: GOOD. THANKS.

THE COURT: WHERE ARE YOU SITTING TODAY?

THE WITNESS: I'M SITTING IN BEAUTIFUL BRONX, NEW YORK.

THE COURT: ALL RIGHT. OKAY. WELL, YOU'RE CLOSE TO MY GRANDCHILDREN WHO ARE IN SCHOOL IN THE BRONX IN NEW YORK.

ALFREDO, CAN YOU HEAR ME?

THE CLERK: YES, YOUR HONOR. I'M READY.

THE COURT: OKAY. GO AHEAD.

THE CLERK: MR. ASCHNER, CAN YOU PLEASE RAISE YOUR RIGHT HAND?

DO YOU SOLEMNLY STATE THAT THE TESTIMONY YOU MAY GIVE IN THE CAUSE NOW PENDING BEFORE THIS COURT SHALL BE THE TRUTH, THE WHOLE TRUTH, AND NOTHING BUT THE TRUTH, SO HELP YOU GOD?

THE WITNESS: YES, I DO.

THE CLERK: PLEASE STATE AND SPELL YOUR FIRST AND LAST NAME FOR THE RECORD.

THE WITNESS: MY FIRST NAME IS MICHAEL. MY LAST NAME IS ASCHNER.

THE CLERK: OKAY. CAN YOU SPELL THOSE, PLEASE. CAN YOU SPELL THEM, PLEASE?

THE WITNESS: MICHAEL IS M-I-C-H-A-E-L AND ASCHNER IS A-S-C-H-N-E-R.

THE CLERK: THANK YOU.

THE WITNESS: THANK YOU.

THE COURT: OKAY. YOU MAY PROCEED.

MR. ESFANDIARY: ALL RIGHT.

DIRECT EXAMINATION

MR. WISNER:

Q GOOD MORNING. OR GOOD AFTERNOON, DOCTOR.

A GOOD -- YES, IT'S RIGHT NOON. YES. GOOD AFTERNOON.

Q ALL RIGHT. CAN YOU PLEASE INTRODUCE YOURSELF TO THE COURT AND BRIEFLY STATE WHAT YOUR CURRENT OCCUPATION IS.

A I WORK IN THE DEPARTMENT OF MOLECULAR PHARMACOLOGY. IT'S MY PRIMARY APPOINTMENT AT ALBERT EINSTEIN COLLEGE OF MEDICINE.

Q VERY GOOD.

AND, DOCTOR, WE'RE GOING TO GET INTO YOUR BACKGROUND AND QUALIFICATIONS IN JUST A SECOND.

BUT BEFORE WE DO THAT, I JUST WANT TO PRESENT TO YOU AND THE COURT -- CAN YOU SEE MY SCREEN HERE?

A NOT YET.

Q OH, IS THAT -- AM I SHARING?

A NO.

Q NO?

THE COURT: I SEE IT.

MS. FREIWALD: PEDRAM, I CAN -- I CAN SEE YOUR SCREEN.

THE WITNESS: THE VIDEOGRAPHER IS GOING TO TRY TO HELP ME. I CANNOT SEE IT ON MY COMPUTER.

MR. ESFANDIARY: OKAY.

THE WITNESS: YEAH, IT'S NOT COMING UP FOR SOME REASON. I DON'T KNOW WHY. I'VE NEVER HAD THIS PROBLEM BEFORE.

(OFF-RECORD COMMENTS)

MR. ESFANDIARY:

Q OKAY. SO, DOCTOR, THIS WILL BE OUR ROADMAP FOR TODAY. THIS IS WHAT WE'RE GOING TO COVER WITH YOU, OKAY. AND WE'RE GOING TO START OFF WITH YOUR QUALIFICATIONS. THEN WE'RE GOING TO MOVE ON TO YOUR METHODOLOGY, THE METHODOLOGY THAT YOU EMPLOYED IN THIS CASE BEFORE REACHING YOUR OPINIONS. WE'RE GOING TO TALK ABOUT THE NEUROTOXICITY OF HEAVY METALS. I'M GOING TO FINISH OFF ON METALS AND ASD, OKAY?

A YES, SIR.

Q VERY GOOD.

NOW, I WANT TO GO THROUGH YOUR QUALIFICATIONS

BRIEFLY, DOCTOR, AND I WANT TO SHOW YOU EXHIBIT 1. ACTUALLY, IT'S YOUR C.V.

CAN YOU SEE THAT, DOCTOR?

A YES, SIR.

Q DOES THIS APPEAR TO BE A TRUE AND ACCURATE VERSION OF YOUR C.V. OR ACADEMIC BIOSKETCH?

A IT'S AN ACADEMIC BIOSKETCH, YES. MY BIOGRAPHICAL SKETCH.

Q AND WHAT IS THE PURPOSE OF AN ACADEMIC BIOSKETCH? DID YOU PUT THIS TOGETHER?

A I PUT THIS TOGETHER AND THIS IS BASICALLY THE TYPE OF BIOSKETCH THAT I WOULD SUBMIT WHEN I APPLY FOR GRANTS FROM THE NIH OR SOME OTHER FUNDING AGENCIES.

Q UNDERSTOOD.

AND IT SAYS RIGHT HERE THAT YOU RECEIVED YOUR BACHELOR OF SCIENCE DEGREE IN 1980 FROM UNIVERSITY OF ROCHESTER; IS THAT CORRECT?

A THAT'S CORRECT.

Q OKAY.

AND WHAT IS NATURAL SCIENCES? WHAT DOES THAT REFER TO? I'M NOT FAMILIAR WITH THAT ACADEMIC --

A WELL, I HAD DIFFERENT COURSES IN BIOLOGY AND THE ARTS, AND I DIDN'T HAVE A MAJOR FOCUS BECAUSE OF MY BACKGROUND. I ACTUALLY CAME HERE WHEN I WAS IN MY 20'S FROM ISRAEL AND I HAD TO COMPLETE COLLEGE, SO I TOOK A VARIETY OF DIFFERENT COURSES. I COMPLETED FOUR YEARS OF COLLEGE AT THE UNIVERSITY OF ROCHESTER AT NIGHT, WORKING DURING THE DAY, AND THIS WAS A SPECIAL PROGRAM THAT

ALLOWED ME TO DO THAT.

Q YES, SIR.

A SO --

Q THINGS ARE A LITTLE DIFFERENT IN THE U.S. AND THE UK. WE DO HAVE A MAJOR FOCUS, IF I UNDERSTAND, IN THE U.S., PEOPLE FOCUS ON A BUNCH OF DIFFERENT THINGS.

LET'S TAKE A LOOK AT YOUR NEXT DEGREE. IT'S ALSO FROM THE UNIVERSITY OF ROCHESTER. IT'S A MASTER OF SCIENCE, CORRECT, IN ANATOMY?

A WELL, THAT'S CORRECT.

AND --

Q AND TO BE CLEAR -- GO AHEAD, PLEASE.

A AND ONCE YOU DEFEND YOUR PROPOSAL FOR THE PH.D. DISSERTATION, IN THOSE DAYS YOU WERE GRANTED AN AUTOMATIC MASTER'S DEGREE.

Q AND JUST TO BE CLEAR, ANATOMY, THAT'S REFERRING TO HUMAN ANATOMY, INCLUDING THE BRAIN?

A THAT -- THE BRAIN WOULD BE A SUBSET. THE MAJOR FOCUS ON THE BRAIN WOULD BE IN NEUROSCIENCE OR NEUROBIOLOGY, YES.

Q AND, IN FACT, THAT'S WHERE YOU WENT NEXT, RIGHT, DOCTOR.

IN 1985, YOU OBTAINED YOUR PH.D. IN NEUROBIOLOGY AND ANATOMY FROM UNIVERSITY OF ROCHESTER SCHOOL OF MEDICINE; CORRECT?

A THAT'S CORRECT.

Q AND NEUROBIOLOGY, WHAT STUDY IS THAT? WHAT KIND OF STUDY IS THAT?

A IT'S BASICALLY THE BIOLOGY FUNCTIONING OF THE BRAIN ALL THE WAY FROM MAJOR STRUCTURAL COMPONENTS OF THE BRAIN TO THE HISTOLOGY OF THE BRAIN, NEUROPHYSIOLOGY OF THE BRAIN, AND COMMUNICATIONS BETWEEN CELLS, ALL THE WAY TO THE MOLECULAR LEVEL.

Q AND THEN, DOCTOR, WHAT WAS THE FOCUS OF YOUR PH.D. THESIS?

A THE FOCUS OF MY PH.D. THESIS WAS ON THE EFFECTS OF METHYLMERCURY ON PROTEIN SYNTHESIS AND TRANSPORT.

Q OKAY.

COULD YOU EXPLAIN THAT A LITTLE BIT MORE?

WHAT DID THAT INVOLVE? WHAT DID THAT RESEARCH SPECIFICALLY INVOLVE, AND WHAT WERE SOME OF YOUR CONCLUSIONS?

A SO THAT RESEARCH -- IN ORDER FOR CELLS, BRAIN CELLS, TO STAY VIABLE, THEY HAVE TO PRODUCE DIFFERENT PROTEINS IN THE CELL BODY AND THEN TRANSPORT THOSE PROTEINS TO THE TERMINALS OF THESE CELLS. SO THEY HAVE TO RELY ON A MACHINERY, WHICH IS CALLED AXONAL TRANSPORT, WHICH IS BASICALLY CARRIED OUT BY DIFFERENT TYPES OF ORGANELLES, MICROTUBULES.

SINCE METHYLMERCURY WAS KNOWN -- IS KNOWN TO BE TOXIC, MY DISSERTATION FOCUSED ON THE SPECIFICS OF HOW METHYLMERCURY INTERFERES WITH THE TRANSPORT OF DIFFERENT ESSENTIAL ELEMENTS, AMNIO ACIDS, IN THE VISUAL SYSTEM, AND THESE STUDIES WERE CARRIED IN RATS.

Q AND WE'RE GOING TO GET TO THOSE SPECIFIC MECHANISMS IN JUST A LITTLE WHILE.

BUT FAIR TO SAY, DOCTOR, HAVE YOU BEEN STUDYING METHYLMERCURY FOR THE BETTER PART OF 30 YEARS?

A I STARTED TO WORK WITH METHYLMERCURY, I BELIEVE, IN 1981.

Q OKAY.

A SO IT'S 41 YEARS, YES.

Q 41 YEARS. ALL RIGHT. VERY GOOD.

NOW, YOU OBTAINED YOUR POST-DOCTORATE AT THE SAME INSTITUTION BUT THIS TIME IN TOXICOLOGY; CORRECT?

A THAT'S CORRECT. I MOVED FROM THE FIFTH FLOOR TO THE FOURTH FLOOR, I BELIEVE. YES, IN THE SAME INSTITUTION DIFFERENT DEPARTMENT, THOUGH.

Q OKAY.

AND WAS IT NEUROTOXICOLOGY SPECIFICALLY OR TOXICOLOGY IN GENERAL THAT WAS THE FOCUS OF YOUR POST-DOC? CAN YOU JUST ELABORATE ON THAT FOR US, PLEASE?

A SO, AS YOU NOTED, BY PH.D WAS IN NEUROBIOLOGY. I HAD INTEREST IN TOXICOLOGY GIVEN THE TYPE OF WORK THAT I DID. SO, IN ORDER TO EXPAND MY HORIZONS, WHAT I BASICALLY DID, I OPTED TO DO A POST-DOCTORATAL FELLOWSHIP IN TOXICOLOGY WHERE I CONTINUED THE STUDIES LOOKING AT -- I STILL WORKED WITH METHYLMERCURY, BUT I DID COMPLETELY DIFFERENT THINGS THAT ARE MUCH MORE GERMANE TO TOXICOLOGY IN GENERAL, AND I TOOK COURSES IN TOXICOLOGY AS WELL.

Q AND YOU OBTAINED THAT POST-DOC IN 1987.

AND THEN WE SEE, IN 2012, YOU OBTAINED A

HONORARY PH.D. FROM THE 4TH MILITARY MEDICAL SCHOOL IN XINJIANG, CHINA.

DOCTOR, HOW ON EARTH DID YOU COME TO OBTAIN AN HONORARY DEGREE FROM CHINA? WHAT WAS THAT ALL ABOUT?

A SO I DID NOT OBTAIN IT. I THINK THEY GAVE IT TO ME.

Q SURE.

A I HAVE HAD RELATIONSHIPS WITH MANY, MANY GROUPS IN DIFFERENT COUNTRIES, AND I'VE PUBLISHED, AGAIN, EXTENSIVELY WITH OTHER GROUPS. I BELIEVE I'VE HAD A VERY PRODUCTIVE RELATIONSHIP WITH -- IT CONTINUES, ACTUALLY TO DATE. WE'RE STILL DOING WORK TOGETHER. AND I WAS INVITED TO XI'AN A COUPLE TIMES, AND IN 2012, I WAS GRANTED THIS HONOR, YES.

Q NOW, DOCTOR, YOU BRING UP AND SINCE WE'RE ON THE TOPIC OF THE FAR EAST, IS IT TRUE THAT SOME OF YOUR WORK WAS PRESENTED AT MUSEUM EXHIBITS IN JAPAN NOT TOO LONG AGO?

A YEAH. SO UNFORTUNATELY, IN JAPAN THEY HAVE EXPERIENCED AN EPIDEMIC OF MERCURY EXPOSURE IN THE 1950S AND '60S, AND THEY HAVE DECIDED, IN THE MINAMATA AREA IN JAPAN, TO BUILD A MUSEUM TO MAKE SURE THAT THIS EVENT WILL BE RECOGNIZED AND REMEMBERED.

I WAS IN MINAMATA SEVERAL TIMES. ACTUALLY, I WAS INVITED TO PRESENT SOME LECTURES ON THE WORK THAT WE DO ON MERCURY AND ON -- ACTUALLY, ON A COUPLE OF THESE OCCASIONS, I WAS INVITED TO THE MUSEUM, WHICH IS FULLY DEDICATED TO MINAMATA DISEASE, AND I WAS SURPRISED TO

SEE A VIDEO THERE WHICH BASICALLY DESCRIBES THE MEANS BY WHICH MERCURY CROSSES THE BLOOD BRAIN BARRIER AND ENTERS INTO THE BRAIN PROPER.

SO YEAH, IT WAS VERY GRATIFYING.

Q SURE.

NOW, LOOKING BACK AT YOUR C.V. AGAIN, DOCTOR, I JUST WANT TO FOCUS, CURRENTLY SINCE 2013 PRESENT, YOU'RE AT THE ALBERT EINSTEIN SCHOOL OF MEDICINE. YOU HAVE THIS VERY LONG TITLE. IT SAYS, HAROLD AND MURIEL BLOCK CHAIR IN MOLECULAR PHARMACOLOGY, PROFESSOR OF MOLECULAR PHARMACOLOGY, PEDIATRICS AND NEUROSCIENCE, INVESTIGATOR, KENNEDY INTELLECTUAL AND DEVELOPMENTAL DISABILITIES RESEARCH CENTER, ALBERT EINSTEIN COLLEGE OF MEDICINE.

DOCTOR, CAN YOU JUST EXPLAIN TO US BRIEFLY WHAT THESE ROLES ENTAIL, WHAT THEY INVOLVE, WHAT IT IS YOU DO AT ALBERT EINSTEIN?

A SO I'M A TENURED FULL PROFESSOR AT ALBERT EINSTEIN. MY PRIMARY APPOINTMENT IS IN MOLECULAR PHARMACOLOGY, BUT I DO HAVE ADJUNCT POSITIONS IN THESE OTHER DEPARTMENTS, NEUROSCIENCE AND THE KENNEDY CENTER IN PEDIATRICS.

I ALSO -- THE FIRST PART OF THIS IS THE HAROLD AND MURIEL BLOCK CHAIR. I HOLD THE CHAIR WHICH IS AN ENDOWED CHAIR WHICH BASICALLY SUPPORTS MY RESEARCH. SO INTERESTS -- THIS IS MONEY THAT HAS BEEN -- IT'S -- HAS BEEN DONATED BY MR. AND MRS. BLOCK TO THE UNIVERSITY, AND I DON'T KNOW HOW MANY ENDOWED CHAIRS WE HAVE, BUT BASICALLY RECOGNIZES, I THINK, INDIVIDUALS THAT HAVE

DONE OKAY IN THEIR SCIENCE, AND THIS IS ADDITIONAL SUPPORT FOR MY WORK.

Q I APPRECIATE THE HUMILITY THERE, DOCTOR.

LET'S LOOK AT THE PREVIOUS POSITION YOU WERE IN FROM 2004 -- OOPS. FROM 2004 TO 2013.

IT SAYS YOU WERE GRAY E.B. STAHLMAN CHAIR IN NEUROSCIENCE, PROFESSOR OF PEDIATRICS IN PHARMACOLOGY, AND SENIOR SCIENTIST AT THE KENNEDY CENTER FOR RESEARCH ON HUMAN HEALTH AT VANDERBILT UNIVERSITY; CORRECT?

A THAT'S CORRECT.

Q OKAY. AND WHAT DID YOUR ROLE INVOLVE AT THAT POSITION?

A SO I WAS IN A -- ACTUALLY IN A CLINICAL DEPARTMENT WHEN I WAS AT VANDERBILT. MY PRIMARY APPOINTMENT WAS IN THE DEPARTMENT OF PEDIATRICS, BUT I HAD SEVERAL OTHER ADJUNCT APPOINTMENTS, WHICH ARE LISTED HERE, AND LIKEWISE, AS AT ALBERT EINSTEIN, I WAS GIVEN AN ENDOWED CHAIR IN 2004, THE GRAY E.B. STAHLMAN CHAIR IN NEUROSCIENCE.

AND BASICALLY -- THE PRINCIPLE IS BASICALLY THE SAME.

Q GOT IT.

AND, DOCTOR, WE SEE THE DEPARTMENT OF PEDIATRICS POPPING UP.

HAS YOUR RESEARCH IN THE PAST FOCUSED UPON THE NEUROTOXICITY OF METALS, SPECIFICALLY ON THE DEVELOPING BRAIN IN CHILDREN?

A SO I ACTUALLY HAVE PUBLISHED SEVERAL STUDIES

ON, FOR EXAMPLE, MANGANESE EXPOSURE IN NEONATES. YES, A LOT OF THE WORK THAT I'VE DONE RELATES TO THE EFFECTS OF METHYLMERCURY AND OTHER METALS ON BRAIN DEVELOPMENT, BRAIN FUNCTION AND -- BUT I THINK I SPEND, ACTUALLY, YOU KNOW, THE WHOLE GAMUT, A LOT OF THE WORK THAT WE DO PERTAINS TO DISEASES THAT ARE INHERENT TO OLDER PEOPLE, SUCH AS PARKINSON'S DISEASE.

SO I WON'T SAY I ONLY FOCUS ON DEVELOPMENTAL EFFECTS OF METALS. I THINK I'VE BEEN ABLE TO DO SO ALSO DURING SYNAPSIS, AGAIN, FOCUSING BASICALLY ON THE INTERACTION BETWEEN GENETICS, METALS AND THE CROSS-STOP BETWEEN THESE TWO IN THE DEGENERATIVE DISEASES.

Q AND HERE IT SAYS -- I'M HAVING TROUBLE WITH THIS LITTLE PEN. FROM 2011 TO 2013, IT SAYS YOU WERE DIRECTOR, NIEHS MOLECULAR TOXICOLOGY CENTER, AND THEN FROM 2011 ALSO TO 2013, YOU WERE DIRECTOR, NIEHS TRAINING PROGRAM IN ENVIRONMENTAL TOXICOLOGY.

NOW, DOCTOR, NIEHS, IS THAT REFERRING TO THE NATIONAL INSTITUTES OF ENVIRONMENTAL HEALTH SCIENCES?

A YES, SIR.

Q AND COULD YOU PLEASE EXPLAIN WHAT YOUR ROLE AS DIRECTOR OF THE MOLECULAR TOXICOLOGY CENTER AND THE TRAINING PROGRAM IN ENVIRONMENTAL TOXICOLOGY PERTAINED TO?

A SO THE P30 GRANT, THE MOLECULAR TOXICOLOGY CENTER, THERE ARE FEW RECOGNIZED PLACES IN THE UNITED STATES, I DON'T KNOW THE EXACT NUMBER, BUT THERE ARE PROBABLY A DOZEN CENTERS THAT ARE BEING RECOGNIZED FOR

THEIR WORK IN TOXICOLOGY, DIFFERENT FACETS OF TOXICOLOGY, AND THESE ARE RELATIVELY BIG GRANTS, BECAUSE THE GRANT IS NOT GIVEN TO AN INDIVIDUAL; IT'S GIVEN TO THE INSTITUTION.

HENCE, YOU NEED A CRITICAL MASS OF INVESTIGATORS IN ORDER TO BE ABLE TO APPLY FOR THOSE.

I WAS THE DIRECTOR OF THIS GRANT FOR SEVERAL YEARS UNTIL I LEFT VANDERBILT. AND THE T32, THE SECOND ONE, IS A TRAINING GRANT IN TOXICOLOGY. AND I DIRECTED A TRAINING GRANT IN TOXICOLOGY, MOLECULAR TOXICOLOGY, BOTH FOR GRADUATE STUDENTS AND POST-DOCTORAL STUDENTS. WE HAD SIX SLOTS FOR PRE-DOCS AND POST-DOCS.

AGAIN, BASICALLY THE SAME PRINCIPLES ARE NEEDED FOR A T32. IT'S NOT GIVEN TO AN INDIVIDUAL. IT'S IN RECOGNITION OF THE INSTITUTION'S MERITS AND WORK IN THIS DOMAIN OF TOXICOLOGY.

Q VERY GOOD.

AND LASTLY, DOCTOR, BEFORE WE MOVE ON -- I MEAN, YOUR HONORS LIST, AS WE CAN SEE HERE ON THE SCREEN, IT'S VERY LARGE. SO I'M NOT GOING TO BELABOR IT AND GO INTO EACH AND EVERY ONE. I DO WANT TO FOCUS ON JUST A COUPLE, THOUGH.

I SEE HERE THAT IN 2011, YOU WERE YOU GRANTED THE MERIT AWARD FROM THE SOCIETY OF TOXICOLOGY.

JUST BRIEFLY, WHAT IS THE SOCIETY OF TOXICOLOGY, AND WHAT IS THE MERIT AWARD, AND WHY DID YOU RECEIVE IT?

A THE SOCIETY OF TOXICOLOGY IS A SOCIETY OF ABOUT

8,000 MEMBERS THAT WORK IN DIFFERENT FIELDS OF TOXICOLOGY. AND IT SPANS REPRODUCTIVE, KIDNEY, BRAIN -- I MEAN, BASICALLY ALL THE ORGANS, BASIC ASSESSMENT, ALL THE WAY FROM ANIMAL STUDIES TO HUMAN STUDIES. WE HAVE A VERY LARGE MEMBERSHIP, AND THIS SAYS, BESTOWED -- THIS AWARD IS BESTOWED ON ONE INDIVIDUAL. IT'S THE MOST PRESTIGIOUS AWARD THAT'S GIVEN BY THE SOCIETY OF TOXICOLOGY ON A YEARLY BASIS. SO I BELIEVE THE SOCIETY WAS FOUNDED IN 1961, AND THIS WAS ACTUALLY THE 50TH ANNIVERSARY OF SOT, AND I WAS THE RECIPIENT OF THIS AWARD.

Q ALL RIGHT. VERY GOOD.

NOW, LET'S TALK ABOUT YOUR METHODOLOGY IN THIS CASE, DOCTOR. SO WE'RE GOING TO GO TO OUR NEXT STOP ON THE ROADMAP.

WHAT -- WELL, I'M JUST -- LET ME JUST MAKE SURE I -- OKAY.

WHAT WAS THE METHODOLOGY YOU EMPLOYED IN THIS CASE IN REACHING YOUR OPINIONS?

A SO I THINK IT'S FAIR TO SAY THAT I'VE HAD A LOT OF PREVIOUS KNOWLEDGE BECAUSE I WORK IN THIS AREA. I DON'T THINK I HAD TO GO AND READ EVERY PAPER ON METHYLMERCURY. I THINK I HAD A FAIRLY GOOD FOUNDATION ABOUT THESE METALS. I SERVED TO ADVISE ON THESE METALS FOR DIFFERENT COMMITTEES, THE NATIONAL ACADEMY OF SCIENCES, AND SO FORTH, SO.

WHAT I DID HERE IS, MY SEARCH INVOLVED TYPING IN A FEW KEY WORDS; MERCURY, LEAD, ADHD, ASD, TRANSPORT,

CHILDREN, AND THEN DOING A VERY EXTENSIVE SEARCH LOOKING AT ALL THE PAPERS, OR TRYING AT LEAST TO LOOK AT ALL THE PAPERS, IRRESPECTIVE OF THE OUTCOMES AND TRY TO DETERMINE THE RELATIONSHIP -- I GUESS TO OPINE ON THE ISSUE THAT WE'RE DISCUSSING TODAY.

Q DOCTOR, I UNDERSTAND YOU CONSIDERED TOXICOLOGICAL DATA; CORRECT?

A YES, I DID.

Q AND MECHANISTIC DATA; CORRECT?

A ABSOLUTELY, YES.

Q DID YOU CONSIDER, IN YOUR ANALYSIS, ISSUES RELATING TO DOSE, USE OF ANIMAL MODELS, USE OF INVITRO MODELS, IN YOUR METHODOLOGY BEFORE RENDERING YOUR OPINION?

A YES, ABSOLUTELY. I THINK I MENTION IT IN MY OPINION. I MEAN, EVERYTHING IS TOXIC, SO WHEN YOU LOOK AT OUTCOMES IN RESPONSE TO CERTAIN EXPOSURE IN ANIMAL STUDIES, YOU ALWAYS HAVE TO CONSIDER WHETHER THE EXPOSURE OF THE ANIMAL HAS ANY PHYSIOLOGICAL RELEVANCE.

SO, I MEAN, I CAN GO ON TO DETAILS, BUT EVERYTHING IS TOXIC. SO YOU DO HAVE TO CONSIDER THE DOSE. AND WHEN YOU DO THE ANIMAL STUDIES, THE DOSES HAVE TO BE RELEVANT TO HUMAN EXPOSURES, YES.

Q AND, DOCTOR, AS A TOX -- I UNDERSTAND YOU ALSO LOOKED AT THE EPIDEMIOLOGICAL DATA; CORRECT?

A YES. YES, SIR.

Q ALL RIGHT.

AS A TOXICOLOGIST, HOW DOES THE EPIDEMIOLOGICAL

DATA FIT INTO YOUR CONSIDERATION OF CAUSATION?

A SO MANY THE PRINCIPLES THAT I USE IN MY OWN RESEARCH ARE VERY SIMILAR. I MEAN, I'M ALSO OBLIGATED TO DO STATISTICAL ANALYSIS TO DETERMINE WHETHER X CAUSES Y.

AS I'VE STATED BEFORE, I'M NOT AN EPIDEMIOLOGIST, BUT I DO HAVE THE ABILITY TO READ THOSE TYPES OF PAPERS, AND I CAN LOOK AT THE SOUNDNESS OF THESE PAPERS TO -- NOT TO A FULL EXTENT, BUT IT GIVES ME COMPLEMENTARY INFORMATION. IT ALLOWS ME TO LOOK AT THE LITERATURE AS A TOTALITY.

I MEAN, I WOULD HAVE NO REASON TO DO ANY EXPERIMENTS ON MERCURY IN ANIMAL STUDIES IF MERCURY WAS NOT TOXIC TO HUMANS. WE DON'T USE RATS, YOU KNOW, TO STUDY WHAT'S THE EFFECT OF HEALTH OF MERCURY ON THE HEALTH OF RATS. WE WANT TO BE ABLE TO EXTRAPOLATE.

SO, YOU KNOW, IT'S IMPOSSIBLE -- OR ONE SHOULD NOT SEPARATE THE TOXICOLOGY ARENA FROM THE EPIDEMIOLOGICAL ARENA. THESE ARE SUPPLEMENTING EACH OTHER, AND THAT'S WHY I HAVE READ BOTH OF THEM.

Q AND, DOCTOR, IS IT FAIR TO SAY THAT, DURING YOUR REGULAR COURSE OF YOUR RESEARCH, ACADEMIC CAREER, DO YOU REGULARLY READ EPIDEMIOLOGICAL PAPERS AND CONFER WITH EPIDEMIOLOGISTS ON RESEARCH INTERESTS?

A ABSOLUTELY, YES.

Q OKAY.

AND, DOCTOR, IS IT FAIR TO SAY THAT THE METHODOLOGY YOU APPLIED -- YOU'RE APPLYING HERE IN THIS

COURTROOM, IS THAT THE SAME METHODOLOGY AND THE SAME INTELLECTUAL RIGOR YOU WOULD APPLY IN YOUR EVERY DAY ACADEMIC RESEARCH AND YOUR CAREER?

A YES. ABSOLUTELY.

Q NOW, DOCTOR, I WANT TO TALK ABOUT THE GENERAL NEUROTOXICITY OF METALS. THAT'S GOING TO BE OUR NEXT STOP ON YOUR ROADMAP.

BUT I WANT TO START WITH SOME BASIC DEFINITIONS BECAUSE WE REALLY -- A LOT OF THE TESTIMONY SO FAR HAVE BEEN FOCUSED ON THE EPIDEMIOLOGICAL DATA. I REALLY WANT TO TALK ABOUT SOME OF THE MECHANISTIC AND BIOLOGICAL FUNCTIONS OF THESE METALS IN THE HUMAN BRAIN.

SO, DOCTOR, WHAT ARE ESSENTIAL AND NONESSENTIAL METALS? COULD YOU JUST GIVE US A VERY BRIEF DISTINCTION BETWEEN THOSE?

A SO ESSENTIAL METALS ARE THOSE METALS THAT ARE REQUIRED FOR BODILY FUNCTIONS. WE WOULD NOT BE ABLE TO SURVIVE, BASICALLY, IN THE ABSENCE OF INGESTION, FOR EXAMPLE, OF THESE HEAVY METALS. IRON IS ONE OF THEM. MANGANESE IS ANOTHER ONE. THERE ARE MANY MORE. AND NONESSENTIAL METALS ARE THOSE THAT ARE NOT REQUIRED FOR ANY BODILY FUNCTION. SO ARSENIC, LEADS, MERCURY, CADMIUM, AND OTHERS, ARE NOT REQUIRED. CHROMIUM IS NOT REQUIRED.

THAT DISTINGUISHES BETWEEN ESSENTIAL AND NONESSENTIAL METALS.

Q AND, DOCTOR, WE'VE SEEN REFERENCES TO THE BLOOD BRAIN BARRIER IN SOME OF THESE STUDIES.

COULD YOU BRIEFLY DESCRIBE FOR US WHAT THE BLOOD BRAIN BARRIER IS.

AND TO HELP US ALONG, WE HAVE THIS EXHIBIT NUMBER 148 AS A DEMONSTRATIVE OF THE BLOOD BRAIN BARRIER.

COULD YOU JUST WALK US THROUGH WHAT THIS ASPECT OF OUR BIOLOGY IS, HOW IT WORKS?

A OKAY. I DON'T HAVE A POINTER, BUT --

Q YES. IF YOU JUST LET ME KNOW WHERE TO GO.

A YOU CAN SEE THE LUMEN. YES, THAT'S THE LUMEN OF THE BLOOD VESSEL. YOU CAN SEE A RED BLOOD VESSEL -- A RED BLOOD CELL INSIDE, FLOWING WITHIN THE CAPILLARY LUMEN.

THE BRAIN IS A VERY PRIVILEGED ORGAN. SO BASICALLY, IT EVOLVED IN SUCH A WAY THAT IT'S PROTECTED FROM THIS SYSTEMIC ENVIRONMENT, WHICH I WOULD REFER TO AS THE BLOOD.

YOU WOULD NOT WANT THE CHANGES IN THE BLOOD TO BE DIRECTLY TRANSLATED INTO THE BRAIN PARENCHYMA, AND I'LL GIVE YOU AN EXAMPLE. POTASSIUM, FOR EXAMPLE, IF YOU EAT A BANANA AND ALL OF THE POTASSIUM THAT YOU HAVE IN THE BLOOD WOULD GO INTO YOUR BRAIN, YOU WOULD HAVE A TECNIS KIND OF REACTION. SO THE BLOOD BRAIN BARRIER IS THERE BASICALLY TO PREVENT THINGS THAT ARE NOT NECESSARY FROM GETTING INTO THE BRAIN AND ASSURE THAT THOSE NECESSARY INGREDIENTS, MACRO MOLECULE NUTRIENTS, ARE VERY TIGHTLY REGULATED.

AND, IN ORDER TO DO SO, THE BLOOD BRAIN BARRIER

EVOLVED IN SUCH A WAY THAT WE DON'T HAVE WHAT'S CALLED FENESTRAE BETWEEN CELLS, AND FENESTRAE IN LATIN FOR THOSE OF YOU WHO KNOW ARE WINDOWS. SO IN CAPILLARIES, IN MOST -- IN ALL OF THE OTHER ORGANS, WITH A COUPLE OF EXCEPTIONS, ALL THE CAPILLARIES HAVE, SORT OF, FENESTRAE. THEY HAVE WINDOWS THAT ALLOW THINGS TO DIFFUSE BETWEEN CELLS IN THE BRAIN. THERE ARE SEVEN AREAS THAT DON'T HAVE THE FENESTRAE. THEY ARE CALLED THE CIRCUMVENTRICULAR ORGANS, BUT THE REST OF THE BRAIN IS COMPOSED OF CAPILLARIES WHERE THE OUTER LEAFLETS OF THE CELLS ADJOIN AND, BASICALLY, FORM A BARRIER FOR THINGS TO DIFFUSE BETWEEN CELLS.

SO EVERYTHING THAT GETS INTO THE BRAIN HAS TO BE EITHER A LIQUID SOLUBLE, WHICH MEANS IT WILL GET THROUGH THE MEMBRANES OR IT HAS TO HAVE A SPECIFIC TRANSPORT MECHANISM.

NOW, HAVING SAID THAT --

Q YES.

A NOW, HAVING SAID THAT, THAT DOES NOT MEAN THAT SOMETHING THAT'S NOT ESSENTIAL IN THE BRAIN IS NOT GOING TO GET IN THERE, AND I'LL GIVE YOU AN EXAMPLE:

ONE THING WOULD BE METHYLMERCURY BECAUSE THOSE THINGS CAN MIMIC. THEY CAN USE WHAT WE CALL MOLECULAR MIMICRY TO MIMIC OTHER COMPOUNDS THAT ARE IN THE BLOOD AND UTILIZE THOSE TRANSPORTERS FOR THEIR OWN TRANSPORT.

Q DOCTOR, YOUR FLOW WAS PERFECT BECAUSE THAT'S EXACTLY WHAT WE'RE GOING TO TALK ABOUT NEXT.

AS YOU JUST SAID, SOME METALS AND SOME

COMPOUNDS CAN CROSS OVER FROM THE BLOOD INTO THE BRAIN, AND THAT INCLUDES, ON THIS DEMONSTRATIVE, THE SAME EXHIBIT NUMBER 148.

WE HAVE METHYLMERCURY IDENTIFIED HERE. WE ALSO HAVE LEAD AS WELL AND SOME OTHER METALS.

CAN YOU JUST BRIEFLY WALK US THROUGH HOW METALS, SUCH AS LEAD, METHYLMERCURY, AND ARSENIC, ALTHOUGH I KNOW ARSENIC IS NOT REPRESENTED ON HERE, HOW DO THEY GET THROUGH FROM THE BLOOD INTO THE BRAIN?

A SO SOME OF THESE METALS THAT ARE HERE ARE ESSENTIAL, ZN TWO PLUS, WHICH IS ZINC. MN TWO PLUS, WHICH IS MANGANESE. FE REFERS TO IRON. THE DIFFERENT BALLS, THE DIFFERENT COLORED BALLS, GLUT ONE AND SO FORTH, MCT. THESE ARE DIFFERENT TRANSPORTERS.

I MEAN, WE CAN GO INTO A LOT OF DETAILS ABOUT THESE TRANSPORTERS, BUT I WON'T BORE YOU WITH THIS.

BASICALLY, THESE MOLECULES, SUCH AS PB2 PLUS, WHICH IS LEAD, CAN TAKE ADVANTAGE OF TRANSPORTERS THAT ARE INHERENT TO THE BLOOD BRAIN BARRIER FOR THE TRANSPORT OF ZINC, FOR EXAMPLE, AND THEY CAN BASICALLY PIGGY-BACK ON THESE TRANSPORTERS TO GET INTO THE BRAIN.

SO METHYLMERCURY, FOR EXAMPLE, WILL BIND TO ANOTHER PROTEIN OR AMINO ACID. IT WILL HAVE A STRUCTURE THAT'S VERY SIMILAR TO METHIONINE, THE METHYLMERCURY CYSTEINE COMPLEX, AND THE BLOOD BRAIN BARRIER IS BASICALLY NOT SMART ENOUGH TO DISTINGUISH BETWEEN WHAT'S GOOD AND WHAT'S BAD. SO IT CANNOT DISCRIMINATE BETWEEN THE METHIONINE OR THE METHYLMERCURY CYSTEINE COMPLEX.

SO BOTH OF THEM WILL BE TRANSPORTED, AND THIS IS VERY SIMPLIFIED. LEAD CAN GET IN ON OTHER TRANSPORTERS. THERE'S ANION TRANSPORTERS. THERE'S CALCIUM CHANNELS ON THE BLOOD BRAIN BARRIER, WHICH ARE NOT DEPICTED HERE, BUT LEAD CAN GET INTO THE BRAIN THROUGH THOSE.

ARSENIC ACTUALLY WILL GET IN THROUGH -- INTO THE BRAIN BY WAY THE GLUC ONE, THE GLUCOSE TRANSPORTERS. SO, ALTHOUGH THEY ARE NOT ESSENTIAL, AND THEY ARE NOT SUPPOSED TO IN THE BRAIN, IF THEY ARE IN THE BLOOD, THOSE METALS WILL GET INTO THE CNS, INTO THE CENTRAL NERVOUS SYSTEM.

Q DOCTOR, WHAT IS THE SIGNIFICANCE OF THAT? RIGHT. I MEAN, THERE ARE IN THE BLOOD. THEY CROSS THE BLOOD BRAIN BARRIER INTO THE BRAIN. WHY IS THAT SIGNIFICANT, IF AT ALL?

A WELL, IT'S SIGNIFICANT BECAUSE THESE METALS DON'T HAVE ANY BIOLOGICAL FUNCTION, BUT THEY DO INTERFERE WITH NORMAL BIOLOGICAL FUNCTIONS.

SO IF YOU ACCUMULATE THE BRAIN -- IN THE BRAIN, LEAD, MERCURY, ARSENIC, OTHER METALS, THEY WILL EXERT TOXIC EFFECTS AND THEY WILL NOT ALLOW THE BRAIN TO FUNCTION PROPERLY. SO THERE'S NO NEED FOR THEM TO BE WITHIN THE BRAIN.

Q AND THAT'S EXACTLY WHAT WE'RE GOING TO TALK ABOUT NEXT.

LET'S TALK ABOUT WHAT THESE METALS DO ONCE THEY GET INTO THE BRAIN AND CROSS THE BLOOD BRAIN BARRIER.

HERE, DOCTOR, WE HAVE A LITTLE ILLUSTRATION,

SAME EXHIBIT 148, OF THE EFFECT OF LEAD ON NEUROTRANSMITTERS.

DOCTOR, CAN YOU JUST WALK US THROUGH WHAT IS GENERALLY BEING DESCRIBED HERE AND SHOWN HERE?

CAN YOU SEE MY SCREEN?

A YES.

SO THE TURQUOISE, I GUESS, OR THE GREEN, I DON'T KNOW, ON THE LEFT PART, YOU SEE THE NEURON. THERE'S LIKE A CHANNEL IN YELLOW, WHICH IS CALCIUM, CA2 PLUS. SO THIS IS WHERE CALCIUM WOULD NORMALLY GET IN. I THINK I'VE MENTIONED BEFORE THAT LEAD CAN PIGGY-BACK INTO NEURONS BY WAY OF USING CALCIUM CHANNELS.

SO WHAT'S DEPICTED HERE IS ABILITY OF LEAD TO ENTER CELLS ON CALCIUM CHANNELS. SO THIS IS NOT A PHYSIOLOGICAL PHENOMENON. IT SHOULD NOT HAPPEN IN ANYONE, BUT UNFORTUNATELY, MOST OF US -- OR IF NOT ALL OF US -- ARE EXPOSED TO LEAD.

SO ONCE IT'S IN THE CELL, THE LEAD WILL INTERFERE WITH NORMAL PROCESSES. IT WILL INTERFERE WITH THE ABILITY OF THESE LITTLE VESICLES THAT ARE SHOWN IN THE GREEN PART OF THE SLIDE. RIGHT. THESE VESICLES ARE IN THE NEURON. A LITTLE BIT TO THE LEFT. THE GREEN -- NO. THE OTHER SIDE. YEAH.

SO THESE VESICLES ARE THE NEUROTRANSMITTERS. WHEN CALCIUM GETS IN WHAT HAPPENS, THESE VESICLES WILL FUSE WITH A MEMBRANE OF THE NEURON, THE TERMINAL OF THE NEURON, AND THOSE LITTLE GREEN DOTS WILL BE THEN WHAT YOU SEE OVER THE WHITE BACKGROUND. THESE LITTLE

NEUROTRANSMITTER VESICLES WILL BE IN WHAT WE CALL THE SYNAPSE. THAT'S THE AREA BETWEEN THE TWO NEURONS.

THEY WILL THEN DIFFUSE TO THE CELL ON THE RIGHT, WHICH IS ANOTHER NEURON. THEY WILL BIND TO RECEPTORS ON THESE NEURONS, AND THAT'S GENERATES A NORMAL RESPONSE.

NOW, WHEN YOU HAVE LEAD IN THE CELL, YOU ABROGATE THIS RESPONSE. YOU HAVE THE SYNAPTIC TRANSMISSION, AS WE REFER TO IT, IS BASICALLY ABROGATED. YOU WILL NOT SEE THIS TYPE OF EFFECT. THERE'S NO RELEASE. THERE'S NO ABILITY TO BIND TO THE POST SYNAPTIC NEURON, AND THIS SYNAPSE IS NOT GOING TO FUNCTION IN A PROPER WAY.

Q DOCTOR, WHEN A SYNAPSE FAILS TO FUNCTION IN A PROPER WAY, WHAT ARE SOME OF THE REPERCUSSIONS OF THAT?

A OH, IT CAN MANIFEST IN ALL KINDS OF DIFFERENT BEHAVIORAL EFFECTS. IT MAY MEAN THAT THE CELL NEXT TO THE ONE THAT'S -- THE CELL THAT'S RECEIVING THE INPUT MAY NOT RELEASE HORMONES. IT MAY IMPEDE MOVEMENT. IT CAN HAVE A WHOLE PLETHORA OF EFFECTS.

Q DOCTOR, TO PUT IT SIMPLY: DO WE CALL THAT BRAIN DAMAGE?

A YEAH, THAT'S BRAIN DAMAGE. YES.

Q AND IS THAT WHAT WE SEE DEPICTED HERE ON THE RIGHT? WE HAVE THIS ILLUSTRATION IN BLACK OF VARIOUS PARTS OF THE BRAIN WITH SOME RED, IT LOOKS LIKE, INFLAMED PARTS.

WHAT'S BEING SHOWN HERE? CAN YOU BRIEFLY

DESCRIBE THAT FOR US?

A SO THIS STUDY WAS LOOKING AT THE VOLUME OF THE BRAIN, AND ACTUALLY IN ADULTS WHERE THERE WAS INFORMATION ABOUT THEIR EXPOSURES WHEN THEY WERE CHILDREN. SO IT'S SORT OF A PROSPECTIVE STUDY WHERE YOU CAN RELATE LEAD EXPOSURE AT EARLY AGE WITH DAMAGE LATER ON IN LIFE, WHICH IS A VERY IMPORTANT CONCEPT. I DON'T KNOW IF WE'LL TALK ABOUT IT TODAY.

BUT BASICALLY, THE DIFFERENT SHAPES OF THE YELLOW, OR SHADES OF YELLOW AND RED, DEPICT DECREASES IN THE VOLUME OF THE GRAY MATTER. BASICALLY, WHERE THE NEURONS, WHERE THE CELL BODIES, ARE SITUATED IN THE BRAIN.

SO THIS SHOWS THAT EARLY LEAD EXPOSURE DECREASES THE AMOUNT OF BRAIN VOLUME IN ADULTS. SO THE EFFECT THAT OCCURS EARLY ON IS -- IT MAY BE SILENT IN TERMS OF SOME OF THE BEHAVIORAL EFFECTS, BUT ON THE MORPHOLOGICAL BASIS, IT'S A PERMANENT EFFECT BECAUSE, AS I SAID, THESE WERE ADULTS.

AND WHAT'S INTERESTING IS THAT THESE EFFECTS ARE ACTUALLY IN AREAS THAT ARE REFERRED TO AS THE ANTERIOR SINGULAR CORTEX, THE PREFRONTAL CORTEX, AND THESE ARE AREAS THAT HAVE VERY IMPORTANT ROLE IN EXECUTIVE FUNCTION IN ALL KINDS OF DIFFERENT BEHAVIORS.

Q AND ARE THOSE -- AND WE'LL GET TO THIS IN A BIT MORE DETAIL IN A SECOND. ARE THOSE AREAS ALSO WHAT IS IMPAIRED IN CHILDREN WITH ASD?

A YES, THEY ARE.

Q NOW, DOCTOR, WHEN -- I WANT TO TALK ABOUT MERCURY. AND WE JUST TALKED LEAD. I WANT TO TALK ABOUT MERCURY AND WHAT IT DOES WHEN IT'S IN THE BRAIN.

NOW, I UNDERSTAND THAT, IN SUPPORT OF YOUR OPINION, YOU REVIEWED A VIDEO WHICH VERY HELPFULLY DEMONSTRATES WHAT MERCURY DOES IN THE BRAIN. IS THAT CORRECT, THERE'S A VIDEO THAT CAN SHOW US THIS?

A THAT'S CORRECT.

Q OKAY.

I'D LIKE TO JUST TAKE A LOOK AT THIS VIDEO -- OH, SHARE SCREEN.

THAT ONE. OKAY.

DOCTOR, CAN YOU SEE MY SCREEN HERE?

A I CAN SEE IT, YES.

Q ALL RIGHT.

LET'S -- I'M GOING TO HIT PLAY.

(VIDEO)

MR. ESFANDIARY: I'M JUST GOING TO STOP IT RIGHT THERE, DOCTOR.

WHAT ARE THESE THINGS STICKING OUT TO THE RIGHT HAND OF THAT, WHAT LOOKS LIKE A GALAXY IN THE MIDDLE, AND WHAT ARE SOME OF THE THINGS STICKING OUT ON THE LEFT HAND? WHAT IS THAT REFERRING TO?

A SO A NEURON BASICALLY HAVE A -- HAS A CELL BODY, WHICH IS THE CENTER. IT'S CALLED A CELL SOMA OR A CELL BODY, AND ALL THE OTHER THINGS THAT ARE COMING OUT ARE BASICALLY THE RECEPTIVE FIELD. THERE ARE DENDRITES, WHERE THE INFORMATION IS GATHERED BY THE NEURON AND

OTHER PROCESSES OR ONE MAJOR PROCESS IS REFERRED TO AS THE AXON, AND THAT'S THE OUTPUT FROM THE CELL.

SO BASICALLY A CELL, WHEN IT GETS ALL KINDS OF INFORMATION FROM ALL THESE DENDRITES HAS TO DO SOME COMPUTING AND DECIDE, AM I GOING TO RESPOND TO ALL OF THIS OR AM I GOING TO DO SOMETHING? THE INPUT COMES FROM THE DENDRITIC FIELD, AND THEN, THE OUTPUT GOES INTO THE AXON.

MS. FREIWALD: YOUR HONOR, IF I MAY -- WOULD I BE -- I DON'T KNOW IF I'M ABLE TO BE HEARD.

THE COURT: YES.

MS. FREIWALD: I JUST WANT TO BE CLEAR. I DIDN'T SAY ANYTHING WHEN I SAW THIS WAS MAYBE A COUPLE OF SECONDS, BUT NOW I'M APPRECIATING IT'S A LONGER EXERCISE. THIS WAS NOT PRODUCED TO US. IT WASN'T PART OF DR. ASCHNER'S REPORT. I'VE NEVER SEEN IT BEFORE. SO --

MR. ESFANDIARY: YOUR HONOR, IF I MAY. THIS IS A DEMONSTRATIVE TO HELP DR. ASCHNER EXPLAIN THE EXACT SAME CONCEPTS THAT HE TALKS ABOUT IN DEPTH IN HIS REPORT. HE'S NOT RELYING ON IT FOR HIS OPINIONS. IT'S SIMPLY A DEMONSTRATIVE TO HELP THE COURT BETTER UNDERSTAND SOME OF THESE VERY COMPLEX MECHANISMS GOING ON IN THE BRAIN. THAT'S WHAT DR. ASCHNER IS REFERRING TO.

THE COURT: JUST A MOMENT. JUST A MOMENT. HOW LONG IS THE VIDEO?

MR. ESFANDIARY: IT'S GOING TO BE ABOUT TWO

MINUTES.

THE COURT: OKAY. THEN I THINK IT'S A PROBLEM. I WOULDN'T LET ANYBODY USE A DEMONSTRATIVE AT TRIAL WITHOUT GIVING THE OTHER SIDE A CHANCE TO LOOK AT IT, AND SO MAYBE THE SOLUTION IS FOR THE COURT TO EXIT FOR A MOMENT, LET YOU PLAY IT FOR OPPOSING COUNSEL.

MR. ESFANDIARY: YEAH.

THE COURT: AND SEE WHETHER SHE HAS SPECIFIC OBJECTIONS.

SO I AM GOING TO DISAPPEAR FOR ABOUT FIVE MINUTES. MAYBE YOU'LL NEED MORE TIME THAN THAT. I DON'T KNOW, BUT THAT SHOULD WORK.

MR. ESFANDIARY: OKAY.

THE COURT: SO LET ME SEE WHAT TIME IT IS.

IN CALIFORNIA IT IS 9:37, SO AT 9... I DON'T KNOW, LET'S SAY, TEN MINUTES. AT 9:50, I'LL COME BACK AND THAT WILL GIVE ME A MINUTE TO DO SOME OTHER WORK.

MR. ESFANDIARY: OKAY. GREAT.

MS. FREIWALD: THAT'S FINE, YOUR HONOR.

(RECESS)

THE COURT: OKAY. HI, COUNSEL. HAVE YOU HAD A CHANCE TO TALK TO EACH OTHER AND FIGURE OUT WHETHER WE'VE GOT A DISPUTE?

MS. FREIWALD: YES, YOUR HONOR. I THINK WE DO.

IT'S -- THERE ARE A COUPLE ISSUES HERE. I MEAN, THIS IS A FAIRLY LENGTHY, NARRATED VIDEO THAT APPEARS TO BE BASED ON THE RESULTS OF A STUDY, BUT IT PRESENTS THE FINDINGS AS IF THEY ARE, KIND OF, ABSOLUTE

UNIVERSAL FINDINGS. I DON'T KNOW WHAT THE STUDY IS, IF IT'S A STUDY THAT WAS PUBLISHED IN THE PEER-REVIEWED LITERATURE. I DON'T BELIEVE WE HAVE IT. IF WE DO HAVE IT, THEN THEY SHOULD TALK ABOUT THE STUDY. BUT SIMPLY HAVING A NARRATOR WHO WE CAN'T CROSS-EXAMINE DESCRIBE THE RESULTS OF A STUDY, SEEMS TO, TO DEFENDANTS, TO GO WELL BEYOND THE SCOPE OF AN APPROPRIATE DEMONSTRATIVE IN THIS CONTEXT.

THE COURT: OKAY.

MR. WISNER, WOULD YOU LIKE TO RESPOND?

MR. WISNER: SURE, YOUR HONOR. I'M SORRY TO JUMP IN ON THIS, BUT IT'S EVIDENTIARY STUFF, AND I'M HANDLING IT FOR US ON THIS SIDE.

A COUPLE THINGS: JUST TO START OFF, THERE WAS AN AGREEMENT THAT WE ALL MADE BEFOREHAND THAT WE WOULD NOT SHARE DEMONSTRATIVES AT THIS STATION OF THE HEARING, THAT WE WOULD SHARE THEM AFTER THEY WERE USED.

NOW, AT TRIAL, OF COURSE, WE WOULD NEVER DO THAT, RIGHT, BECAUSE WE HAVE TO MAKE SURE EVERYTHING'S VETTED BEFORE IT GETS TO A JURY, BUT DUE TO THE ACCELERATED PACE THIS, WE AGREED TO THAT PROCESS.

SO THIS IS BEING USED PURELY AS A DEMONSTRATIVE.

COUPLE THINGS FACTUALLY: MS. FREIWALD HAS POINTED OUT THAT THIS IS BASED ON A STUDY. IT'S NOT REALLY BASED ON A STUDY. WHAT WE'RE SEEING HERE IS THIS VIDEOGRAPHIC EVIDENCE OF NEURON CELLS AND WHAT HAPPENS WHEN YOU EXPOSE MERCURY. THE VIDEO SPECIFIES THE EXACT

AMOUNT OF DOSE, IT SPECIFIES THE AMOUNT OF TIME, AND IT VISUALLY SHOWS WHAT HAPPENS TO THE NEURON.

NOW, DURING THE VIDEO WE INTEND -- MR. ESFANDIARY INTENDS TO PAUSE IT, ASK DR. ASCHNER WHAT WE'RE SEEING, EXPLAIN DIFFERENT CONCEPTS, AND IT'S BEING PURELY USED AS A DEMONSTRATIVE.

ALL OF THE OPINIONS, THE ASPECTS, THE TESTIMONY, THAT HE'S GOING TO BE OFFERING USING THIS AS AN ILLUSTRATIVE GUIDE, IS IN HIS REPORT.

SO WE'RE NOT SUBMITTING THIS THING AS AN EXHIBIT THAT'S GOING TO PROVE ANYTHING. IT'S LITERALLY BEING USED AS A GUIDE TO DEMONSTRATE HIS TESTIMONY.

NOW, ONE POSSIBLE COMPROMISE --

THE COURT: I THINK -- WELL, WHAT WERE YOU GOING TO SUGGEST? I'M ALL FOR COMPROMISE.

MR. WISNER: YEAH, I KNOW.

SO ONE POSSIBLE COMPROMISE WOULD BE WE JUST MUTE IT AND HAVE DR. ASCHNER TALK ABOUT WHAT WE'RE SEEING INSTEAD OF HAVING THE NARRATOR SPEAK. IT SEEMS LIKE ALMOST ALL THE OBJECTIONS WERE WHAT THE NARRATOR WAS SAYING. AND SO, IF IT'S JUST DR. ASCHNER TALKING ABOUT WHAT WE'RE SEEING, THEN IT'S PURELY DEMONSTRATIVE.

THE COURT: I THINK THAT'S A VERY GOOD IDEA.

MR. WISNER: OKAY.

THE COURT: IT'S MUCH MORE CLEARLY A DEMONSTRATIVE IF WE HAVE DR. ASCHNER SPEAKING AND NOT SOME UNKNOWN PERSON.

SO I WILL ACCEPT THE OBJECTION AS AN OBJECTION

TO IT AND -- BUT I THINK ALLOWING IT, I WOULD OVERRULE THE OBJECTION TO THE EXTENT WE ARE JUST SEEING THE VIDEO.

CAN YOU LIVE WITH THAT, MS. FREIWALD?

MS. FREIWALD: CAN I HAVE A PROFFER? IS THIS SUPPOSED TO NEURONS IN UTERO OR IS THIS SUPPOSED TO NEURONS IN A CHILD OR AN ADULT OR IS THERE ANY KIND OF PROFFER ABOUT WHAT THIS IS?

MR. WISNER: SURE. DR. ASCHNER WILL TESTIFY --

MS. FREIWALD: OR IN A SNAIL? I THINK IT'S IN A SNAIL MAYBE, BUT I'M NOT SURE.

MR. WISNER: SO, SORRY. I DIDN'T MEAN TO INTERRUPT YOU. DR. ASCHNER WILL TESTIFY ABOUT WHAT NEURONS WE ARE SEEING, HOW IT IS IN FACT A NEURON FROM A NAIL, BUT THAT IN FACT THAT IT IS IN THE SAME STRUCTURE AS ANY MAMMALIAN NEURON, BUT THEY OFTEN USE THEM BECAUSE THEY ARE BIGGER AND YOU CAN SEE WHAT HAPPENS VISUALLY. HE'S GOING TO EXPLAIN ALL OF THAT.

SO ALL OF THE FOUNDATIONAL QUESTIONS THAT YOU ARE CONCERNED ABOUT WILL BE EXPLAINED AS HE TESTIFIES AND, OF COURSE, WILL BE SUBJECT TO CROSS-EXAMINATION, YOUR HONOR.

THE COURT: OKAY. LET'S PROCEED. THANK YOU.

MS. FREIWALD: THANK YOU, YOUR HONOR.

MR. WISNER: GIVE ME TWO SECONDS TO MAKE SURE WE HAVE THE TECH, BUT IT SHOULD BE JUST REALLY QUICK.

THE COURT: SURE. OF COURSE.

(PAUSE IN THE PROCEEDINGS)

MS. FREIWALD: YOUR HONOR, IF I MAY, IS IT POSSIBLE TO GET ANY KIND OF A PROFFER FROM COUNSEL AS TO WHETHER THIS REPRESENTATION TRACKS ANYTHING THAT'S IN THE PEER-REVIEWED LITERATURE, WHETHER THIS IS A STUDY THAT HAS BEEN PUBLISHED OR NOT?

MR. ESFANDIARY: I CAN HAVE DR. ASCHNER TALK ABOUT THAT AT LENGTH, YOUR HONOR, AND WHERE THIS COMES FROM. I BELIEVE HE ACTUALLY KNOWS THE GUY THAT PUT THIS TOGETHER. SO I THINK THAT DR. ASCHNER CAN TALK ABOUT FOUNDATION FOR THIS AND WHERE IT'S COME FROM AND WHERE IT STANDS IN THE LITERATURE. I DON'T THINK THAT'S A PROBLEM.

THE COURT: ALL RIGHT. SO I THINK LET'S LET THE PLAINTIFFS PROCEED AS THEY WISH, AND OF COURSE YOU CAN OBJECT AS APPROPRIATE.

MS. FREIWALD: THANK YOU, YOUR HONOR.

THE COURT: I THINK WE LOST DR. ASCHNER, THOUGH.

(OFF-RECORD COMMENTS)

MR. ESFANDIARY: ALL RIGHT. THERE WE GO, DOCTOR, CAN YOU HEAR US?

A YES, SIR.

Q SO, DOCTOR, WE'RE GOING TO PLAY THE VIDEO, BUT WE'RE GOING TO DO IT WITHOUT THE AUDIO. SO, AS WE'RE PLAYING IT, YOU CAN JUST EXPLAIN TO THE COURT AND TO COUNSEL WHAT IS OCCURRING IN THE VIDEO; IS THAT OKAY?

A THAT'S FINE.

Q ALL RIGHT. SO I'M JUST GOING TO TAKE IT FROM

WHERE WE LEFT OFF WITH THE GROWTH CONES.

DOCTOR, WALK US THROUGH WHAT WE'RE SEEING HERE.

A OKAY.

SO BASICALLY, WHAT'S SHOWN HERE IS THE GROWTH CONE OF A NERVE CELL. IT'S VERY SMALL ON MY SCREEN. I'M TRYING TO DO MY BEST.

THE COURT: YEAH, ONE SECOND. I NEED TO FIND IT ON MY SCREEN TOO. YOU CAN CLICK ON IT. NO. SORRY. I'M NOT FINDING IT EITHER. JUST GIVE ME A MINUTE.

THE WITNESS: OKAY. I CAN SEE IT NOW, YOUR HONOR. I CAN SEE IT.

THE COURT: YEAH, BUT I CAN'T. GIVE ME A MINUTE. I DON'T KNOW WHY I CAN'T SEE IT. OH, HERE IT IS. OKAY. LET ME PIN THAT. ALL RIGHT, I'M WITH YOU.

MR. ESFANDIARY: ALL RIGHT. VERY GOOD.

Q DOCTOR, THAT'S -- GO AHEAD.

A OKAY. SO THESE LITTLE PURPLE BALLS ARE THE NERVE FIBRILS WHICH ARE BASICALLY STARTING TO FORM A HIGHWAY BY WHICH VARIOUS NUTRIENTS, MACRO MOLECULES, ARE THEN TRANSPORTED ALONG THE AXON, WHAT WE'VE TALKED ABOUT BEFORE.

WHAT'S SHOWN HERE IS, I GUESS, THEY ARE NOTING THAT ONE SECOND IN THE MOVIE IS EQUIVALENT TO 30 SECONDS, SO IT'S A TIME-LAPSED MOVIE, AND THEY ARE SHOWING, BASICALLY, THE NORMAL DEVELOPMENT OF THE GROWTH CONE WITH ALL KINDS OF MACRO MOLECULES GETTING TO THE TERMINAL OF THE CELL AND, AS YOU CAN SEE, IT CONTINUES TO GROW.

Q DOCTOR, I WANT TO PAUSE IT RIGHT THERE.

I UNDERSTAND THAT THEY DID THIS DEMONSTRATION USING SNAIL NEURONS; IS THAT CORRECT? FROM A SNAIL'S BRAIN?

A YEAH, THEY -- YES. YES, SIR.

Q OKAY. IS THAT -- HOW IS THAT IN ANY WAY RELEVANT TO UNDERSTANDING THE EFFECTS OF METHYLMERCURY ON A HUMAN NEURON?

A IT WOULD BE THE SAME. THEY USE SNAIL NEURONS BECAUSE THEY ARE OBVIOUSLY EASIER TO GET, AND THEY ARE ACTUALLY ALSO A LITTLE BIT LARGER THAN HUMANS, SNAILS.

SO IN TERMS OF THE TECHNIQUES THAT ARE REQUIRED FOR THIS TYPE OF STUDY, IT WOULD BE EASIER TO MANIFEST IN A SNAIL, BUT IN TERMS OF A PHYSIOLOGY, WHAT WE TALKED ABOUT BEFORE, THE RELEASE OF NEUROTRANSMITTERS, AND SO FORTH, THE GROWTH OF THE CONE, IT WOULD BE EXACTLY THE SAME. IT'S BASICALLY THE SAME PRINCIPALS.

Q WHAT ARE WE SEEING HERE?

A SO I STILL BELIEVE THIS IS JUST SHOWING THE NORMAL GROWTH CONE IN THE SNAIL NEURON.

Q THEN HERE IT SAYS --

A OKAY. SO HERE THEY ARE ADDING TEN TO THE MINUS SEVEN MOLAR. THIS IS THE CONCENTRATION, AND TO PUT IT INTO PERSPECTIVE, TEN TO THE MINUS SIXTH WOULD BE ONE PART A MILLION. SO IF YOU HAVE A MILLION DROPS, ONE PART OF THOSE MILLION WOULD BE MERCURY. TEN TO THE MINUS SEVEN MEANS THAT ONE TENTH OF ONE DROP WOULD BE PUT TOGETHER WITH ONE MILLION OTHER DROPS.

SO THIS IS A INFINITESIMAL CONCENTRATION OF MERCURY.

Q AND THE NEURON IS BEING EXPOSED TO THIS INFINITESIMAL NUMBER --

A THE NEURON, YES, I THINK IT WAS IN THE BEGINNING OF THIS MOVIE, THEY -- YOU COULD SEE ACTUALLY THE PIPETTES.

THEY PUT THE MERCURY IN THE FLUID, WHICH IS BATHING THIS NEURON, AND I THINK WE'VE STARTED TO SEE, ACTUALLY, BEFORE YOU EVEN STOPPED THIS, HOW THE NEURON IS STARTING TO RETRACT, OKAY. SO RATHER THAN GROWING, THE NEURON IS NOW MOVING IN THE WRONG DIRECTION.

WHAT YOU'RE SEEING HERE IS WHAT'S REFERRED TO AS DEGENERATION. THERE ARE DIFFERENT TYPES OF DEGENERATION. AND THE REASON FOR THAT IS YOU HAVE DESTROYED THE HIGHWAY, SO YOU CANNOT DELIVER, NEURO -- FED EX CANNOT -- IF THEY DON'T HAVE ANY TIRES ON THEIR TRUCK, THEY AREN'T GOING TO BE ABLE TO DELIVER YOUR GOODS. BASICALLY, IT'S THE SAME THING HERE.

SO GIVEN THE FACT THAT THE NEURON CANNOT MAINTAIN HOMOEOSTASIS WITHIN THE TERMINAL, WITHIN THE GROWTH CONE, IT STARTS TO RETRACT. SO IT'S MOVING BACKWARDS, RATHER THAN MOVING FORWARD.

Q DOCTOR, WHAT ARE THE NEUROBIOLOGICAL CONSEQUENCES OF A NEURON RETRACTING LIKE THIS, AS YOU JUST DESCRIBED?

A WELL, SO MAYBE THE EASIEST THING TO COMPARE IT TO IS ONE OF THE PREVIOUS SLIDES THAT WE DISCUSSED WHEN

WE TALKED ABOUT THE MRI. IF THE NEURON IS DYING, YOU'RE GOING TO HAVE LESS VOLUME IN THE BRAIN, LESSER NUMBER OF CELLS. THESE NEURONS ARE EVENTUALLY GOING TO COMPLETELY DISAPPEAR. EVEN IF THEY STAYED WITHIN THE BRAIN, THESE NEURONS WOULD NOT MAKE THE PROPER CONNECTIONS.

SO ALL THESE FUNCTIONS THAT WE TALKED ABOUT BEFORE, ABOUT NEUROTRANSMITTER, ABOUT TALKING TO OTHER NEURONS, GETTING ALL THE INPUT FROM THE OTHER NEURONS, MAKING EXECUTIVE DECISIONS IN TERMS OF OUTPUT, BEHAVIOR, MOTOR FUNCTION, ALL OF THIS WOULD BE COMPROMISED.

Q LET'S CONTINUE.

THIS IS THE HIGHWAY AGAIN; CORRECT?

A YEAH, I THINK THIS IS THE HIGHWAY, AND I THINK THEY ARE CONTINUING TO SHOW HERE THE RETRACTION OF THE NEURON.

Q OKAY.

AND HERE COMES THE METHYLMERCURY; IS THAT CORRECT?

A THAT'S A DROP OF METHYLMERCURY OR MERCURY. ACTUALLY, I DON'T EVEN KNOW WHAT SPECIES THEY USED.

OKAY. AND I THINK THEY EXPLAIN HERE THE REASON FOR THAT. WHAT YOU SEE IS THE HIGHWAY IS BASICALLY FALLING APART LIKE THE BRIDGE IN PITTSBURGH A FEW DAYS AGO, AND WHAT'S HAPPENING HERE IS THE MERCURY BINDS TO THE GTP, GUANOSINE TRIPHOSPHATE, WHICH IS PART OF THE -- WHICH IS THE ENERGY THAT'S NECESSARY FOR THESE NEUROFIBRILS TO FUNCTION THE PROPER WAY, AND WHEN THE MERCURY BINDS AND PREVENTS THE GTP FROM EXERTING ITS

NORMAL FUNCTION, THESE HIGHWAYS START COMING APART. SO THAT'S THE REASON FOR THE RETRACTION OF THE NEURON, FOR THE RETRACTION OF THE GROWTH CONE.

Q YOU SEE HERE, THESE DENUDED NEUROFIBRILS KIND OF, YOU KNOW, SQUISHING UP.

A YEAH. AND SO I THINK WHAT THEY'RE SHOWING HERE IS WHAT YOU'D EXPECT TO SEE IN A NORMAL NEURON GROWTH CONE, WHICH IS ON THE LEFT SIDE OF MY SCREEN, THE BRIGHTER GREEN, WITH A TUBULIN, YES.

THIS WOULD BE A NORMAL -- YOU CAN SEE MUCH LARGER VOLUME THAN THE ONE ON THE RIGHT-HAND SIDE, WHICH HAS BEEN EXPOSED TO MERCURY. AND AGAIN, THIS IS ALL RELATED TO THE FACT THAT METHYLMERCURY HAS VERY HIGH AFFINITY FOR CERTAIN COMPONENTS, SPECIFICALLY SULFHYDRYL GROUPS IN THE TUBULIN AND THIS HIGHWAY IS BASICALLY DISASSEMBLED. SO NEUROFIBRILS, NEUROTUBULES, THEY ALL FALL APART. AND, AS YOU CAN SEE HERE, I BELIEVE THE NEURON STARTS TO RETRACT. IT'S MOVING BACKWARDS, RATHER THAN FORWARDS.

Q THAT LIGHT, THAT'S THE METHYLMERCURY; CORRECT?

A YEAH. I THINK -- I BELIEVE THAT'S WHEN THEY APPLY THE --

Q YEAH.

A -- THE DROP, YES.

Q ALL RIGHT. DOCTOR, WELL, THAT'S IT FOR THIS VIDEO.

I'M GOING TO PAUSE IT RIGHT THERE.

AND LET'S TALK BRIEFLY ABOUT ARSENIC.

OKAY. AND TO DO THAT, WE'RE GOING TO GO BACK TO OUR SLIDES HERE.

CAN YOU JUST BRIEFLY WALK US THROUGH WHAT THIS DIAGRAM IS SHOWING IN TERMS OF WHAT ARSENIC DOES TO THE BRAIN?

A SO ARSENIC IS DEPICTED HERE AS ARSENIC AS203 IN TOP OF THIS FIGURE, AND THE LITTLE BLUE BALLS ON THE TOP, SPHERES, ARE BASICALLY THE CELL MEMBRANE. THEY DON'T DISCUSS SPECIFICALLY HOW THE ARSENIC GETS INTO THE CELLS, BUT WE TALKED ABOUT IT BEFORE. IT'S UTILIZING GLUCOSE TRANSPORTERS AND, BASICALLY, IT SHOWS SOME OF THE MECHANISMS BY WHICH ARSENIC EXERTS ITS TOXICITY.

THE GREEN SPHERE THAT YOU SEE IS LABELED AS MITOCHONDRIA, WHICH IS BASICALLY THE ENGINE OF THE CELL. IT PRODUCES THE ATP. IT PRODUCES THE REQUIRED ENERGY FOR THE CELL TO FUNCTION. AND THROUGH VARIOUS MECHANISMS, AGAIN, INTERFERING WITH THE DIFFERENT ENZYMES, SUCH AS CATALASE, SUPEROXIDE DISMUTASE, WHAT ARSENIC WILL DO IS INCREASE OXIDATIVE STRESS, AND THIS WILL IMPEDE MITOCHONDRIA FUNCTION.

THEY ARE -- MITOCHONDRIA ARE NOT GOING TO BE ABLE TO GENERATE OPTIMAL LEVELS OF ATP. THIS WILL RESULT IN ACTIVATION OF VARIOUS COMPONENTS THAT INDUCE CELL DEATH BY SPECIFIC MEANS, WHICH IS REFERRED TO AS APOPTOSIS. THOSE ARE KNOWN AS DIFFERENT TASK PHASES. SOME OF THE TASK PHASES ARE INHIBITORY TO APOPTOSIS, SUCH AS BCL, BCLX. YOU CAN SEE THEM IN THE FIGURE. SOME OF THEM ARE PRO-APOPTOTIC AND YOU CAN SEE, I THINK,

FROM -- IF YOU LOOK FROM THE ROSS, THE ARROW MOVES TOWARDS THE BACK. THEY ARE ACTIVATED. THEY AFFECT THE MITOCHONDRIA. IT'S LIKE A BRUSH FIRE AND, ULTIMATELY, YOU GET CELL DEATH BY MEANS OF APOPTOSIS, WHICH IS ONE OF THE MECHANISMS FOR CELL DEATH.

Q OKAY. DOCTOR, CELL DEATH, THAT'S CELL DEATH IN THE BRAIN SPECIFICALLY; RIGHT?

A NO. APOPTOSIS REFERS TO CELL DEATH IN ANY TISSUE.

Q OKAY. BUT IF WE'RE TALKING ABOUT THE NEUROTOXICITY OF ARSENIC, WE'RE TALKING ABOUT APOPTOSIS THE ARSENIC IS CAPABLE OF CAUSING IN THE BRAIN; CORRECT?

A YES, YES. YES, SIR.

Q AND THEN, VERY BRIEFLY, I WANT TO KEEP THIS BRIEF, WHAT ABOUT NEUROINFLAMMATION? HOW DOES ARSENIC INDUCE THAT, AND WHY IS THAT RELEVANT?

A SO THIS IS RELEVANT BECAUSE, ONCE YOU START HAVING DEBRIS, FOR EXAMPLE, IN THE BRAIN AS YOU'D EXPECT IF WE GO BACK TO THE MOVIE, IF THE NEURONS ARE DISINTEGRATING, THOSE ARE USUALLY TAKEN UP BY MICROGLIAL, WHICH ARE DEPICTED HERE.

FROM THE LEFT YOU SEE A RESTING MICROGLIAL. WHEN THESE CELLS COME INTO CONTACT WITH DEBRIS, OR WHEN THEY ARE ACTIVATED BY DIFFERENT MECHANISMS RELATED TO LEAD OR ARSENIC OR MERCURY EXPOSURE, THEY START TO PRODUCE ALL KINDS OF CYTOKINES, HEMOKINES. THEY'RE SHOWN ON THE RIGHT-HAND SIDE OF THIS SLIDE. THE TUMOR NECROSIS FACTOR, INTERLEUKIN, INTERFERON, GAMMA TASK

PHASES WHICH WE TALKED ABOUT BEFORE, WHICH ARE RELATED TO APOPTOSIS NITROUS OXIDE WHICH INDUCES OXIDATIVE STRESS.

SO MICROGLIAL ARE BASICALLY IMPORTANT PARTS, YOU KNOW, IN THE ORCHESTRA. WHEN YOU HAVE CELL DEATH, WHEN THEY GET ACTIVATED THEY PARTICIPATE BASICALLY IN THE PARTY.

Q NOW, DOCTOR, WE'VE COVERED THE VARIOUS WAYS THESE METALS CAN CAUSE BRAIN DAMAGE AND THE MECHANISMS BY WHICH THEY CAN CAUSE BRAIN DAMAGE.

ARE THESE MECHANISMS, AND THE WAYS IN WHICH THESE METALS CAUSE BRAIN DAMAGE, GENERALLY ACCEPTED IN THE SCIENTIFIC COMMUNITY?

A YES, THEY ARE.

Q AND, DOCTOR, YOU KNOW, WE TALKED ABOUT THE MECHANISMS, BUT WHAT ON EARTH DOES ANY OF THIS HAVE TO DO WITH ASD?

A SO ALL THESE MECHANISMS THAT WE'VE JUST DESCRIBED WILL LEAD TO THE MORPHOLOGICAL EVIDENCE THAT'S INHERENT TO THESE DISORDERS. I THINK I TOUCHED UPON THE DECREASED BRAIN MATTER. IF YOU HAVE ANY OF THESE MECHANISMS THAT INDUCE APOPTOSIS, IF YOU HAVE INFLAMMATION, ALL OF THESE, IF YOU -- IF YOU INTERFERE WITH THE NEURONTRANSMISSION, IF YOU INTERFERE WITH THE PRODUCTION OF ENERGY, ALL OF THIS IS GOING TO MANIFEST IN ABNORMAL BRAIN FUNCTION, BRAIN STRUCTURE, AND ALL OF THESE ARE INHERENT TO ASD AND ADHD.

Q LET'S JUST BRIEFLY TAKE A LOOK AT THIS. WE

HAVE HERE A DIAGRAM FOR THE LIMBIC SYSTEM. IT'S THE SAME EXHIBIT NUMBER 148. AND WE HAVE HERE VARIOUS PARTS OF THE BRAIN, I BELIEVE, THE AMYGDALA, HYPOTHALAMUS, HIPPOCAMPUS, THALAMUS, BASAL GANGLIA.

DOCTOR, CAN YOU BRIEFLY JUST EXPLAIN WHAT THESE PARTS OF THE BRAIN ARE RESPONSIBLE FOR, AND HOW AND IF METALS CAN AFFECT THESE PARTS?

A SO THESE ARE DIFFERENT BRAIN REGIONS, VERY FEW OF THEM ARE SHOWN HERE. IF WE START AT 1:00 O'CLOCK, THE BASAL GANGLIA, THEY ARE IMPORTANT IN MOVEMENTS, LEARNING, COGNITION.

GO DOWN TO THE THALAMUS, CONSCIOUSNESS AND ALERTNESS. THE BEAUTIFUL TREE UNDERNEATH IN YELLOW IS ACTUALLY THE CEREBELLUM, WHICH IS VERY IMPORTANT FOR MOVEMENT. ALL THESE -- THE GRAY ON THE TOP IS BASICALLY DIFFERENT PARTS OF THE CORTEX. WE TALKED ABOUT PREFRONTAL CORTEX BEFORE. THAT WOULD BE UP IN THE FRONT.

AND WHAT YOU SEE IN GREEN IS THE AMYGDALA, WHICH IS VERY IMPORTANT IN MEMORY, DECISION. IT'S THOUGHT TO BE AN EMOTIONAL AREA, AN AREA THAT AFFECTS EMOTIONS IN HUMANS. THE HYPOTHALAMUS IS MOSTLY IMPORTANT IN TERMS OF REGULATING TEMPERATURE, HUNGER, RELEASE OF HORMONES, FOR EXAMPLE. SLEEP.

BUT ALL -- THERE'S NO DISTINCTION, ACTUALLY, IN TERMS OF WHERE THESE METALS ACCUMULATE, ESPECIALLY IN KIDS. THERE ARE SOME DISTINCTIONS FOR MERCURY, FOR EXAMPLE, BETWEEN YOUNG INDIVIDUALS AND OLDER

INDIVIDUALS, BUT IN GROWING INDIVIDUALS, IN UTERO OR POST-NATALLY, THERE'S GENERALLY A FAIRLY UBIQUITOUS DISTRIBUTION OF THESE METALS. IT'S NOT NECESSARILY HIGHER IN ONE OF THESE REGIONS VERSUS THE OTHER.

SO ALL OF THESE BRAIN AREAS MIGHT BE AFFECTED LEADING TO ABHORRENT BRAIN FUNCTION.

Q AND SOME OF THESE VERY SAME BRAIN AREAS, IS WHAT IS IMPAIRED IN AUTISTIC CHILDREN; CORRECT?

A THAT'S CORRECT.

Q NOW, DOCTOR -- NOW, HERE WE HAVE -- AND YOUR REPORT DISCUSSES HUNDREDS OF STUDIES. I MEAN, THE TOXICOLOGICAL DATA, THE MECHANISTIC DATA, AND OF COURSE, THE NEUROLOGICAL DATA HERE IS VAST.

INSTEAD OF GOING THROUGH ALL THE STUDIES THAT ARE LISTED IN YOUR REPORT, I WANT TO TAKE A LOOK AT SOME OF YOUR OWN PUBLICATIONS PREDATING YOUR INVOLVEMENT IN THIS LITIGATION, OKAY, TO HELP US FLESH OUT YOUR OPINION IN THIS MATTER.

AND I'M GOING TO START WITH EXHIBIT NUMBER 28.

CAN YOU SEE MY SCREEN HERE, DOCTOR?

A YES, I CAN.

Q ALL RIGHT. AND THIS IS A STUDY BY YOURSELF; CORRECT? AND AANYA GOEL; IS THAT RIGHT?

A AANYA.

Q AANYA. AND IT PUBLISHED IN THE INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES; CORRECT?

A THAT'S CORRECT.

Q IS THAT A DECENTLY WELL RESPECTED JOURNAL?

MS. FREIWALD: YOUR HONOR, MAY I JUST OBJECT? THIS IS ACTUALLY NOT A STUDY. IT'S A REVIEW ARTICLE. IT'S NOT ANY ORIGINAL RESEARCH.

THE COURT: FAIR ENOUGH.

YOU CAN BRING THAT OUT ON CROSS-EXAMINATION, BUT THANK YOU. IT'S AUTHORED BY DR. ASCHNER.

MR. ESFANDIARY:

Q AND, DOCTOR, IS THAT A WELL RESPECTED JOURNAL?

A I DON'T RECALL THE IMPACT FACTOR, BUT I BELIEVE IT'S PROBABLY AROUND FIVE, SIX. SO I WOULD SAY I CAN DEFINE IMPACT FACTOR, BUT IT'S A REPUTABLE JOURNAL, YES.

Q AND THE TITLE OF THIS IS "THE EFFECT OF LEAD EXPOSURES ON AUTISM DEVELOPMENT."

CORRECT?

A THAT'S CORRECT.

Q ALL RIGHT. AND YOU PUBLISHED THIS BEFORE GETTING INVOLVED IN THIS LITIGATION; IS THAT RIGHT, DOCTOR?

A THAT'S CORRECT. I THINK IT WAS SUBMITTED PROBABLY IN 2020 AND IT WAS PUBLISHED IN 2021. THERE'S A REVIEW PROCESS. IT TAKES TIME.

Q THAT'S RIGHT. IT SAYS IT WAS PUBLISHED IN -- 6 OF FEBRUARY 2021.

A SO IT WAS SUBMITTED IN 2020, LONG BEFORE, I THINK, YOU CONTACTED ME.

Q ALL RIGHT. DOCTOR, I WANT TO TAKE A LOOK AT WHAT YOU SAID IN THIS ARTICLE.

IT SAYS HERE, IN THE ABSTRACT THAT "PREVIOUS

STUDIES HAVE HIGHLIGHTED EXPOSURE TO LEAD MAY PLAY A ROLE IN ASD."

CAN YOU SEE THAT, DOCTOR?

A YES, SIR.

Q ARE YOU REFERRING THERE TO PRIOR EPIDEMIOLOGICAL AND TOXICOLOGICAL STUDIES?

A YES, SIR.

Q NEXT HERE YOU SAY, "IN ADDITION, LEAD HAS BEEN SHOWN TO BE ONE OF THE MOST PREVALENT METAL EXPOSURES ASSOCIATED WITH NEUROLOGICAL DEFICITS."

DO YOU SEE THAT, DOCTOR?

A YES, SIR.

Q AND WHAT DO YOU MEAN BY "HAVING SHOWN TO BE MOST PREVALENT METAL EXPOSURES ASSOCIATED WITH NEUROLOGICAL DEFICITS"?

A SO WE WOULD REFER TO ADHD, FOR EXAMPLE, OTHER NEUROLOGICAL DEFICITS.

Q AND IT SAYS HERE THAT THE PURPOSE -- I'M JUST GOING TO BLOW IT UP SO WE CAN SEE.

IT SAYS HERE, "A SEMI-SYSTEMATIC REVIEW WAS CONDUCTED USING PUBLIC DATABASES IN ORDER TO EVALUATE THE EXTENT OF LEAD'S ROLE IN THE ETIOLOGY OF AUTISM."

CORRECT?

A THAT'S CORRECT.

Q AND WHAT IS A SEMI-SYSTEMATIC REVIEW, DOCTOR?

A SO, WE BASICALLY GATHERED ALL THE INFO -- WELL, NEVER SAY NEVER AND NEVER SAY ALL, BECAUSE WE MAY HAVE MISSED SOME PAPERS, BUT AGAIN, I THINK WITHOUT ANY BIAS,

WE TRY TO GATHER ALL THE PAPERS AND ANALYZE THEM SYSTEMATICALLY TO SEE WHETHER THEY SHOW A RELATIONSHIP BETWEEN BLOOD LEVELS OR OTHER BIOLOGICAL MARKERS OF LEAD EXPOSURE WITH THE PRESENCE OF ASD.

Q AND WHY DID YOU TAKE THAT APPROACH OF DOING A SEMI-SYSTEMATIC REVIEW?

A BECAUSE IT'S MUCH STRONGER EVIDENCE THAN JUST REVIEWING ONE OR TWO PAPERS. YOU KNOW, THE LARGER THE N, OBVIOUSLY, YOU ELIMINATE A LOT OF CONFOUNDERS, ESPECIALLY WHEN YOU CONSIDER THE FACT THAT YOU MIGHT BE DOING STUDIES IN DIFFERENT POPULATIONS, THEN OBVIOUSLY YOU'RE ELIMINATING POTENTIAL FOR THE GENETICS TO INFLUENCE THE DISEASE.

SO THE GREATER THE NUMBER OF STUDIES, THE GREATER THE NUMBER OF INDIVIDUALS, THE GREATER THE POWER OF THE STUDY.

Q AND, DOCTOR, IS THAT THE SAME APPROACH THAT YOU EMPLOYED HERE IN THIS CASE?

A YES, THAT'S CORRECT.

Q OKAY.

NOW, IT SAYS HERE -- OOPS.

"SPECIFICALLY THE MECHANISMS OF ACTION OF LEAD EXPOSURE, INCLUDING CHANGES WITHIN THE CHOLINERGIC, DOPAMINERGIC, GLUTAMATERGIC, GAMMA-AMINOBUTYRIC ACID ARE DISCUSSED."

CAN YOU SEE THAT, DOCTOR?

A YES, SIR.

Q DOCTOR, WHAT THE ON EARTH ARE THESE SYSTEMS?

A OKAY. SO YOU ACTUALLY DIDN'T PRONOUNCE THEM RIGHT. IT'S DOPAMINERGIC, CHOLINERGIC, GABAERGIC, AND GLUTAMATERGIC.

SO THESE REFER TO DIFFERENT PHENOTYPES OF NEURONS THAT PRODUCE DIFFERENT TYPES OF NEUROTRANSMITTERS. AND SOME OF YOU MAY HAVE HEARD ABOUT DOPAMINE. DOPAMINE IS A CHEMICAL. IT'S A NEUROTRANSMITTER THAT'S BEEN IMPLICATED IN PARKINSON'S DISEASE, FOR EXAMPLE. IT'S VERY IMPORTANT IN TERMS OF THE AWARD SYSTEM, AND WE'VE SEEN, ACTUALLY, DOPAMINE IN THE PREVIOUS SLIDE WHEN WE TALKED ABOUT THE BASAL GANGLIA. THERE'S A LOT OF DOPAMINE THERE.

BUT THE POINT OF THIS IS TO SHOW THAT LEAD AFFECTS ALL OF THESE NEUROTRANSMITTERS. IT DOESN'T HAVE A PREFERENCE FOR ONE OR THE OTHER. THERE ARE, AGAIN, ENOUGH STUDIES TO DEMONSTRATE THAT LEAD WILL DECREASE THE LEVELS OF GABA, DOPAMINE, GLUTAMATE IN THE BRAIN.

AND THE SIGNIFICANCE OF THIS, AGAIN, GOES BACK TO WHAT WE'VE TALKED ABOUT BEFORE. ONCE YOU REDUCE THE LEVELS OF THESE NEUROTRANSMITTERS, YOU'D EXPECT TO SEE CHANGES IN BRAIN FUNCTION. THE SYNAPTIC TRANSMISSION IS IT GOING TO BE COMPROMISED, FOR EXAMPLE.

Q DOCTOR, JUST TO TIE IT TOGETHER, IT SAYS HERE THAT CONSIDERATIONS OF THE CURRENT DATA AND TRENDS SUGGEST A POTENTIAL STRONG ROLE FOR LEAD IN ASD.

DOCTOR, WHAT DO YOU MEAN BY A "STRONG ROLE FOR LEAD IN ASD"?

A SO, AGAIN, FROM THE STUDIES THAT I'VE READ THAT

ARE CITED THIS PAPER AND SUBSEQUENT STUDIES THAT I'VE READ, I THINK THAT THE DATA ARE SUPPORTIVE OF AN ASSOCIATION BETWEEN EXPOSURE TO LEAD AND ASD.

Q AND, DOCTOR, IT SAYS HERE THAT YOU FOCUSED ON AUTISTIC -- THE LEAD'S CAPABILITY FOR INDUCING AUTISTIC COMORBID SYMPTOMS OF AUTISM.

LET ME JUST HIGHLIGHT IT SO YOU CAN SEE.

FURTHERING OF COMORBIDITIES OF AUTISM.

DOCTOR, WHAT IS THE -- HOW IS STUDYING THE COMORBIDITIES OF AUTISM IN ANY WAY RELEVANT TO UNDERSTANDING OF HOW LEAD CAN CAUSE ASD?

A I'M NOT SURE I UNDERSTAND THE QUESTION.

Q SURE.

IT SAYS HERE THAT YOU WERE STUDYING THE COMORBIDITIES OF AUTISM.

WHY?

A WELL, BECAUSE, I MEAN, LEAD WOULD HAVE EFFECTS ON MANY SYSTEMS, AND IT MIGHT BE BEYOND JUST ASD. I'M NOT SURE I'M ANSWERING YOUR QUESTION, BUT THERE IS COMORBIDITIES BETWEEN ASD, FOR EXAMPLE, AND ADHD. SO WHILE THIS IS SPECIFIC TO ASD, YOU COULD PROBABLY PERFORM THE SAME STUDY AND LOOK AT ADHD AND SEE THE SAME KIND OF RELATIONSHIPS.

Q AND PAGE 3, IT SAYS HERE, DOCTOR, "PRIOR TO DISTINGUISHING SPECIFIC AREAS OF FOCUS WITHIN THE REVIEW, BACKGROUND RESEARCH WAS CONDUCTED ON AUTISM AND ITS PRIMARY SYMPTOMS TO MAKE ADEQUATE CONNECTIONS TO THE EFFECTS OF LEAD

EXPOSURE."

DO YOU SEE THAT, DOCTOR?

A YES, I DO.

Q NOW, I KNOW, DOCTOR, THERE'S BEEN SOME ALLEGATIONS MADE BY DEFENDANTS IN THIS CASE THAT YOU ARE NOT SUFFICIENTLY -- IN PREPARING YOUR REPORT IN THIS CASE, YOU WERE NOT SUFFICIENTLY FAMILIAR WITH THE SYMPTOMS OF ASD AND ASD ITSELF IN ORDER TO BE REACHING YOUR OPINIONS.

I JUST WANT TO BE VERY CLEAR. IN THIS STUDY, YOU SAY THAT YOU CONDUCTED BACKGROUND RESEARCH TO UNDERSTAND THE SYMPTOMS OF AUTISM AND HOW LEAD COULD CAUSE THOSE SYMPTOMS.

AND IS THAT WHAT YOU DID IN THAT STUDY, DOCTOR?

A YES, SIR.

Q OKAY. AND DID YOU DO THAT SAME PROCESS HERE?

A YES, SIR.

Q AND WHY DID YOU DO THAT?

A WELL, WE OBVIOUSLY WANT TO KNOW WHETHER OUR KNOWLEDGE, APPLIED KNOWLEDGE FROM THE MECHANISTIC STUDIES, LOOKING AT MODES OF ACTION AND THE MEANS BY WHICH THESE METALS, OR LEAD SPECIFICALLY IN THIS CASE, HOW THE EFFECTS THAT MANIFEST IN A SINGLE CELL MIGHT BE TRANSLATED TO ASD OR OTHER DISORDERS.

SO, YOU KNOW, I SAID BEFORE, I'M NOT A CLINICIAN. I'M NOT AN EXPERT IN DIAGNOSING ASD, BUT I THINK I HAVE A REASONABLE COMMAND OF THE RELATIONSHIP BETWEEN LEAD AND SOME OF THESE CLINICAL MANIFESTATIONS.

Q DOCTOR, TO BE CLEAR, THIS ARTICLE -- WAS THIS PEER-REVIEWED?

A YES, SIR.

Q OKAY. AND WAS IT SUBJECT TO RIGOROUS SCIENTIFIC METHOD AND REVIEW?

A WELL, I CAN'T SPEAK ON BEHALF OF THE REVIEWERS, BUT I'VE HAD PAPERS THAT WERE REJECTED BEFORE. IT'S COMMON. SOMETIMES YOU'RE ASKED TO REVISE A PAPER, BUT I'VE PUBLISHED IN THE VICINITY OF 860 PAPERS, SO I THINK IT'S A REASONABLE NUMBER.

Q YES, IT CERTAINLY IS.

NOW, DEFENDANTS ARE CLAIMING THAT THIS IS NOT ORIGINAL RESEARCH.

IS THAT TRUE, THIS PAPER?

A WELL, THIS IS REVIEW OF THE LITERATURE, THAT'S CORRECT.

Q OKAY.

A I MEAN, THERE IS NOTHING WRONG WITH REVIEWS. ACTUALLY, THEY ARE VERY HELPFUL BECAUSE AT TIMES WHAT THEY DO IS THEY SYNTHESIZE DIFFERENT TYPES OF RESEARCH ARTICLES THAT HAVE BEEN PUT TOGETHER AND IT PUTS IT IN A MUCH MORE COHERENT FRAME. YOU KNOW, IT PUTS IT UNDER THE MICROSCOPE TO SEE WHETHER DIFFERENT STUDIES CONDUCTED BY OTHER PEOPLE HAVE REACHED THE SAME TYPES OF CONCLUSIONS.

SO THERE'S GREAT MERIT ACTUALLY TO REVIEW PAPERS BECAUSE THEY ARE VERY INFORMATIVE. THEY LOOK AT CONSISTENCIES, AND THEY ARE STRONG IN TERMS OF DEFINING

ASSOCIATIONS BETWEEN EXPOSURES AND OUTCOMES. SO I WOULD SAY THE FACT THAT IT'S A REVIEW REALLY DOESN'T MAKE MUCH OF A DIFFERENCE.

Q NOW, DOCTOR --

A TO THE CONTRARY.

Q UNDERSTOOD.

NOW, MY PEN IS BEING VERY TEMPERAMENTAL HERE, BUT BEAR WITH ME WHILE I TRY TO GET THIS UP.

IT SAYS HERE ON PAGE 2 -- I WANT TO BREAK THIS DOWN IN QUITE A BIT A DETAIL.

"THE ADVERSE HEALTH CONSEQUENCES OF LEAD SHOULD BE INVESTIGATED IN THE CONTEXT OF ITS LONG HALF LIFE AND MODERATE TURNOVER WITHIN THE BODY."

DO YOU SEE THAT, DOCTOR?

A YES, SIR.

Q ALL RIGHT.

CAN YOU JUST BRIEFLY WALK US THROUGH WHAT THAT'S REFERRING TO? WHAT IS HALF LIFE? WHAT IS LEAD'S HALF LIFE? WHAT IS MODERATE TURNOVER WITHIN THE BODY? WHAT ARE THESE CONCEPTS GETTING AT?

A SO THE HALF LIFE LEAD OF REALLY DEPENDS ON THE TISSUE, WHERE IT'S -- WHERE IT IS THE POSITIVE. IT CAN BE FROM DECADES IF WE TAKE, FOR EXAMPLE, BONE OR TEETH. LEAD IN BONE CAN BE THERE FOR, THE LENGTH OF IT, FOR THE DURATION OF HUMAN LIFE, FOR SEVERAL DECADES AT A MINIMUM. AND THE REASON FOR THAT IS THAT THE REMODELLING OF THE BONE IS A VERY SLOW PROCESS. SO ONCE IT'S DEPOSITED, AGAIN, BECAUSE IT'S SUBSTITUTES CALCIUM,

IT'S THERE AND IT MAY NOT BE RELEASED FROM THE BONE INTO THE BLOOD STREAM FOR DECADES. IN OTHER TISSUES, THE HALF LIFE OF LEAD CAN BE VERY SHORT. IT CAN BE IN THE ORDERS OF DAYS, BLOOD, FOR EXAMPLE.

IN THE BRAIN, IT'S INTERMEDIATE. IT'S PROBABLY MONTHS TO YEARS, AND THAT'S IMPORTANT WHEN WE TALK ABOUT NEUROLOGICAL DISORDERS BECAUSE LEAD THAT GETS INTO THE BRAIN IS THERE FOR A LONG TIME.

AND ANOTHER IMPORTANT CONCEPT THAT I SHOULD NOTE IS THAT WE DON'T HAVE REALLY ANY MEANS TO GET THE LEAD OUT OF THE BRAIN. THERE ARE SOME TREATMENTS FOR BRAIN EXPOSURE -- FOR LEAD EXPOSURE. PEOPLE USE SODIUM CALCIUM EDTA. THERE'S ANOTHER DRUG KNOWN AS SUCCIMER. THEY ARE VERY EFFECTIVE.

WHAT THEY WILL DO IS, THEY WILL GET THE LEAD FROM THE SOFT TISSUES, LIKE KIDNEY AND LIVER, FROM MUSCLE, BUT BECAUSE THESE DRUGS ARE TOO BIG, GOING BACK TO THE CONCEPT OF THE BLOOD-BRAIN BARRIER, THEY ARE NOT ABLE TO GET INTO THE BRAIN. SO ACTUALLY, THE CONCENTRATION OF LEAD IN THE BRAIN STAYS THERE FOR A VERY, VERY LONG TIME.

Q NOW, I WANT TO FOCUS IN ON THAT A LITTLE BIT.

IT SAYS HERE THAT, "LEAD ALSO DEPOSITS IN THE BONE, FROM WHICH IT MAY REENTER THE BLOODSTREAM UPON INCREASED VISCOELASTIC ACTIVITIES, SUCH AS DURING PREGNANCY, AGING AND MENOPAUSE."

AND THEN IT SAYS, "FURTHERMORE, THE TYPICAL HALF LIFE OF LEAD IN THE BONE IS 20 TO 30

YEARS."

DO YOU SEE THAT, DOCTOR?

A YES, SIR.

Q NOW, DOCTOR, I WANT TO PUT THIS IN A BIT OF A CONTEXT.

SO IF A CHILD AROUND ABOUT THE AGE OF ONE AND TWO IS EXPOSED TO LEAD AND THAT LEAD STICKS TO -- INTO THEIR BONE, CAN THAT SAME SOURCE OF LEAD EXPOSURE OF LEAD THAT'S ENTERED THEIR BODY, MANIFEST IN THE BLOOD YEARS DOWN THE LINE BASED ON THE PROCESS THAT YOU JUST DESCRIBED?

A YES. THAT'S EXACTLY WHAT I'M REFERRING TO.

THE LEAD IN THE BONE WILL BE THERE, AND IT WILL LEECH OUT INTO THE BLOOD AS THE BONE IS REMODELLING, WHICH IS A VERY SLOW PROCESS. IT'S HASTENED BY DIFFERENT PHYSIOLOGICAL CONDITIONS, FOR EXAMPLE, LEAD ABSORPTION IS INCREASED IN PREGNANCY. IT'S INCREASED IN OLDER INDIVIDUALS. OSTEOPOROSIS WOULD BE ONE EXAMPLE, SO OLDER AGE.

BUT, YOU KNOW, THE LEAD THAT'S IN THE BONE IS NOT GOING TO STAY THERE. IT'S AN INFINITESIMAL AMOUNT. IT'S NOT A VERY LARGE AMOUNT OF LEAD, BUT THE PRINCIPLE BASICALLY IS THAT, OVER TIME, IT'S GOING TO BE RELEASED IN INTO THE BLOOD. YES.

Q IF A CHILD AT ONE AND TWO IS EXPOSED TO LEAD, AND IT ENDS UP IN THEIR BONE, THE PROCESS OF AGING, AS THEIR BONE GROWS AND SO FORTH, COULD THAT LEAD BE FOUND IN THE BLOOD WHEN THAT CHILD REACHES THE AGES OF FOUR,

FIVE, SIX, AND SO ON?

A YES, ABSOLUTELY. YES.

Q ALL RIGHT. DOCTOR, I WANT TO GO BACK TO YOUR STUDY.

HOW DOES THE HALF LIFE AND TURNOVER OF LEAD IN THE BODY COMPARE WITH THAT OF MERCURY AND ARSENIC?

A SO LEAD HAS GENERALLY, AT LEAST IN BONE, MUCH LONGER HALF LIFE COMPARED TO MERCURY OR ARSENIC, AND THE REASON FOR THAT IS THAT MERCURY AND ARSENIC ARE NOT CALCIUM NEMETICS, SO THEY DON'T TEND TO ACCUMULATE IN THE BONE, BUT, YOU KNOW, IN SOFT TISSUES AND, AGAIN, IN THE BRAIN, THEY WILL HAVE -- BOTH OF THESE METALS WILL HAVE LONGER HALF LIVES THAN ARSENIC AND MERCURY IN THE BLOOD. AGAIN, THAT MAY BE IN THE ORDER OF DAYS. IN THE BRAIN, IT'S PROBABLY -- OR IT IS, NOT PROBABLY. THE HALF LIFE OF MERCURY, FOR EXAMPLE, IN THE BRAIN IS THREE MONTHS.

Q OKAY.

AND, DOCTOR, HERE IT SAYS, "CURRENTLY THERE ARE NO SAFE BLOOD LEVELS, AND MINUTE TRACES OF BLOOD LEAD ARE CONSIDERED HARMFUL, INCREASING THE CONCERN REGARDING LEAD EXPOSURE."

DO YOU SEE THAT, DOCTOR?

A YES, SIR.

Q ALL RIGHT. I WANT TO TALK ABOUT THIS IDEA OF DOSE AND WHAT THAT MEANS TO BE NO SAFE BLOOD LEVELS.

CAN YOU JUST -- LET'S START OFF BY YOUR EXPLANATION, DOCTOR.

WHAT DOES IT MEAN FOR THERE BE NO, AS YOU PUT IT HERE, NO SAFE BLOOD LEVEL? WHAT IS THAT GETTING AT?

A WELL, IT'S BEEN STATED BY MANY AUTHORITIES THAT THE SAFEST BLOOD LEVEL IN THE BLOOD IS ZERO. SO -- BECAUSE WE DON'T KNOW, BASICALLY. WE DO KNOW -- WELL, I'LL GIVE YOU A HISTORICAL PERSPECTIVE. I BELIEVE 20, 30 YEARS AGO, SAFE BLOOD LEAD LEVELS WERE 60 MICROGRAMS PER DECILITER, AND THEN WE'VE STARTED TO REALIZE THAT IT DOES HAVE SOME ILL EFFECTS IN CHILDREN, SO IT WAS REDUCED TO 25.

WE'VE STARTED TO DO STUDIES -- OR OTHER PEOPLE, I SHOULD SAY, I DID NOT DO THESE STUDIES, HAVE LOOKED AT LOWER BLOOD LEAD LEVELS, AND CDC LOWERED BLOOD LEAD LEVELS TO 10 MICROGRAMS PER DECILITER. WE NOW HAVE PLENTY OF EVIDENCE THAT EVEN LOWER LEVELS OF BLOOD, LEAD IN THE BLOOD, AT LEVELS AS LOW AS 2 MICROGRAMS PER DECILITER ARE ASSOCIATED WITH MANY OF THE BEHAVIORS THAT ARE INHERENT TO ASD AND ADHD.

SO AS WE GET BETTER WITH OUR TECHNOLOGY, AS STUDIES ARE BETTER REFINED TO LOOK AT BEHAVIORAL DEFICITS, WE ARE REVISING OUR STANDARDS, BASICALLY, HAVING GONE FROM 60 TO 10. AND I DON'T WANT TO GUESS, BUT PROBABLY IN THE FUTURE, THE 10 MICROGRAM PER DECILITER WILL GO DOWN.

AND I SAY THERE'S NO LEVEL BECAUSE WE DON'T KNOW WHAT HAPPENS AT LEVELS OF A POINT MICROGRAM PER DECILITER. WE DON'T HAVE THAT INFORMATION YET. BUT AGAIN, GIVEN THE FACT THAT IT'S NOT ESSENTIAL, GIVEN

THAT WE KNOW THAT IT INTERFERES WITH CALCIUM SIGNALLING AND ALL THE OTHER THINGS WE MENTIONED BEFORE, THERE'S NO REASON TO BELIEVE THAT THERE'S A SAFE LEVEL OF LEAD.

Q DOCTOR, ARE THERE SAFE LEVELS FOR MERCURY AND ARSENIC?

A NO. IT'S THE SAME PRINCIPLE.

Q OH, SORRY, DOCTOR. I THINK WE JUST LOST YOU. I...

A OH.

Q YOUR CAMERA HAS DIED.

A AM I THERE?

Q YOU'RE BACK, YES.

A OKAY. IT'S MY FAULT. I GOT EXCITED AND I MOVED SOMETHING ON THE SIDE OF MY COMPUTER. SO...

Q NOT A PROBLEM, DOCTOR.

A OKAY. CAN YOU REPEAT THE QUESTION, PLEASE?

Q YES.

A YOU ASKED ME WHETHER MERCURY AND ARSENIC ARE BASICALLY NO SAFE LEVELS FOR THOSE, AND I SAID, YES, THERE'S NO SAFE LEVELS FOR MERCURY AND ARSENIC.

Q OKAY. GREAT.

NOW, DOCTOR, TO BE CLEAR, ARE YOU SAYING THAT LEAD, MERCURY AND ARSENIC, THEN CAN CAUSE ASD AT ANY LEVEL OF EXPOSURE?

A NO, I'M NOT SAYING THAT.

Q YEAH.

A NO, ABSOLUTELY NOT. NO.

Q AND COULD YOU ELABORATE?

A YEAH. I MEAN, I WOULD NEVER SAY THAT THE ONLY THING THAT CAUSES ASD IS LEAD. I MEAN, IT'S INTERACTION BETWEEN MANY, MANY OTHER THINGS AND LEAD. I MEAN, I HAVE SAID DURING MY DEPOSITION AND MY REPORT, I BELIEVE, THAT THERE'S GENETIC COMPONENTS TO ASD. SO JUST TO IMPLY THAT ASD IS THE ONLY THING THAT WOULD CAUSE -- I'M SORRY -- THAT LEAD IS THE ONLY CAUSE FOR ASD OR YOU JUST NEED SOME LEAD IN YOUR BLOOD TO CAUSE ASD, I DON'T THINK THAT WOULD BE ACCURATE.

Q I APOLOGIZE. WE'RE HAVING SOME TECHNICAL ISSUES. I'M GOING TO -- I WANT TO SHOW YOU A DOCUMENT, BUT IT LOOKS LIKE IT'S NOT GOING TO APPEAR FOR A COUPLE OF MINUTES. SO I'M GOING TO MOVE ON, AND WE'RE GOING TO THIS, TO COME BACK TO THIS DISCUSSION OF DOSE, IN JUST A SECOND.

ALL RIGHT. LET'S GO BACK TO YOUR STUDY. LET ME JUST PULL IT UP.

AND I APOLOGIZE, YOUR HONOR, IT'S JUST TECHNICAL ISSUES.

CAN YOU SEE THAT, THE PAGE, DOCTOR?

A YES.

Q OKAY.

A YES.

Q NOW, YOU HAVE HERE A REALLY HANDY-DANDY DIAGRAM OF THE WAY IN WHICH LEAD ENTERS THE BODY.

CAN YOU JUST BRIEFLY EXPLAIN HOW THIS ROUTE OF ENTRY MAY BE DIFFERENT OR SAME COMPARED TO MERCURY AND ARSENIC?

A SO SOURCES OF EXPOSURE FOR THESE METALS ARE IDENTICAL. IT CAN BE THROUGH THE SKIN. IT COULD BE BY INHALATION, BY INGESTION AND, YOU KNOW, I DIDN'T GO INTO IT, BUT THESE METALS CAN EXIST IN DIFFERENT OXIDATION STATES. THEY CAN BE IN THE ORGANIC OR INORGANIC FORM. SO THERE'S A LOT OF PHYSICAL AND CHEMICAL PROPERTIES THAT ARE GOING TO GUIDE AND DETERMINE HOW MUCH OF EACH OF THESE METALS IS GOING TO BE ABSORBED.

BUT THE POINT OF THIS SLIDE IS THAT LEAD AND, AGAIN, THE OTHER METALS AS WELL, IT WOULD BE THE SAME THING. THEY WOULD BE EITHER INGESTED, GETTING THROUGH THE SKIN, INHALED. THEY WILL FIND THEIR WAY BECAUSE THEY GET TRANSPORTED, OR BY OTHER MEANS, INTO THE BLOODSTREAM AND THEN THEY DISTRIBUTE TO DIFFERENT TISSUES.

HERE THERE'S EMPHASIS ON THE BONES, WHICH WOULD NOT BE THE CASE WITH LEAD -- WITH MERCURY OR WITH ARSENIC, AND THEN THE ARROW POINTING DOWNWARDS, ITS AFFECT ON BRAIN AND DIFFERENT NEUROTRANSMITTER SYSTEMS. IT WOULD BE APPROPRIATE FOR THE OTHER ONES AS WELL.

Q NOW, PAGE 3, YOU TALK ABOUT -- OOPS -- YOU TALK ABOUT THE ASSOCIATION BETWEEN LEAD EXPOSURE AND THE COMORBIDITIES OF AUTISM; RIGHT? IS THAT HERE ON THE SCREEN?

A I CAN SEE IT, YES.

Q OKAY.

AND THEN YOU GIVE A SUMMARY OF YOUR FINDINGS ON PAGE 5. I'D JUST LIKE TO LOOK AT THIS.

IT SAYS, "THE PREVALENCE OF SOCIAL WITHDRAWAL, LOSS OF INTELLIGENCE SCORES, DECLINE IN MEMORY, AND LANGUAGE DIFFICULTIES IN LEAD-EXPOSED INDIVIDUALS FURTHER SUGGEST THE PROBABLE ROLE OF LEAD IN FURTHERING COMORBIDITIES ASSOCIATED WITH AUTISM."

DO YOU SEE THAT, DOCTOR?

A YES.

Q CAN YOU JUST BRIEFLY EXPLAIN WHAT YOU MEAN BY THAT.

A SO, AGAIN, ASD HAS, YOU KNOW, SPECIFIC -- THE CRITERIA FOR DETERMINING AUTISM ARE FAIRLY SPECIFIC. I DON'T DO THAT NECESSARILY CLINICALLY, BUT THE IDEA HERE IS THAT THERE ARE SOME COMORBIDITIES THAT YOU SEE IN OTHER SYNDROMES, SYMPTOMS IN THE BRAIN IN INDIVIDUALS THAT DO NOT NECESSARILY HAVE ASD.

FOR EXAMPLE, YOU KNOW, WHEN YOU THINK ABOUT IQ, IT'S BEEN ESTIMATED THAT EACH EXCESS, CERTAIN AMOUNT OF MICROGRAMS PER DECILITER OF LEAD IS RELATED TO A DECREMENT OF ONE POINT IQ, AND THERE HAVE BEEN SOME BEAUTIFUL BELL-SHAPED CURVES THAT SHOW YOU EXACTLY WHAT YOU'D EXPECT TO SEE WITH A POPULATION OF A HUNDRED MILLION WITH IQ OF 100 AND WHAT HAPPENS TO THEM WHEN THEY ARE EXPOSED TO LEAD AND THE IQ GOES TO 95. SO WHILE NOT ALL KIDS THAT HAVE ASD HAVE NECESSARILY A DECREMENT IN IQ, MANY OF THEM DO.

SO BY COMORBIDITIES, SOME OF THESE STUDIES WERE NOT DESIGNED NECESSARILY TO STUDY ASD. THEY LOOKED AT

OTHER KINDS OF BEHAVIORS OR END POINTS, BUT THEY ARE COMORBID TO ASD. THAT'S WHAT'S MEANT HERE.

Q DOCTOR, IT SAYS, "WHILE LEAD HAS BEEN SCIENTIFICALLY PROVEN TO CAUSE THESE COMORBIDITIES, THE PRESENCE OF THESE COMORBIDITIES DOES NOT NECESSARILY MEAN THAT THEY WERE INDUCED BY LEAD."

CORRECT?

A YES.

Q ALL RIGHT. AND IS THAT WHAT YOU'RE GETTING AT? THAT JUST BECAUSE YOU MAY HAVE SOME OF THESE SYMPTOMS AND COMORBIDITIES OF AUTISM, ARE THERE OTHER CAUSES BESIDES LEAD FOR THESE SYMPTOMS?

A YES, ABSOLUTELY.

Q OKAY. ALL RIGHT. DOCTOR, I WANT TO LOOK AT SPECIFICALLY SOME OF THE MECHANISMS THAT YOU HIGHLIGHT IN THIS PAPER. I WANT TO CALL OUT THIS IS PAGE.

ON PAGE 5, YOU TALK ABOUT THE IMPACT ON CHOLINERGIC SYSTEM AND ENERGY METABOLISM -- I PRONOUNCING THAT INCORRECTLY.

HOW IS IT PRONOUNCED, DOCTOR?

A CHOLINERGIC.

Q CHOLINERGIC. OKAY.

CAN YOU JUST -- YOU KNOW WHAT? LET'S PULL UP THE PART WHERE YOU TALK ABOUT THIS.

IT SAYS HERE, "AUTISTIC INDIVIDUALS HAVE BEEN SHOWN TO POSSESS A VARIETY OF DYSFUNCTIONALITIES WITHIN THE" -- CAN YOU READ

THAT OUT FOR US, DOCTOR?

A YOU'D LIKE ME TO READ IT?

Q PLEASE.

A OH, OKAY.

SO, "AUTISTIC INDIVIDUALS HAVE SHOWN TO POSSESS A VARIETY OF DYSFUNCTIONALITIES WITHIN THEIR DOPAMINERGIC, CHOLINERGIC AND GLUTAMATERGIC SYSTEMS..." AND NOW IT DISAPPEARED FROM MY SCREEN.

MR. ESFANDIARY: SORRY, IT'S JUST TECHNICAL ISSUES.

CAN WE JUST TAKE A -- YOUR HONOR, DO YOU MIND INDULGING US WITH A QUICK TWO- OR THREE-MINUTE BREAK?

THE COURT: WELL, I THINK WE SHOULD ACTUALLY TAKE A BREAK UNTIL -- FOR ABOUT 15 MINUTES.

SO WHY DON'T WE TAKE A BREAK ACTUALLY UNTIL 11:00 O' CLOCK CALIFORNIA TIME.

MR. ESFANDIARY: THANK YOU, YOUR HONOR.

THE COURT: THANK YOU.

MS. FREIWALD: THANK YOU, YOUR HONOR.

THE WITNESS: THANK YOU.

(RECESS)

THE COURT: THANK YOU. YOU MAY PROCEED.

MR. ESFANDIARY:

Q ALL RIGHT. DOCTOR, WE'RE JUST GOING TO WRAP UP OUR DISCUSSION OF YOUR PAPER. I DON'T WANT TO SPEND TOO MUCH TIME ON IT.

LET'S GO TO YOUR PAPER AGAIN AND JUST LOOK AT

WHAT YOU SAY HERE ON PAGE 9.

IT SAYS, -- YOU SAY HERE THAT, "MOREOVER, THE ROOT CAUSE OF AUTISM ASD ETIOLOGY STILL REMAINS UNCLEAR, BUT METAL EXPOSURES HAVE BEEN SHOWN TO CONTRIBUTE TO THE IMPACT OF ASD."

ALL RIGHT. YOU SEE THAT, DOCTOR?

A YES, SIR.

Q OKAY. WHAT DO YOU MEAN THAT THE ROOT CAUSE REMAINS UNCLEAR?

A WELL, FOR EXAMPLE, THERE'S A LOT OF GENE CANDIDATES THAT HAVE BEEN CONSIDERED IN TERMS OF RENDERING OR INCREASING SUSCEPTIBILITY TO THE DISORDER, BUT IT'S A MULTI-FACTORIAL DISEASE. SO HOW MANY GENES MIGHT BE INVOLVED, WHETHER IT'S 5, 10 OR 50 OR 100, WE DON'T KNOW. AND, AS I SAID IN THE BEGINNING, I BELIEVE, LIKE MOST OTHER NEUROLOGICAL DISORDERS, THERE IS BOTH AN ENVIRONMENTAL COMPONENT AND A GENETIC COMPONENT.

SO YOU CAN IMAGINE THAT YOU WOULD HAVE TO DO A LOT OF STUDIES TO ASCERTAIN EXACTLY WHAT GENES ARE ASSOCIATED WITH THIS DISEASE BECAUSE YOU'D HAVE TO GENOTYPE HUNDREDS OF THOUSANDS OF PEOPLE, PRETTY MUCH EVERYBODY THAT HAS ASD.

SO THAT'S WHAT I MEAN BY WE DON'T KNOW THE ROOT OF THE DISEASE, BUT I POINT OUT TO THE FACT THAT THERE IS KNOWLEDGE THAT SUBSTANTIATES THAT EXPOSURE TO HEAVY METALS, IN THIS CASE LEAD, ARE CAUSAL IN TERMS OF INTERACTION BETWEEN THE GENETICS AND THE DEVELOPMENT OF ASD.

THE COURT: I HAVE A QUESTION FOR THE WITNESS. EXCUSE ME FOR INTERRUPTING.

MR. ESFANDIARY: NO PLEASE, YOUR HONOR.

THE COURT: I SEE THE WAY IT'S PHRASED, DOCTOR. IT SAYS THAT THE METAL EXPOSURE HAS BEEN SHOWN TO CONTRIBUTE TO THE IMPACT OF ASD. IT DOESN'T SAY TO THE CAUSE OF ASD OR TO THE GENERATION OF ASD. WHAT DO YOU MEAN BY CONTRIBUTE TO THE IMPACT OF ASD? IN OTHER WORDS, ARE YOU SAYING IT WORSENS THE SYMPTOMS? WHAT DOES THAT MEAN, THE IMPACT OF ASD?

THE WITNESS: SO THANK YOU, YOUR HONOR. YOU KNOW, IT MIGHT BE POOR LANGUAGE ON MY PART, BUT I WOULD SAY ACTUALLY BOTH ARE CORRECT.

I WOULD SAY, IF WE GO BACK, I DON'T KNOW IF YOU'LL RECALL THE STUDY OF CECIL WHERE WE TALKED ABOUT THE GRAY MATTER AND THE REDUCTION IN THE SIZE OF THE GRAY MATTER OF THE BRAIN. WHAT THEY HAVE DONE THERE IS TO ACTUALLY CORRELATE THE REDUCTION, THE VOLUME, OF THE REDUCTION IN THE BRAIN MATTER, AND THAT WAS ACTUALLY CORRELATED WITH THE AMOUNT OF LEAD THAT THESE ADULTS WERE EXPOSED TO WHEN THEY WERE CHILDREN.

SO, WHAT I MEAN IS NOT JUST -- IT'S NOT JUST THAT THERE'S A RELATIONSHIP BETWEEN THESE METALS AND THE DISEASE, ALSO, THE SEVERITY OF THE DISEASE WILL BE DEPENDENT UPON THE LEVEL OF EXPOSURE.

THE COURT: I SEE.

MR. ESFANDIARY: YOUR HONOR? ALL RIGHT. YOUR HONOR, MAY I PROCEED?

THE COURT: YES, PLEASE.

MR. ESFANDIARY: OH, SORRY.

Q OKAY.

DOCTOR, WHEN WE WERE TALKING ABOUT DOSE A LITTLE WHILE AGO, I JUST WANT TO WRAP UP THAT DISCUSSION BY BRIEFLY LOOKING AT A DOCUMENT.

THIS IS EXHIBIT -- I DON'T REMEMBER THE EXACT EXHIBIT NUMBER. IT'S NOT POPPING UP ON THERE. I THINK IT'S 74. WE CAN CLEAR THAT UP LATER.

THIS IS A PUBLICATION BY THE U.S. DEPARTMENT OF HEALTH AND HUMAN SCIENCES -- SERVICES, SPECIFICALLY, THE DIVISION OF AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY.

CAN YOU SEE THAT, DOCTOR?

A YES, SIR.

Q IS THE ATSDR, IS THAT A BRANCH OF THE CDC?

A YES, IT'S A BRANCH OF THE CDC.

Q OKAY.

AND WHAT IS THE -- WHAT IS THE PURPOSE OF THE ATSDR? DO YOU KNOW WHAT THEIR ROLE IS WITH RESPECT TO THE ENVIRONMENTAL CAUSES OF DISEASE?

A WELL, I KNOW THAT THEY PUBLISH A LOT OF TOXICOLOGICAL PROFILES. SO YOU'LL FIND PROFILES, NOT JUST ON METALS, BUT A LOT OF CHEMICALS THAT WE'RE EXPOSED TO. AND THEY ARE VERY ACTIVE IN SUPER FUNDS. I GUESS, THEY ARE JUST ADVISORY TO THE CDC, BUT I DON'T KNOW EXACTLY THE RELATIONSHIP BETWEEN THEM.

Q IS THE ATSDR, THESE TOXICOLOGICAL PROFILES THAT

THEY DO, ARE THEY USUALLY CONSIDERED RELIABLE SOURCES FOR UNDERSTANDING THE ETIOLOGIES OF VARIOUS DISEASES AS POSED BY ENVIRONMENTAL TOXINS?

A YES, ABSOLUTELY. THIS IS ACTUALLY AUTHORED OR OR CO-AUTHORED BY INDIVIDUALS WHO ARE EXPERTS IN THIS AREA. I BELIEVE THEY ACTUALLY INCLUDE THE NAMES OF THE INDIVIDUALS WHO HAVE CO-AUTHORED THIS, AND IT'S ALSO THEN PEER-REVIEWED.

Q YES.

A AND, I MEAN, I SERVED ON SOME OF THEIR REVIEWS AND I MAY ACTUALLY HAVE CO-AUTHORED, I DON'T REMEMBER, THE ONE ON MANGANESE.

SO, YEAH, IT'S VERY REPUTABLE. IT'S VERY SYSTEMATIC, AND IT'S A VERY RELIABLE SOURCE FOR INFORMATION FOR THOSE OF US IN THE SCIENTIFIC COMMUNITY.

Q THIS IS OVER 500 PAGES DEVOTED EXCLUSIVELY TO UNDERSTANDING THE TOXICITY OF LEAD; CORRECT?

A THAT'S CORRECT.

Q OKAY. I WANT TO JUST TAKE A LOOK AT WHAT THEY SAY ON PAGE 133.

IT'S NOT TAKING ME TO... THERE WE GO.

AND HERE, DOCTOR, IT SAYS, AFTER IT DISCUSSES THE AVAILABLE SCIENTIFIC LITERATURE ON LEAD IT SAYS, "THE FOLLOWING NEUROBEHAVIORAL EFFECTS IN CHILDREN HAVE BEEN ASSOCIATED WITH LEAD."

CAN YOU SEE THAT, DOCTOR?

A YES, SIR.

Q AND IT GIVES US A DOSE MEASUREMENT; CORRECT?

IT SAYS LESS THAN OR EQUAL TO 10 MICROGRAMS PER LEAD DECILITER; CORRECT?

A THAT'S CORRECT.

Q WHAT IS THAT MEASUREMENT REFERRING TO? JUST GIVE US SOME CONTEXT FOR THAT DOSE. HOW MUCH LEAD IS THAT?

A SO AS I SAID, 10 MICROGRAMS PER DECILITER WILL BE .1 PART PER MILLION. SO IT WOULD BE ONE TENTH OF A PARTICLE WITH ANOTHER ONE MILLION PARTICLES.

Q IS THAT A LOT OF LEAD?

A I DON'T THINK SO.

Q AND, DOCTOR, THEY SAY HERE, "SPECIFICALLY, THE NEUROBEHAVIORAL EFFECTS HAVE BEEN OBSERVED WITH THIS MINISCULE AMOUNT OF LEAD INCLUDE ALTERED MOOD AND BEHAVIORS THAT MAY CONTRIBUTE TO LEARNING DEFICITS, INCLUDING ATTENTION DEFICIT, HYPER ACTIVITY, AUTISTIC BEHAVIORS, CONDUCT DISORDERS, AND DELINQUENCY."

DO YOU SEE THAT, DOCTOR?

A YES, SIR.

Q OKAY.

IS THAT CONSISTENT WITH YOUR REVIEW OF THE DATA, THAT THE AVAILABLE EVIDENCE HAS DEMONSTRATED THAT LEAD IS CAPABLE OF CAUSING ASD AND THESE BEHAVIORS AT LOW LEVELS?

A YES, IT IS.

Q AND JUST TO GO TO PAGE 173 OF THIS DOCUMENT, AND IT SAYS HERE AT THE TOP, "PROSPECTIVE STUDIES HAVE

ALSO PROVIDED EVIDENCE FOR ASSOCIATIONS BETWEEN NEONATAL OR EARLY CHILDHOOD LEAD AND OTHER NEUROBEHAVIORAL OUTCOMES, INCLUDING."

AND THEY HAVE HERE, "HYPER ACTIVITY AND IMPULSIVITY AND AUTISTIC BEHAVIORS."

DO YOU SEE THAT, DOCTOR?

A YES, SIR.

Q OKAY. IS THAT ALSO CONSISTENT WITH YOUR REVIEW OF THE DATA IN THIS CASE?

A YES, IT IS.

Q AND THEY GIVE A STRING CITATION TO NUMEROUS STUDIES HERE; CORRECT?

A THAT'S CORRECT.

Q OKAY.

A AND I'M NOT INVOLVED IN ANY OF THESE STUDIES, SO I SHOULD POINT THAT OUT.

Q SURE. UNDERSTOOD.

ALL RIGHT. DOCTOR, I GUESS MY QUESTION IS: IS IT CONFIRMATORY OR REFRESHING TO SEE THAT THE CDC, ESSENTIALLY, AGREES WITH YOUR OPINION IN THIS CASE?

A I BELIEVE SO, YES.

Q OKAY. ALL RIGHT. DOCTOR, I JUST WANT TO WRAP UP HERE.

WE TALKED ABOUT THE SYMPTOMS OF ASD AND THE MECHANISMS BY WHICH METALS CAN CAUSE ASD AND THE SYMPTOMS.

DOCTOR, IF SOMEONE WERE TO SAY THAT THE MECHANISMS BY WHICH METALS CAUSE ASD AND THE POTENTIAL

FOR CAUSING ASD IS HYPOTHETICAL OR SPECULATIVE THEORIES, WHAT IS YOUR RESPONSE TO THAT?

A SO I THINK I'VE PROVIDED YOU TODAY WITH A NUMBER OF MECHANISMS RANGING FROM ALTERED SYNAPTOGENESIS, SYNAPTIC TRANSMISSION, CALCIUM SIGNALLING, DIMINISHED BRAIN VOLUME, INCREASED APOPTOSIS, AND I CAN GO ON AND ON, INCREASED OXIDATIVE STRESS; I MEAN, ALL OF THESE ARE CONSISTENT -- THEY ARE THE UNDERLYING MECHANISMS OF NEURODEGENERATIVE DISEASES, INCLUDING ASD.

SO THERE'S PLENTY OF INFORMATION THAT AT LEVELS THAT ARE INHERENT TO EXPOSURES IN CHILDREN, ANIMALS CAN RECAPITULATE SOME OF THE BEHAVIORS WITH THE UNDERPINNING MECHANISMS THAT ARE ASSOCIATED WITH IT.

Q DOCTOR, TO A REASONABLE DEGREE OF SCIENTIFIC CERTAINTY, CAN EXPOSURE TO LEAD, ARSENIC AND MERCURY CAUSE ASD?

A YES.

Q AND TO A REASONABLE DEGREE OF SCIENTIFIC CERTAINTY, CAN EXPOSURE TO LEAD CAUSE ADHD?

A YES.

Q ALL RIGHT. DOCTOR, THANK YOU SO MUCH FOR YOUR TIME.

MR. ESFANDIARY: I HAVE NO FURTHER QUESTIONS. I PASS THE WITNESS.

THE COURT: THANK YOU.

THE WITNESS: THANK YOU.

THE COURT: ALL RIGHT. MS. FREIWALD, YOU'RE

UP. THANK YOU.

MS. FREIWALD: MAY I PROCEED, YOUR HONOR?

THE COURT: PLEASE.

CROSS EXAMINATION

MS. FREIWALD:

Q OKAY. GOOD AFTERNOON, DR. ASCHNER.

I NEED TO CHECK TO MAKE SURE IT'S WHAT -- GET MY EAST COAST, WEST TIMES -- COAST TIMES STRAIGHT.

SO GOOD AFTERNOON. IT'S GOOD TO SEE YOU AGAIN, DR. ASCHNER.

A THANK YOU. GOOD AFTERNOON.

Q SO LET'S JUST START QUICKLY AND TALK A LITTLE BIT ABOUT BIOMARKERS.

SO I THINK YOU AND I COULD AGREE THAT IN ALL OF THE HUMAN STUDIES THAT WE'RE TALKING ABOUT IN THIS CASE, THE HEAVY METAL, WHETHER IT'S ARSENIC, LEAD OR MERCURY, THAT IS BEING MEASURED, IS BEING MEASURED VIA SOME BIOMARKER; CORRECT?

A THAT'S CORRECT.

Q OKAY.

AND THERE ARE BIOMARKERS THAT YOU CAN USE TO MEASURE EXTERNAL AMOUNTS OF A HEAVY METAL, LIKE YOU COULD MEASURE DIRECTLY HOW MUCH OF A HEAVY METAL THERE IS IN WATER OR HOW MUCH THERE IS IN AIR OR HOW MUCH THERE IS IN SOIL; CORRECT?

A THAT'S CORRECT.

Q AND THEN THERE ARE INTERNAL TOOLS FOR MEASURING

BIOMARKERS WITHIN THE HUMAN BODY; CORRECT?

A YES, MA'AM.

Q AND THOSE INTERNAL MEASUREMENTS THAT THE COURT'S ALREADY HEARD ABOUT IN THIS CASE WOULD INCLUDE HAIR, BLOOD AND URINE; CORRECT?

A I WOULD ARGUE THAT NOT ALL THE MEASUREMENTS IN HAIR ACTUALLY REFLECT INTERNAL EXPOSURE BECAUSE SOMETIMES A METAL MAY BE ON THE OUTSIDE OF THE HAIR. BUT I WOULD AGREE WITH YOU, BLOOD AND URINE ARE PROBABLY THE BEST INDICATORS OF BIOMARKERS FOR EXPOSURE.

Q THANK YOU FOR THAT CLARIFICATION, SIR.

AND WE'RE GOING TO TALK ABOUT SOME OF THE LIMITATIONS OF THE BIOMARKERS.

A OKAY.

Q BUT JUST AS A GENERAL PROPOSITION, WHEN WE'RE TALKING ABOUT USING HAIR OR BLOOD OR URINE AS A BIOMARKER, WHAT WE'RE TALKING ABOUT IS MEASURING WHAT IS INSIDE THE BODY; CORRECT?

A YES, MA'AM.

Q AND I THINK YOU TAUGHT ME, WHEN WE CHATTED THE LAST TIME, THAT THERE ACTUALLY ISN'T A DIRECT FORMULA THAT YOU CAN USE TO TRANSLATE WHAT IS INSIDE THE BODY TO AN EXTERNAL LEVEL OF EXPOSURE. IT'S NOT LIKE YOU CAN SAY X IS OUTSIDE EQUALS Y INSIDE; CORRECT?

A YES, BECAUSE IT MAY DEPEND ON THE DURATION OF THE EXPOSURE. IF SOMEBODY WAS EXPOSED TO, LET'S SAY, LEAD FOR ONE MONTH AND THEY HAVE 2-MICROGRAMS PER DECILITER, AND SOMEBODY MAY HAVE BEEN EXPOSED TO A LOWER

CONCENTRATION FOR A LONGER PERIOD, THEY MIGHT HAVE THE SAME BLOOD LEVELS.

SO, I MEAN, I WOULDN'T VENTURE TO SAY IT WAS X AMOUNT OVER A CERTAIN AMOUNT OF TIME. YOU'RE CORRECT, YES.

Q OKAY.

AND I THINK THAT YOU ALSO TAUGHT ME THAT THERE IS INDIVIDUAL VARIABILITY IN THESE BLOOD MARKERS. TWO PEOPLE CAN BE EXPOSED TO THE EXACT SAME LEVELS IN THE AIR OR WATER OR THE SOIL OR THE FOOD THEY EAT, AND THEIR MEASUREMENTS ARE NOT GOING TO COME UP THE SAME; CORRECT?

A THAT'S CORRECT. JUST LIKE TWO GUYS CAN SMOKE AND ONE OF THEM DEVELOPS CANCER AND THE OTHER ONE DOES NOT. CORRECT.

Q OKAY.

AND SOME OF THAT IS JUST BECAUSE THERE ISN'T THIS DIRECT TRANSLATION, BUT SOME OF IT IS ALSO BECAUSE THERE ARE INDIVIDUAL GENETIC, AND OTHER DIFFERENCES, IN HOW EACH AND EVERY ONE OF US PROCESSES METALS IN OUR BODY; IS THAT FAIR?

A AND I'D SAY, GENERALLY, THE WAY WE PROCESS THESE METALS IS THE SAME. THERE MIGHT BE SOME DIFFERENCES AND THAT MAY BE RELATED TO -- I THINK I MENTIONED IT EARLIER TODAY. SOMEBODY MAY HAVE A SNIP OR WHAT'S CALLED A POLYMORPHISM IN ONE OF THE GENES AND THEY MIGHT BE BETTER EXCRETERS OF LEAD OR BETTER ABSORBERS OF LEAD.

SO, AGAIN, FOR THE SAME AMOUNT OF LEAD THAT

THEY MIGHT ABSORB, TWO INDIVIDUALS MAY HAVE DIFFERENT BLOOD LEVELS. I WOULD AGREE WITH THAT.

Q OKAY.

AND SO, IF PEOPLE HAVE POLYMORPHISMS JUST BECAUSE THEY HAVE THEM OR BECAUSE THOSE POLYMORPHISMS ARE ASSOCIATED WITH OTHER UNDERLYING CONDITIONS THEY HAVE, THAT COULD AFFECT HOW THEY PROCESS METALS; RIGHT?

A SO I -- WHEN YOU SAY "OTHER POLYMORPHISMS," WHAT -- CAN YOU KINDLY EXPLAIN TO ME WHAT YOU MEAN?

Q OH, I'M SORRY.

I THINK YOU TESTIFIED THAT THERE MIGHT BE MUTATIONS OF DIFFERENT KINDS THAT AFFECT HOW PEOPLE PROCESS DIFFERENT METALS; CORRECT?

A CORRECT. YES, THAT'S CORRECT.

Q OKAY. THERE ARE SOME GENETIC DIFFERENCES THAT AFFECT HOW YOU PROCESS LEAD AND DIFFERENT ONES THAT MIGHT EVEN AFFECT HOW YOU PROCESS ARSENIC, ET CETERA; CORRECT?

A THAT'S RIGHT. YES, MA'AM.

Q OKAY.

SO THERE'S A WHOLE LOT -- THERE'S A FAIR BIT OF VARIABILITY THAT IS GENETIC, AND THOSE POLYMORPHISMS, SOME OF THEM -- PEOPLE WHO DON'T HAVE ANYTHING DIFFERENT ABOUT THEM MAY HAVE -- YOU MAY JUST NOT KNOW THAT YOU HAVE THEM, AND SOME OF THEM MAY BE TIED TO OTHER UNDERLYING GENETIC CONDITIONS; CORRECT?

A WE ARE ALL DIFFERENT, YES, BUT THEY PROBABLY HAVE DIFFERENT KIND OF EXPRESSION OF OTHER GENES AS

WELL. YES, I'D AGREE WITH THAT.

Q AND EVEN DIFFERENCES IN OUR NUTRITIONAL STATUS CAN AFFECT HOW WE PROCESS METALS, YOU AGREE WITH THAT; RIGHT?

A I DEFINITELY AGREE WITH THAT BECAUSE METALS, THEY TEND TO UTILIZE THE SAME KINDS OF TRANSPORTERS, SO ABSOLUTELY. ONE METAL MAY AFFECT THE OTHER. IT MAY SYNERGIZE WITH THE OTHER, ACTUALLY. IT MAY INCREASE THE CONCENTRATION OF A GIVEN METAL. IT CAN WORK BOTH WAYS, I WOULD AGREE. YES, MA'AM.

Q AND I THINK YOU'VE ACTUALLY WRITTEN THAT, IN A BUNCH OF PLACES, THAT HOW MUCH CALCIUM WE EAT, HOW MUCH IRON WE GET, HOW MUCH ZINC WE GET, HOW MUCH SELENIUM WE GET, ALL CAN AFFECT HOW EFFECTIVELY OUR BODIES HANDLE METALS; CORRECT?

A THAT'S CORRECT, YES.

Q OKAY.

AND WHEN I SAY HOW EFFECTIVELY OUR BODIES CAN HANDLE METALS, WE ALL HANDLE METALS, RIGHT, EVERY SINGLE DAY, WE'RE ALL EXPOSED TO METALS?

A WELL, EVERYBODY MY AGE HAS A LEAD BURDEN FOR SURE, YES.

Q OKAY. AND MY AGE TOO, I THINK.

PRETTY MUCH IF YOU WERE BORN BEFORE ABOUT 1995, RIGHT, YOU ARE GOING TO HAVE BEEN EXPOSED TO METALS AT A MUCH HIGHER RATE THAN WHAT CHILDREN TODAY ARE EXPOSED TO; ISN'T THAT TRUE?

A I WOULD AGREE WITH THAT, THAT THE LEAD LEVELS

HAVE GONE DOWN SIGNIFICANTLY --

Q OKAY.

A -- OVER THE LAST FEW YEARS, YES.

Q OKAY.

SO, I MEAN, WE'LL TALK ABOUT THAT A LITTLE BIT MORE LATER, BUT JUST FOR NOW IN TERMS OF TALKING ABOUT BIOMARKERS, IT'S -- WE CAN BE EXPOSED ON AN ALMOST DAILY BASIS TO SOME LEVEL OF METAL, AND WHAT WE EAT THAT HAS GOOD THINGS IN IT, LIKE CALCIUM OR IRON OR SELENIUM -- DID WE LOSE THE WITNESS? I'M SORRY, YOUR HONOR.

MR. ESFANDIARY: LOOKS LIKE DR. ASCHNER IS --

THE WITNESS: I CAN HEAR YOU. I JUST -- MY VIDEO, AGAIN, I TOUCHED IT. I'M SORRY.

MS. FREIWALD: OKAY.

THE WITNESS: I APOLOGIZE.

MS. FREIWALD: NOT AT ALL. NOT AT ALL. WE'RE ALL GETTING USED TO TECHNOLOGY.

THE WITNESS: ...FOR A FEW MORE YEARS, YEAH.

MS. FREIWALD: I THINK WE ALL FEEL THE SAME WAY, SIR. ALTHOUGH, IT IS VERY NICE TO BE ABLE TO SEE EVERYBODY. I WILL ADMIT I -- THANK YOU, YOUR HONOR, THIS IS A VERY CONVENIENT FORMAT.

Q SO, SIR, WE'RE ALL EXPOSED TO METALS ON A DAILY BASIS, AND HOW MUCH WE CONSUME OF HEALTHY THINGS, LIKE CALCIUM AND ZINC AND IRON AND SELENIUM, EVEN FIBER, ALL AFFECTS HOW WELL OR NOT WE PROCESS METALS; CORRECT?

A THAT'S CORRECT.

Q OKAY.

AND JUST STICKING ON THE SUBJECT OF BIOMARKERS FOR A BIT, YOU WOULD AGREE WITH ME THAT WHILE HAIR, URINE, AND BLOOD, INCLUDING RED BLOOD CELLS OR PLASMA, KIND OF ARE USED GENERALLY, THEY ARE NOT ALL EQUALLY GOOD FOR ALL METALS; CORRECT?

A ABSOLUTELY, MA'AM, YES.

Q OKAY.

AND YOU ALLUDED TO A POINT THAT I WANTED TO GET TO, WHICH IS WHEN YOU ARE MEASURING MERCURY IN HAIR, FOR EXAMPLE, YOU HAVE TO BE SUPER CAREFUL BECAUSE THERE'S MERCURY IN THE AIR; RIGHT?

A THERE'S A CERTAIN AMOUNT, YES. IT DEPENDS WHERE YOU LIVE.

Q OKAY.

A YES.

Q AND I THINK WHAT YOU WERE GETTING AT WHEN YOU SAID THAT HAIR MERCURY MAY NOT MEASURE JUST INTERNAL, IT MAY ALSO MEASURE EXTERNAL, IS THAT LITERALLY MERCURY FROM THE ENVIRONMENT DROPS ON THE STRANDS OF HAIR. EVEN PRODUCTS WE USE ON OUR HAIR CAN AFFECT THE HEAVY METAL BURDEN ON THE HAIR; RIGHT?

A YEAH. BUT TO PUT IT IN PERSPECTIVE, I -- YOU KNOW, YOU'RE TALKING ABOUT CERTAIN STUDIES THAT HAVE HAIR MEASUREMENTS. I THINK THERE'S PLENTY OF DATA THAT WE CAN GATHER FROM LEAD LEVELS IN BLOOD. SO, I MEAN, YOU CAN -- EVEN IF YOU EXCLUDE THOSE STUDIES, I DON'T THINK ANY OF MY CONCLUSIONS WOULD CHANGE.

BUT I THINK IT'S IMPORTANT TO DETERMINE WHETHER

THE DIGESTION OF THE HAIR, FOR EXAMPLE, WAS DONE THE RIGHT WAY. I'VE PUBLISHED ON THAT. SO IT'S AN IMPORTANT CRITERION, BUT --

Q OKAY.

A -- YOU KNOW, IT'S ONE APPLE ON A TREE, YES.

Q I'M JUST TRYING TO UNDERSTAND -- YOU KNOW, FROM YOUR PERSPECTIVE AS A TOXICOLOGIST, MAKE SURE WE'RE ALL TALKING ABOUT THE SAME THING.

AND I THINK YOU ACTUALLY TOLD ME THAT WHEN YOU'RE DOING STUDIES IN COUNTRIES, FOR EXAMPLE, WHERE THERE'S A LOT OF ARSENIC IN THE WATER, YOU HAVE TO BE CAREFUL ABOUT HAIR MEASUREMENT. IF PEOPLE ARE WASHING THEIR HAIR IN WATER THAT HAS A HIGH ARSENIC BURDEN, THAT CAN AFFECT THE ARSENIC IN THE HAIR; CORRECT?

A YES. MANY THINGS WILL DETERMINE LEVELS OF ARSENIC IN THE HAIR, YES.

Q OKAY.

AND I THINK YOU'VE ALSO TOLD ME THAT URINE IS NOT A GREAT BIOMARKER FOR LEAD, IF I'M GETTING THAT CORRECTLY?

A URINE IS NOT GREAT FOR LEAD. URINE IS NOT GREAT FOR ALL THE MERCURY SPECIES. URINE IS GOOD FOR ARSENIC. SO WE WOULD HAVE TO TALK SPECIFICALLY ABOUT THE SPECIATION OF THE METAL, WHETHER IT'S ORGANIC OR INORGANIC, BUT, YES.

Q RIGHT.

A I WOULD SAY THAT THE BEST MARKER IS BLOOD LEVELS.

Q OKAY.

SO YOU JUST MENTIONED SPECIATION. I'M NOT SURE THAT'S A CONCEPT WE'VE GOTTEN INTO QUITE YET AND I WANT TO PAUSE ON THAT.

SO, WITHIN ARSENIC AND WITHIN MERCURY, IN PARTICULAR, THERE'S MORE THAN ONE TYPE; RIGHT?

A THAT'S CORRECT.

Q OKAY.

AND THEY HAVE -- THE TYPES HAVE DIFFERENT LEVELS OF ASSOCIATION WITH POTENTIAL HEALTH OUTCOMES; CORRECT?

A YES, MA'AM. THAT'S CORRECT.

Q OKAY.

AND I THINK, IN FACT, YOUR COUNSEL MADE A POINT THAT ETHYLMERCURY, WHICH IS THE KIND OF MERCURY THAT WAS IN VACCINES, WHICH THE CDC HAS NOW SAID DOES NOT CREATE A RISK OF AUTISM, IS DIFFERENT FROM METHYLMERCURY; CORRECT?

A CORRECT. AND I'VE SAID THE SAME THING AS WELL.

Q OKAY.

AND ARSENIC, TOTAL ARSENIC, IS NOT THE SAME THING AS WHEN YOU DIVIDE INORGANIC ARSENIC AND ORGANIC ARSENIC; CORRECT?

A THAT'S CORRECT, MA'AM, YES.

Q AND SO IF YOU'RE DOING JUST A TOTAL MEASURE, THEN YOU'RE GETTING A NUMBER THAT MAY BE GREATER THAN THE PART OF THE WHOLE THAT REPRESENTS THE MORE TOXIC OR MORE OF CONCERN PART OF THE WHOLE; FAIR ENOUGH?

A NO, I DON'T AGREE WITH THAT.
Q OKAY.
A NO, I DON'T AGREE WITH THAT. BECAUSE WHAT YOU'RE JUDGING IS THE TOTAL -- LET'S TALK ABOUT MERCURY, FOR EXAMPLE. SO WHEN YOU DO MERCURY ANALYSIS, YOU CAN ACTUALLY DETERMINE THE TOTAL MERCURY, AND THEN YOU CAN SPECIATE IT. THERE ARE VARIOUS METHODS BY MEANS OF PCPSC, BY A MERCURY VAPOR ANALYSIS, WHERE YOU CAN SPECIATE THE MERCURY.
Q OKAY.
A UNFORTUNATELY, MANY TIMES WE HAVE TO DIGEST THE BLOOD SAMPLE BECAUSE SOME OF THE METAL MAY BE BOUND. JUST LIKE ANALOGOUS TO WHAT WE TALKED ABOUT THE HAIR, YOU HAVE TO USE DIFFERENT ACIDS TO DIGEST THE BLOOD SO THAT ULTIMATELY THE ARSENIC OR THE MERCURY OR THE LEAD ARE IN THE FREE FORM.
Q OKAY.
A SO YOU CAN TELL THE SPECIATION, BUT IT STILL -- IT DOESN'T TAKE AWAY THE FACT THAT THE LEVELS OF ARSENIC OR THE LEVELS OF BLOOD ARE FIVE TIMES HIGHER THAN WHAT'S NORMAL. IT MUST BE COMING FROM SOMEWHERE.
Q OKAY.
SO IF YOU SPECIATE, THEN YOU CAN TELL WHAT THE DIFFERENT PARTS ARE, BUT WHEN YOU READ A STUDY, YOU NEED TO LEAST LOOK AT WHETHER THEY HAVE TRIED TO SPECIATE OR NOT; CORRECT?
A SO, I DO SO. I MEAN, I DON'T THINK IT'S AN ISSUE REALLY WITH LEAD. I READ THE STUDIES. I PAY

GREAT ATTENTION, BECAUSE WE MAY HAVE TALKED ABOUT IT BEFORE, I APOLOGIZE IF I'M REPEATING MYSELF, BUT INORGANIC MERCURY IS A DIFFERENT BEAST COMPARED TO METHYLMERCURY, WHICH IS AN ORGANIC SPECIES, OR ETHYLMERCURY, WHICH YOU JUST MENTIONED. SO IT'S VERY INFORMATIVE. I WOULD AGREE WITH YOU, COUNSEL, THAT IT'S IMPORTANT TO KNOW WHAT'S THE SPECIATION OF MERCURY. YES.

Q OKAY.

AND THERE ARE ALSO THINGS THAT AFFECT HOW MUCH OF DIFFERENT METALS CAN BE MEASURED IN THE BIOMARKER.

LIKE, I THINK YOU TAUGHT ME THAT HOW MUCH WATER YOU DRINK CAN AFFECT HOW MUCH LEAD YOU GET IN A BLOOD SAMPLE?

A I WOULD SAY THAT PROBABLY IS MORE -- IT WILL AFFECT TO A GREATER EXTENT THE URINARY EXCRETION. I WOULD THINK THAT THE BLOOD LEVELS ARE GOING TO STAY ABOUT THE SAME. THEY ARE GOING TO FLUCTUATE A LITTLE BIT, BUT I THINK IT'S GOING TO AFFECT MUCH MORE THE KIDNEY LEVELS OF THESE METALS.

YOU'RE FAMILIAR WITH DIURESIS. I'VE HAD SIX COFFEES TODAY, SO I'VE BEEN -- WELL, TOO MUCH INFORMATION. BUT THE DIURESIS IS IMPORTANT, AND THAT'S WHY, WHEN YOU MEASURE URINE SAMPLES OF WHATEVER IT IS, WHAT YOU HAVE TO CORRECT IS FOR THE FILTRATION RATE BECAUSE THE MORE COFFEE YOU HAVE, THE GREATER THE FILTRATION. SO YOU WANT TO KNOW HOW CONCENTRATED THE URINE IS.

Q OKAY.

A SO THAT'S WHAT I WOULD LOOK FOR IN A STUDY. I WOULD LIKE TO SEE THAT THEY HAVE CORRECTED IT FOR CREATININE LEVELS IN THE URINE, FOR EXAMPLE. SO IT'S NOT JUST A SAMPLE.

Q OKAY. ALL RIGHT.

SO URINE MEASUREMENTS HAVE TO BE CORRECTED FOR KIDNEY FUNCTION AND --

A YES.

Q -- UNDERSTANDING HOW ALL OF THAT IS WORKING?

ALL RIGHT. SO WHEN WE MEASURE BLOOD LEAD LEVELS, AND THAT'S SOMETIMES WRITTEN AS BLL IN THE STUDIES, WHEN WE MEASURE BLOOD LEVELS -- WELL, NOT WE, I DON'T DO IT -- BUT, WHEN YOU SEE BLOOD LEVELS THAT ARE MEASURED, WHAT ONE IS ACTUALLY SEEING IS ABOUT A 30-DAY WINDOW OF EXPOSURE; CORRECT?

A I WOULD AGREE WITH THAT, YES.

Q OKAY. AND I GUESS IT'S IMPORTANT, BEFORE WE GET INTO THIS A LITTLE MORE, TO MAKE SURE THAT IT'S CLEAR ON THE RECORD THAT EACH ONE OF THESE BIOMARKERS HAS AN AMOUNT OF TIME THAT IT'S INHERENTLY CAPABLE OF MEASURING; RIGHT?

SO --

A RIGHT. IF THEORETICALLY, SOMEBODY WAS EXPOSED TO MERCURY 30 YEARS AGO AND YOU WOULD -- THERE WAS NO EXPOSURE SINCE THEN, AND YOU WOULD TRY TO SEE IF THERE'S ANY MERCURY IN THEIR BLOOD TODAY, I WOULD SAY YOU PROBABLY WOULD FIND IT.

Q OKAY.
A AND WE AGREE.
Q SO FOR -- DEPENDING UPON THE METAL AND DEPENDING UPON THE BIOMARKER USED -- AND I'M GOING TO PUT HAIR ASIDE FOR JUST ONE SECOND, OKAY, BECAUSE IT'S A LITTLE BIT MORE COMPLICATED -- BUT BLOOD OR URINE, YOU'RE TALKING, KIND OF, DAYS TO ABOUT A MONTH, RIGHT, OF EXPOSURE THAT YOU'RE TALK -- THAT YOU'RE GOING TO MEASURE?
A YES, MA'AM.
Q OKAY.
NOW, HAIR IS A LITTLE DIFFERENT BECAUSE HAIR COMES IN DIFFERENT LENGTHS. AND SO, WHEN YOU MEASURE HAIR, IT DEPENDS WHERE ON THE HAIR YOU'RE MEASURING AND HOW LONG THE HAIR IS; CORRECT?
A THAT'S CORRECT. I WOULD BE A BAD EXAMPLE FOR MEASURING MERCURY IN MY HAIR. YES, MA'AM.
Q OKAY. WELL, I THINK WHAT YOU TAUGHT ME IS THAT ABOUT ONE CENTIMETER OF HAIR EQUALS ABOUT ONE MONTH OF EXPOSURE; RIGHT?
A I SAID THAT. THAT'S CORRECT.
Q MEASURING FROM THE SCALP, SO THAT IF YOU HAD A CHILD AND YOU WERE TAKING RIGHT FROM THE SCALP, THAT FIRST CENTIMETER OF HAIR, YOU WOULD BE GETTING ABOUT A MONTH'S WORTH OF EXPOSURE; CORRECT?
A THAT'S CORRECT.
Q AND THEN YOU LITERALLY COULD ADD, AND IF YOU HAD SOMEBODY WHO HAD EIGHT MONTHS, EIGHT CENTIMETERS OF

HAIR, THAT'S MORE OR LESS EIGHT MONTHS, AND TEN CENTIMETERS OF HAIR, THAT'S MORE OR LESS TEN MONTHS, AND YOU GET THE PICTURE, RIGHT? I'VE GOT THIS MORE OR LESS CORRECT?

A YES, MA'AM.

Q OKAY.

AND WITH LEAD, IT'S ABOUT 30 DAYS, RIGHT, IN THE BLOOD?

A I'M SORRY. OKAY.

Q I'M SORRY. IN THE BLOOD?

A (INDICATING).

Q AND I WANT TO BE CLEAR THAT YOU'RE NOT SUGGESTING, SIR, ARE YOU, THAT WHEN YOU MEASURE A CHILD'S BLOOD, YOU'RE GETTING ANY SIGNIFICANT AMOUNT OF LEAD FROM THE CHILD'S BONES?

A NO, I DID NOT SAY THAT. I SAID THAT INFINITESIMAL AMOUNT. THAT'S WHAT I ACTUALLY SAID OF --

Q OKAY.

A -- LEAD IS COMING, PRESUMABLY, FROM THE BONE BECAUSE REMODELING IS INHERENT TO ALL STAGES OF LIFE.

Q BUT JUST TO BE CLEAR ABOUT WHAT REMODELING IS: LEAD STORES ITSELF IN THE BONE; CORRECT?

A PART OF THE LEAD, YES.

Q IT GETS INTO THE BONE VIA CALCIUM; RIGHT?

A NO, IT DOESN'T GET IN VIA CALCIUM. WHAT IT DOES IS, THE BONE STRUCTURE IS REFERRED TO AS HYDROXY APPETITE. IT'S A VERY COMPLEX STRUCTURE. IN THE MIDDLE, THERE'S AN IRON OF -- THERE'S A MOLECULE OF

CALCIUM, AND WHAT LEAD IS ABLE TO IS SUBSTITUTE THE LEAD FOR THE CALCIUM.

Q OKAY.

AND BASICALLY, IT GETS IN THERE AND IT TAKES YEARS TO ACCUMULATE IN THE BONE; CORRECT?

A IT CONTINUOUSLY ACCUMULATES. WHAT I'M SAYING IS THAT, OVER TIME, THE LEVEL OF LEAD WILL INCREASE, YES --

Q OKAY.

A -- IF THERE'S CONTINUOUS EXPOSURE.

Q BUT, GENERALLY SPEAKING, IN THE BONE -- STAYS IN THE BONE EXCEPT FOR UNDER CERTAIN CONDITIONS, LIKE PREGNANCY, FOR EXAMPLE?

A YES.

Q OKAY.

AND SO WHEN WE'RE TALKING ABOUT A CHILD WHO IS 5, 7, 9, 14, AND YOU'RE MEASURING BLOOD LEVELS IN THAT CHILD, YOU'RE NOT GETTING ANY MEANINGFUL AMOUNT OF BONE CALCIUM IN THAT MEASUREMENT; CORRECT?

A THAT'S CORRECT. AND IT'S -- ACTUALLY, IT'S VERY IMPORTANT BECAUSE WHAT YOU'RE SAYING IS THEIR BLOOD LEVELS IS TEN MICROGRAMS PER DECILITER. IT'S COMING FROM ELSEWHERE. THEY ARE CONTINUOUSLY EXPOSED. THEY ARE NOT GETTING IT FROM THEIR BONE. I WOULD AGREE WITH THAT.

Q OKAY.

A SO WE AGREE, YES.

Q SO WHEN WE SEE STUDIES WHERE WE'RE MEASURING

KIDS' BLOOD LEVELS, WE'RE SEEING BASICALLY A 30-DAY WINDOW INTO THEIR EXPOSURE TO LEAD?

A OKAY.

Q YOU AGREE?

A YEAH.

Q OKAY.

A YES, I DO.

Q ALL RIGHT.

SO LET'S -- AND YOU WOULD AGREE WITH ME THAT MOST OF THE STUDIES THAT YOU HAVE LOOKED AT IN THIS CASE THAT LOOK AT HUMAN EXPOSURE TO SOME METAL, WITH THE EXCEPTION OF SOME THAT ARE FOCUSED ON LIKE, SAY, YOU KNOW, CHILDREN IN BANGLADESH WHO HAVE, YOU KNOW, KNOWN VERY HIGH LEVELS OF ARSENIC IN WATER, OR OTHER PLACES WHERE THERE ARE BIG ENVIRONMENTAL ISSUES, PUTTING ASIDE THOSE STUDIES, FOR THE MOST PART, THE STUDIES THAT WE'RE LOOKING AT IN THIS CASE DON'T ACTUALLY MEASURE THE EXTERNAL SOURCES OF LEAD, CORRECT? THEY ONLY MEASURE THE INTERNAL SOURCES OF LEAD?

A IN MOST CASES WHAT'S AVAILABLE IS, I AGREE, BLOOD LEVELS, URINE LEVELS, YES.

Q OKAY.

AND SO THEY CAN'T -- THEY DON'T ACTUALLY TELL US HOW DIFFERENT THE KIDS' EXTERNAL EXPOSURES WERE; CORRECT?

A AGAIN, I -- YES, I WOULD AGREE WITH YOU. IF A CHILD HAS FIVE MICROGRAMS PER DECILITER TODAY, WHICH IS THE CDC STANDARD, OR THRESHOLD, IT DOES NOT MEAN THAT,

YOU KNOW, THEY HAD FIVE MICROGRAMS PER DECILITER FIVE YEARS BEFORE. WE DON'T HAVE THE MEANS TO DETERMINE THAT.

Q OKAY. ALL RIGHT.

LET'S JUST GO BACK, SINCE WE'RE KIND OF TALKING ABOUT THE HUMAN STUDIES BEFORE WE MOVE ON TO MORE OF YOUR MECHANISM OPINIONS. AND I JUST WANT TO BE CLEAR ABOUT A FEW THINGS.

AM I OKAY, YOUR HONOR, OR DO YOU NEED TO --

THE COURT: NO, YOU'RE GOOD.

MS. FREIWALD: OKAY. I'M NOT -- I'M NOT -- I DON'T HAVE A CLOCK THAT IS VERY VISIBLE TO ME. SO I APOLOGIZE. AND I DON'T WANT TO MISS A QUEUE IF THE COURT NEEDS A BREAK.

THE COURT: NO, I'M FINE.

MS. FREIWALD: OKAY.

Q SO I JUST WANT TO GO BACK AND JUST KIND OF LEVEL SET ON WHO YOU ARE AND WHAT YOU DO.

YOU ARE A BENCH SCIENTIST; CORRECT?

A I'D LIKE TO THINK SO. YES, MA'AM.

Q OKAY. YOU'RE NOT INVOLVED IN HUMAN RESEARCH; CORRECT?

A I HAVE BEEN INVOLVED IN SOME HUMAN STUDIES.

Q I THINK YOU TOLD ME THAT THE ONE HUMAN STUDY YOU WERE INVOLVED RECENTLY WAS THE ONE ABOUT WHETHER COVID VACCINES WERE CAUSING RISKS?

A THAT'S ONE OF THEM, AND I WAS INVOLVED -- I THINK I MENTIONED IT EARLIER. I WAS INVOLVED IN ONE

STUDY LOOKING AT LEVELS OF MANGANESE IN BASAL GANGLIA OF NEONATES EXPOSED TO PARENTAL ATTRITION. SO IF I OMITTED IT, PLEASE PARDON ME.

Q OKAY.

A AGAIN, I'M NOT A EPIDEMIOLOGIST, BUT I HAVE BEEN INVOLVED IN SEVERAL STUDIES, AND PRESUMABLY SO BECAUSE I BRING THE MECHANISTIC INSIGHT. SO IT HELPS THE CLINICIANS TO DEFINE WHAT TO LOOK AT.

Q GENERALLY SPEAKING, YOUR WORK IS IN WISTAR RATS. THERE'S SOMETHING CALLED A C. ELEGANS, RIGHT, THAT YOU DO A LOT OF WORK IN.

CAN WE HAVE SLIDE 5.

AND IN CELL LINES, RIGHT? THAT'S THE MAJORITY OF YOUR WORK?

A PETRI DISH, WISTAR -- I'VE DONE SOME WORK IN WISTAR RATS, YES. I'VE DONE SOME WORK, A LOT OF WORK, IN C. ELEGANS. YES.

Q AM I SAYING THAT RIGHT? C. ELEGANS? THAT'S WHAT THAT LITTLE WORMY THING IS?

A YES.

MR. ESFANDIARY: COUNSEL, I'M SORRY. I CAN'T SEE YOUR SCREEN. IF YOU'RE SHARING SOMETHING, THAT'S NOT VISIBLE.

THE WITNESS: I CAN SEE IT.

THE COURT: I CAN SEE IT TOO. YOU MIGHT HAVE TO PIN IT.

MS. FREIWALD: LET US KNOW WHEN YOU ARE READY, MR. ESFANDIARY.

MR. ESFANDIARY: JUST ONE SECOND.

THE COURT: TRYING TO GALLERY AND CLICKING ON THE ONE THAT HAS THE PICTURE, NOT THAT I'M AN EXPERT.

MR. ESFANDIARY: I'M SORRY. GO AHEAD, MS. FREIWALD.

MS. FREIWALD: OKAY.

Q SO MOST OF YOUR WORK -- I THINK, AGAIN, I REMEMBER YOU TELLING ME THAT YOU WERE INVOLVED IN THE STUDY ABOUT WHETHER COVID VACCINES WERE MAYBE KILLING MORE PEOPLE THAN THEY WERE SAVING. I THINK I READ ABOUT THAT.

BUT BY AND LARGE, YOU DO LABORATORY WORK -- RESEARCH; CORRECT?

A I -- YES, MA'AM.

Q OKAY.

AND WE CAN AGREE THAT THERE IS ACTUALLY NO ANIMAL MODEL OR ASD?

A WELL, THERE IS NO ANIMAL MODEL THAT CAN RECAPITULATE ALL THE SYMPTOMS OF ASD, JUST THE WAY THAT THERE'S NO ANIMAL MODEL THAT CAN RECAPITULATE THE TREMOR IN PARKINSON'S DISEASE.

Q OKAY.

A BUT THAT DOES NOT DIMINISH FROM THE FACT THAT YOU CAN LEARN A LOT IN TERMS OF THE MECHANISTIC UNDERPINNINGS OF THESE DISORDERS BY USING CELL LINES, BY USING RATS, OR BY USING SOMETHING LIKE A NEMATODE, WHICH YOU CAN'T EVEN SEE WITH YOUR NAKED EYE. YEAH.

Q SO, BUT JUST -- A WISTAR RAT, A C. ELEGANS,

CANNOT GET ASD; CORRECT?

A NO, BUT IT CAN GET A LOT OF SYMPTOMS THAT ARE INHERENT TO ASD.

Q OKAY. AND SO THAT'S WHAT YOU DO. YOU STUDY BEHAVIORS OR SYMPTOMS THAT YOU THINK ARE EITHER, TO SOME DEGREE, CHARACTERISTIC OF ASD OR, TO PICK UP ON A TERM THAT I THINK HER HONOR NOTED, AS COMORBID WITH ASD; CORRECT?

A YES, MA'AM.

Q OKAY.

A WE DO THAT BECAUSE, OBVIOUSLY, WE WOULDN'T BE ABLE TO DO THOSE KIND OF STUDIES. IT WOULD BE UNETHICAL TO DO THEM IN HUMANS. SO THAT'S WHY WE HAVE TO RELY ON THE ANIMAL LITERATURE. SO I JUST DON'T WANT TO DISMISS THIS LITERATURE BECAUSE I THINK IT'S VERY IMPORTANT IN TERMS OF UNDERSTANDING THE MECHANISTIC UNDERPINNINGS OF THESE DISEASE DISORDERS.

Q AND, SIR, ALL I WANT TO DO IS PUT IT IN THE CONTEXT OF WHAT IT IS AND, FRANKLY, WHAT IT IS NOT.

SO IT LOOKS AT SYMPTOMS OR BEHAVIORS, AND ASKS THE QUESTION WHETHER THOSE SYMPTOMS OR BEHAVIORS ARE LIKE SYMPTOMS AND BEHAVIORS THAT YOU MIGHT SEE IN SOMEBODY WHO HAS ASD; CORRECT?

A THAT'S THE BEST THAT WE COULD DO WITH ANIMAL STUDIES. I WOULD AGREE, YES.

Q SO, FOR EXAMPLE, YOU MIGHT DO A STUDY IN WHETHER A RAT PUSHES A MARBLE A CERTAIN AMOUNT, OR MORE OR LESS, AND THAT BECOMES A PROXY FOR CERTAIN LEARNING

BEHAVIORS, FOR EXAMPLE; CORRECT?

A SO I'VE BEEN INVOLVED IN A NUMBER OF STUDIES THAT HAVE LOOKED AT BEHAVIOR. BEHAVIORAL TOXICOLOGY IS ACTUALLY AN AREA INTO ITSELF, AND I WOULD NOT PRETEND TO BE A BEHAVIORAL TOXICOLOGIST.

Q OKAY. SO YOU --

A SO THESE JUST HELP ME TO UNDERSTAND WHAT KIND OF MECHANISMS I MIGHT BE REQUIRED TO LOOK AT TO DETERMINE THE UNDERPINNINGS OF THOSE BEHAVIORS, AND THEY JUST HAPPEN TO BE SIMILAR TO ASD.

SO I'M NOT A BEHAVIORAL TOXICOLOGIST. I THINK I DO HAVE SOME KNOWLEDGE. I'VE BEEN, AGAIN, JUST LIKE THE EPIDEMIOLOGY, I'VE PUBLISHED SOME PAPERS WITH OTHERS AS A CO-AUTHOR FOR THE SAME REASONS I'M INVOLVED IN THESE STUDIES USING THE EPIDEMIOLOGICAL STUDIES.

BUT AGAIN, I WANT TO FOCUS ON THE FACT THAT I WOULD AGREE WITH YOU THAT THERE'S NO ANIMAL MODEL FOR ASD. BUT WE CAN GATHER A LOT OF PERTINENT INFORMATION FROM THE BEHAVIORS FROM THE MECHANISTIC LITERATURE THAT IS DIRECTLY RELATED TO THE ETIOLOGY OF DISORDERS IN HUMANS; OTHERWISE, WE WOULDN'T BE DOING EXPERIMENTS ON ANIMALS.

Q OKAY.

SO YOU'RE NOT -- THERE IS LITERATURE, BUT YOU'RE NOT SOMEBODY WHO ACTUALLY DOES A LOT OF THE THINGS LIKE LOOKING TO SEE WHETHER A MOUSE FOLLOWS A MAZE OR PUSHES A MARBLE? THAT'S BEHAVIORAL TOXICOLOGY, AND THAT'S NOT REALLY THE WORK YOU DO; CORRECT?

A I'VE DONE SOME. I'VE DONE SOME.
Q BUT --
A BUT IT'S NOT SOMETHING THAT I DO AT MY BENCH IN MY LAB.
Q OKAY.
SO, BUT YOU MIGHT DO SOMETHING LIKE LOOK TO SEE IF, WHEN YOU DIRECTLY PUT A CERTAIN DOSE OF, LET'S SAY, MERCURY OR MANGANESE ON A CELL LINE, THAT DIRECT EXPOSURE OF THE CELL TO MERCURY OR MANGANESE HAS CERTAIN REACTIONS; CORRECT?
A YES, MA'AM. SO I WOULD BE INVOLVED MUCH MORE IN DETERMINING IF A PHYSIOLOGICALLY RELEVANT CONCENTRATION OF MERCURY, FOR EXAMPLE, WOULD ELICIT OXIDATIVE STRESS. HOW DOES THE MERCURY GET INTO THE CELL? HOW DO GENETIC SNIPS DETERMINE HOW MUCH MERCURY WOULD ACCUMULATE IN THE CELL? HOW IS THE MERCURY EXCRETED FROM THE CELL? HOW CAN I AMELIORATE THE EFFECTS OF MERCURY ON OXIDATIVE STRESS, OR SIGNAL TRANSDUCTION. SO IT'S BASIC MECHANISTIC WORK, YES.
Q OKAY.
SO THAT BASIC MECHANISTIC WORK WHEN, LET'S SAY, YOU'RE USING A C. ELEGANS REQUIRES YOU -- STRIKE THAT. I WON'T SAY REQUIRES YOU.
WHEN YOU'RE USING A C. ELEGANS, YOU MAY BE LOOKING AT WHETHER YOU CAN LITERALLY INDUCE, AT A CELLULAR LEVEL, CERTAIN EFFECTS THAT YOU CAN SEE WHEN YOU DIRECTLY EXPOSE THAT CELL OR GROUP OF CELLS TO, LET'S SAY, MERCURY; RIGHT?

A YES. SO, FOR EXAMPLE --

Q OKAY.

A -- IF I'D LIKE TO KNOW IF MERCURY IS ASSOCIATED WITH PARKINSON'S DISEASE, WHAT I WOULD DO IS I WOULD GET DIFFERENT STRAINS OF C. ELEGANS WITH DIFFERENT MUTATIONS, AND THEN DETERMINE WHETHER THE EFFECT OF MERCURY ON CERTAIN CELL SIGNALLING PATHWAY IS IDENTICAL IN THE DIFFERENT STRAINS.

Q OKAY.

A THAT WOULD INFORM ME AS TO WHETHER CERTAIN GENETIC SNIP OR MUTATION IS ASSOCIATED WITH INCREASED RISK FOR MERCURY DOING WHATEVER THAT END POINT IS OR REDUCING THE EFFECT. THE SAME CAN BE DONE, OBVIOUSLY, WITH LEAD. THE SAME CAN BE DONE WITH ARSENIC.

SO I'M TRYING TO FIND WHY PEOPLE MIGHT BE SUSCEPTIBLE TO MERCURY AND WHY THEY MAY NOT BE ABLE TO DEFEND THEMSELVES. NOT PEOPLE, NECESSARILY. IF I SAID PEOPLE, IT'S MY MISTAKE. I DO IT IN ANIMAL MODELS.

BUT THAT'S THE TYPE OF WORK THAT I DO IN MY LAB.

Q OKAY.

SO THAT'S THE KIND OF WORK THAT BECOMES, POTENTIALLY, THE BASIS FOR PEOPLE THEN ASKING THE NEXT QUESTION, WHICH IS MAYBE MECHANISTICALLY WOULD YOU SEE -- WOULD THIS SAME MECHANISM WORK IN A HIGHER LIFE FORM, IN A MOUSE OR IN A MONKEY OR, EVENTUALLY, IN A PERSON? AND THEN, YOU'D ALSO HAVE TO ALSO ASK WHETHER THE MECHANISM THAT YOU SEE IN THE C. ELEGANS, EVEN IF IT

LOOKS LIKE SOMETHING THAT MIGHT CAUSE, LET'S SAY, PARKINSON'S, REALLY DOES CAUSE PARKINSON'S, IF THE HUMAN BIOLOGY WORKS THE SAME WAY; CORRECT?

A AND IT DOES. IT'S AMAZING, BECAUSE, GENICALLY, WE'RE SO SIMILAR -- THE WORM IS ABOUT 70 PERCENT SIMILAR IN TERMS OF ITS GENETIC HOMOGENEITY TO HUMANS. THAT'S WHY WE USE THEM; OTHERWISE, WE WOULD BE WASTING OUR TIME IN THE LAB. SO THERE'S GREAT ADVANTAGES TO USING THE ANIMALS.

I JUST WANT TO MAKE SURE WE DON'T, SORT OF, BRUSH OFF TO THE SIDE THE FACT THAT THESE ARE VERY INFORMATIVE STUDIES, AND I THINK WE SHOULD RECOGNIZE THAT.

Q SO TO BE CLEAR, SIR, I'M NOT QUESTIONING THE VALUE OF THE STUDIES FOR WHAT THEY ARE. I JUST THINK IT'S IMPORTANT FOR US TO BE IN AGREEMENT THAT THERE ARE MULTIPLE STEPS OF SCIENTIFIC UNDERSTANDING THAT HAVE TO HAPPEN BETWEEN THE C. ELEGANS AND DRAWING A CONCLUSION IN A HUMAN BEING; CORRECT?

A I WOULD NOT EXTRAPOLATE FROM A WORM TO A HUMAN.

Q OKAY.

A BUT I WOULD LIKE TO THINK THAT WHAT I FIND IN A WORM IS GOING TO BE THEN STUDIED IN A MOUSE OR IN A RAT.

Q OKAY.

A AND, IF NECESSARY, SOMEBODY WOULD STUDY THE SAME THING IN A HUMAN.

ONE THING TO KEEP IN MIND IS THAT A LOT OF THE STUDIES THAT WE PERFORM IN WORMS, YOU WOULDN'T BE ABLE

TO DO THEM IN HUMAN BEINGS. AND I DON'T THINK YOU CAN LOOK AT THE EFFECTS OF LEAD IN A HUMAN ON PKC OR -- I DON'T KNOW. MAP KINASE SIGNALLING. IT WOULD BE UNETHICAL.

Q OKAY.

A SO THE ONLY SOURCE FOR THIS KIND OF INFORMATION IS TO DO THOSE KINDS OF STUDIES IN ANIMALS.

Q AND YOU'RE NOT FAMILIAR -- YOU ARE NOT AN EXPERT IN DIAGNOSING ASD IN HUMANS; CORRECT?

A NO, I'M NOT, MA'AM.

Q OKAY. AND YOU'RE NOT EVEN AN EXPERT IN THE WHAT DSM REQUIREMENTS ARE FOR MAKING THE DIAGNOSIS; CORRECT?

A I'VE GLANCED OVER THEM. I WOULDN'T PRETEND THAT I HAVE MEMORIZED IT. SO, NO. I'M NOT A CLINICIAN, SO I DO NOT DIAGNOSE PATIENTS WITH ASD OR ADHD. I DO NOT.

Q OKAY.

AND BEFORE OFFERING YOUR OPINIONS IN THIS CASE, YOU DIDN'T FAMILIARIZE YOURSELF WITH WHETHER ASD EXPERTS THINK THAT THE PRENATAL PERIOD IS REALLY THE WHOLE BALL GAME IN TERMS OF ASD, DID YOU?

A WELL, I HAVE -- I THINK I HAVE A REASONABLE COMMAND OF THE ASD LITERATURE. I WAS INVOLVED IN SOME THINK TANKS ON ASD. I WAS INVITED TO PARTICIPATE IN RELATIONSHIP TO MERCURY EXPOSURE.

SO, AGAIN, I DON'T THINK IT'S FAIR TO SAY THAT I DON'T KNOW ANYTHING ABOUT ASD. I WOULD NOT AGREE WITH

THAT.

MS. FREIWALD: CAN I HAVE SLIDE 2, PLEASE.

Q DO YOU REMEMBER, SIR, AT YOUR DEPOSITION I ACTUALLY ASKED YOU THIS QUESTION, AND THE ANSWER YOU GAVE ME AT YOUR DEPOSITION, PAGE 240, LINE 13 TO 15 WAS:

"I HAVE NOT LOOKED SPECIFICALLY AT WHETHER PRENATAL EXPOSURE IS THE WHOLE GAME OF ASD."

MR. ESFANDIARY: OBJECTION, YOUR HONOR, TO COMPLETENESS. IT'S NOT SHOWING --

THE COURT: OVERRULED.

MR. ESFANDIARY: -- PART OF HIS QUESTION AND ANSWER.

THE WITNESS: YEAH. I MEAN, I WOULD LIKE TO SEE -- IS THIS THE ONLY THING THAT I SAID? I MEAN, IS THERE ANY OTHER CONTEXT TO THIS, OR...

MS. FREIWALD:

Q NOW, WHEN YOU WERE SHOWING WITH YOUR COUNSEL THE LITTLE VIDEO THAT YOU WERE NARRATING ON THE CELL LINES AND THE EFFECT OF MERCURY, JUST TO BE CLEAR -- CAN I HAVE THAT, PLEASE, IAN. NO, THE PAPER.

THAT ACTUALLY IS FROM A PUBLISHED PAPER, SIR; CORRECT?

A THE MOVIE?

Q YEAH. THE VIDEO WAS THE RESULT OF RESEARCH THAT WAS A PUBLISHED PAPER ABOUT 20 YEARS AGO?

A THE RESULTS HAVE BEEN PUBLISHED, BUT I DON'T THINK THE VIDEO IS EMBEDDED IN THE PAPER. SO MAYBE I DID NOT --

Q NO.
A YEAH.
Q I'M JUST ASKING YOU ABOUT THE PAPER. THERE'S A PAPER THAT IS THE BASIS FOR THAT VIDEO, AND THAT'S ABOUT -- IT'S ABOUT 20 YEARS OLD; RIGHT?
A YEAH. THAT'S RIGHT, YEAH.
Q OKAY. AND IT WASN'T ON YOUR RELIANCE LIST; RIGHT?
A NO, IT WAS NOT AS FAR AS I REMEMBER.
Q AND -- AND THAT PAPER WAS LOOKING AT SNAIL CELLS IN DEVELOPMENT?
A THAT PAPER WAS USING SNAIL IN DEVELOPMENT. YES, MA'AM.
Q OKAY.
AND IT WAS TO TEST THE POSSIBILITY THAT NEURONS FROM THE CENTRAL RING GANGLIA OF THE SNAIL, BLAH, BLAH, BLAH, WHAT HAPPENED TO THEM WHEN THEY WERE EXPOSED TO, I BELIEVE, IF YOU CALL IT OUT, IT WAS MERCURY, ALUMINUM, LEAD, CADMIUM AND MANGANESE; RIGHT?
A I HAVEN'T LOOKED AT THIS PAPER, BUT, I MEAN, YOU'VE UNDERLINED IT IN RED, AND I DEFINITELY AGREE WITH YOU, YES.
Q OKAY. AND, IN FACT, IF WE GO TO THE DISCUSSION SECTION.
A YES, MA'AM.
Q RIGHT UNDER THE DISCUSSION IT SAYS, "THE RESULTS OF THE INVESTIGATION" -- AND THEY WERE PUTTING, YOU SAID, PARTS PER MILLION DIRECTLY ON THE

CELL LINE; CORRECT?

A THEY PUT TEN TO THE MINUS SEVEN.

Q OKAY.

A IT SO IT'S ONE TENTH OF PARTS PER MILLION, YES.

Q AND TODAY, WHEN WE TALK ABOUT LEVELS, WE OFTEN ARE TALKING ABOUT PARTS PER BILLION; RIGHT?

A PARTS PER MILLION IS ONE MICROGRAM PER MILLILITER. SO IT'S NOT THAT OFF WHEN WE TALK ABOUT ONE PART PER MILLION IN TERMS OF LEAD AND WHAT WE FIND IN HUMAN BLOOD. IT'S BASICALLY THE SAME LEVELS.

Q OFTEN WE EXPRESS IT AS PARTS PER BILLION TODAY?

A IN SOME CASES WHEN IT'S VERY LOW, BUT THE LEVELS THAT WE ARE TALKING ABOUT ARE PARTS PER MILLION.

Q OKAY. IN THIS STUDY ARE PARTS PER MILLION?

A .1 POINT PER MILLION, YES.

Q AND IT SAYS: "THE RESULTS OF THE INVESTIGATION DESCRIBED HEREIN CLEARLY DEMONSTRATE THAT EXPOSURE TO MERCURY MARKEDLY DISRUPTED THE MEMBRANE."

AND THEN IT SAYS: "THIS PHENOMENON APPEARS TO BE SPECIFIC FOR MERCURY SINCE EXPOSURE TO FOUR OTHER HEAVY METALS HAD NO OBSERVABLE EFFECT ON EITHER GROWTH CONE MORPHOLOGY OR INDIVIDUAL NEURITES."

RIGHT?

A THAT'S WHAT THIS SAYS. YES, MA'AM.

Q OKAY.

A THEY ALSO SAY THE SAME THING IN THE MOVIE, AND

I JUST WANT TO CLARIFY. I THINK IT CAME ACROSS BEFORE. THIS IS ONLY ONE SPECIFIC MECHANISM BY WHICH THESE METALS CAN AFFECT DEVELOPMENT AND PROPER FUNCTIONING.

SO I ACTUALLY -- IT'S -- I'M ENCOURAGED BY THOSE KINDS OF RESULTS BECAUSE I WOULD NOT EXPECT THE DIFFERENT METALS TO HAVE DIFFERENT MECHANISMS.

SO THE FACT THAT ALUMINUM DOESN'T CAUSE SAME THE EFFECT, OR LEAD DOESN'T CAUSE THE SAME EFFECT, DOES NOT PRECLUDE THAT, THROUGH OTHER MECHANISMS, THEY WILL INTERFERE WITH SYNAPTIC TRANSMISSION, FOR EXAMPLE, BECAUSE IT MAY NOT BE VIA THE TUBULE. LEAD DOES NOT HAVE HIGH AFFINITY FOR THOSE GROUPS. SO I WOULDN'T EXPECT IT TO AFFECT THE GROWTH CONE, BUT LEAD WILL AFFECT CALCIUM SIGNALLING, WHICH IS VERY IMPORTANT FOR THE RELEASE OF NEUROTRANSMITTERS.

SO, YOU KNOW, YOU CAN BASICALLY END UP WITH THE SAME KIND OF RESPONSE VIA COMPROMISED MECHANISMS THAT ARE VERY DISTINCT. SO THERE'S NO REASON -- I MEAN, THIS IS ENCOURAGING DATA BECAUSE IT JUST SHOWS WHAT YOU'D EXPECT. THEY WORK THROUGH DIFFERENT MECHANISMS. I WOULDN'T EXPECT LEAD TO WORK THE SAME WAY THAT MERCURY DOES.

Q OKAY.

SO YOU HAVE TO LOOK METAL BY METAL AND MECHANISM BY MECHANISM TO SEE WHETHER THE DATA ARE THERE TO SUPPORT?

A ABSOLUTELY.

Q OKAY.

A I THINK WE'VE TALKED ABOUT IT BEFORE. THE METAL, THE OXIDATION STATE, THE -- WHETHER IT'S ORGANIC OR INORGANIC. YOU KNOW, ONE SIZE DOESN'T FIT EVERYTHING -- EVERYONE. IT'S THE SAME THING.

Q ALL RIGHT.

SO LET'S JUST BE -- BEFORE WE GET IN A LITTLE BIT MORE, LET'S JUST TALK VERY BRIEFLY, AS YOUR COUNSEL DID WITH YOU, ABOUT YOUR REVIEW OF THE EPI LITERATURE.

AND TO BE CLEAR, SIR, YOU'VE BEEN VERY CANDID. YOU'RE NOT AN EPIDEMIOLOGIST, AND YOU DON'T WANT TO WEAR THE HAT OF AN EPIDEMIOLOGIST; RIGHT?

A THAT'S CORRECT. I'M NOT AN EPIDEMIOLOGIST. I DON'T PRETEND TO BE ONE.

Q OKAY. AND YOU DIDN'T WANT TO TALK AT YOUR DEPOSITION ABOUT THE DESIGN OF DIFFERENT STUDIES OR WHETHER DIFFERENT STUDIES WERE ADEQUATE FOR PURPOSES OF DETERMINING CAUSE AND EFFECT; CORRECT?

A WELL, I DON'T KNOW IF I SAID I DIDN'T WANT TO TALK ABOUT IT. I SAID I MIGHT NOT BE THE MOST QUALIFIED INDIVIDUAL TO DETERMINE WHETHER THEY USE THE PROPER -- THEY ACCOUNTED FOR PROPERLY FOR CONFOUNDERS, THINGS LIKE THAT.

SO, YEAH, I -- YOU KNOW, IT'S -- I WILL NOT -- I THINK IT'S REFLECTIVE IN THE KIND OF WORK THAT I DO. I DO NOT GET PAPERS, FOR EXAMPLE, FOR REVIEW THAT ARE EPIDEMIOLOGICAL IN NATURE. CONSISTENT WITH EVERYTHING THAT I HAVE -- I'VE SAID BEFORE. SO I DON'T PRETEND TO WEAR THE HAT. I CAN STILL READ THOSE PAPERS, AND I

THINK I CAN ARRIVE AT A REASONABLE CONCLUSION.

MS. FREIWALD: CAN I HAVE DEPOSITION 106, PAGE 106, PLEASE? AND CAN WE BLOW OUT SEVEN TO TEN?

Q SO, SIR, DO YOU REMEMBER AT YOUR DEPOSITION, I ASKED YOU SPECIFICALLY ABOUT WHETHER YOU HAD AN OPINION ON THE ADEQUACY THE STUDIES, AND YOU SAID, "I PREFER NOT TO TALK ABOUT THE DESIGN OF THE STUDIES AND WHETHER THEY ARE ADEQUATE OR NOT"?

A I DEFER IT TO THE EPIDEMIOLOGISTS. YES, ABSOLUTELY.

Q AND YOU'VE BEEN CLEAR THAT YOU DON'T WANT TO TALK ABOUT THE BASIC LIMITATIONS OF THE OBSERVATIONAL STUDIES; CORRECT?

A I AM NOT IN POSITION TO CRITICIZE THOSE STUDIES. AND I'LL REPEAT WHAT I SAID IN MY DEPOSITION. THESE PAPERS HAVE BEEN PEER-REVIEWED. THEY HAVE BEEN PEER-REVIEWED BY EPIDEMIOLOGISTS. SO WHEN I READ THEM, I BELIEVE THAT MOST OF THEM ARE SOUND IN TERMS OF THE METHODOLOGY, BECAUSE OTHERWISE, THEY WOULD NOT BE PUBLISHED.

SO I USE THOSE PAPERS, NOT TO OPINE ABOUT ASD OR ADHD. I USE THOSE PAPERS TO SUPPLEMENT INFORMATION THAT I NEED IN MY TOXICOLOGICAL BENCH SCIENCES AND TO TRY TO RELATE MY FINDINGS TO THOSE THAT HAVE BEEN REPORTED IN THE EPIDEMIOLOGICAL LITERATURE.

I AM NOT HERE TO OPINE AS AN EPIDEMIOLOGIST. I BELIEVE BOTH YOU AND THE PLAINTIFFS HAVE OTHERS THAT ARE RESPONSIBLE FOR THIS ARENA OF SCIENCE.

Q BUT JUST TO BE CLEAR, SIR -- AND THAT'S FINE. BUT JUST TO BE CLEAR, WHEN YOU REVIEWED THE EPI LITERATURE, YOU DIDN'T CONSIDER THINGS LIKE THE DESIGN OF THE STUDY, WHAT THE CONFOUNDERS WERE, WHETHER THEY WERE ADEQUATELY ABLE TO ASSESS CAUSATION, EVEN TEMPORALITY, YOU DIDN'T LOOK AT?

A NO, I DID NOT, BUT, YOU KNOW, IF YOU'RE IMPLYING THAT ALL THESE PAPERS -- WELL, MAYBE I'M NOT THE RIGHT INDIVIDUAL TO ASSESS THESE PAPERS, BUT THE FACT OF THE MATTER IS THAT THE CONCLUSIONS FROM THOSE PAPERS, APPROXIMATELY 80 PERCENT OF THOSE PAPERS, ARE CONSISTENT. THEY ALL TALK ABOUT A CAUSAL RELATIONSHIP BETWEEN LEAD EXPOSURE.

SO IT'S -- I DON'T HAVE TO EVALUATE THOSE PAPERS. I -- YOU KNOW, IF IT WAS BY CHANCE, IT WOULD BE 50/50. THE FACT THAT THERE IS A CONSENSUS BASICALLY BETWEEN EPIDEMIOLOGISTS DOESN'T NECESSARILY MEAN THAT I HAVE TO GO BACK AND REVIEW ALL THESE PAPERS AND DETERMINE WHETHER THEY FORGOT ONE CONFOUNDER. I THINK THAT'S BEEN DONE ALREADY.

Q AND WHEN -- WITHOUT DOING THE THINGS THAT AN EPI WOULD DO, WITHOUT USING A METHODOLOGY, YOU COUNTED STUDIES; RIGHT? THAT'S WHAT YOU SAID YOU DID, YOU COUNTED THE --

A THAT'S ACTUALLY ONE OF THE THINGS I DID, YES. I WAS INTERESTED TO SEE WHETHER IT'S BY CHANCE, AND IT'S NOT. AS I SAID, AND AS I PUBLISHED IN MANY OF MY PAPERS LONG BEFORE THIS LITIGATION, ANYWHERE UPWARDS TO

80 PERCENT OF THE PAPERS THAT HAVE DONE STUDIES TO LOOK AT ASSOCIATIONS BETWEEN THESE METALS AND ASD, ARE POSITIVE.

Q OKAY.

A SO I DON'T THINK IT'S BY CHANCE. AND MAYBE I'M MISSING ONE CONFOUNDER, BUT WHAT YOU'RE DOING IS YOU'RE STRIKING OUT, BASICALLY, ALL THE EPIDEMIOLOGICAL LITERATURE BECAUSE DR. ASCHNER DIDN'T REVIEW IT.

Q AND YOU DIDN'T REVIEW WHETHER OTHERS WHO HAVE DONE MORE SYSTEMATIC ASSESSMENTS OF THE LITERATURE, LIKE, FOR EXAMPLE, THE AUTHORS OF THE WANG PAPER, COUNTED DIFFERENTLY AND FOUND THAT THE SPLIT WAS CLOSER TO 50/50? YOU DIDN'T DO THAT EITHER; CORRECT?

A SO I WAS -- I'M SORRY FOR INTERRUPTING, COUNSEL.

I THINK I WAS VERY UNBIASSED IN MY REPORT, IN MY DEPOSITION, IN MY REPORT, BECAUSE I EVEN POINTED OUT TO THOSE STUDIES THAT HAVE SHOWN THAT THERE'S NO ASSOCIATION. SO...

Q MY QUESTION IS JUST --

A SO I DID NOT --

Q IF I MAY JUST FINISH MY QUESTION, SIR.

IT'S JUST YOU DIDN'T LOOK TO SEE WHETHER OTHERS WHO DID SYSTEMATIC REVIEWS COUNTED DIFFERENTLY FROM YOU?

MR. ESFANDIARY: I'D JUST ASK COUNSEL TO LET THE WITNESS FINISH ANSWERING YOUR QUESTION BEFORE --

THE COURT: I'D LIKE HIM TO ANSWER THE PENDING QUESTION, ACTUALLY.

THE WITNESS: I HAVE LOOKED AT ALL THE PAPERS THAT I'VE REVIEWED, AND I DON'T KNOW IF THE PAPER THAT YOU JUST MENTIONED WAS IN MY REFERENCE LIST. I DON'T HAVE A RECOLLECTION OF THAT, BUT I WENT ONE-BY-ONE AND COUNTED THE PAPERS, WHETHER THEY FOUND A POSITIVE ASSOCIATION OR A NEGATIVE ONE, AND I PROVIDED, ACTUALLY, THE PICTURE FROM MY COMPUTER WHERE I'VE DONE SO.

AND IN SOME CASES THEY FOUND SOME POSITIVE, SOME NEGATIVE ASSOCIATIONS OR NO ASSOCIATIONS. I MARKED IT WITH DIFFERENT COLORS. SO I WAS COMPLETELY UNBIASSED. I'M NOT SAYING IT'S, YOU KNOW, THE RIGHT METHOD TO DETERMINE AND -- BUT I THINK IT GIVES YOU A FAIRLY COMPREHENSIVE PICTURE AS TO WHERE THE LITERATURE IS.

AND AGAIN, I GO BACK TO CANCER. SAYING THAT LEAD IS NOT CAUSING NEUROLOGICAL DISORDERS IS AKIN TO SAYING THAT SMOKING IS NOT ASSOCIATED WITH LUNG CANCER. I MEAN, THAT'S MY BEST ANALOGY.

THE COURT: I HAVE TO BREAK UNTIL 1:30. ARE WE GOING TO PICK UP WITH DR. ASCHNER THEN?

MS. FREIWALD: YES, I WOULD LIKE TO DO THAT, YOUR HONOR. THANK YOU.

THE COURT: LET'S DO THAT.

THANKS FOR YOUR PATIENCE, DOCTOR. SEE YOU IN A LITTLE WHILE.

THE WITNESS: THANK YOU, YOUR HONOR.

THE COURT: BYE.

{LUNCHEON RECESS}

CASE NUMBER: 21STCV22822
CASE NAME: NC VS. HAIN, ET AL.
LOS ANGELES, CALIFORNIA FRIDAY, FEBRUARY 4, 2022
DEPARTMENT 7 HON. AMY D. HOGUE, JUDGE
APPEARANCES: (AS HERETOFORE NOTED.)
REPORTER: JEANESE JOHNSON, CSR 11635
TIME: 1:30 P.M.

--OOO--

AFTERNOON SESSION

THE COURT: OKAY. YOU MAY PROCEED.

MS. FREIWALD: THANK YOU, YOUR HONOR.

CROSS EXAMINATION (RESUMED)

MS. FREIWALD:

Q GOOD AFTERNOON AGAIN, DR. ASCHNER.

A GOOD AFTERNOON, MA'AM. THANK YOU.

Q THANK YOU. OR CLOSER TO EVENING FOR YOU AND ME.

LET'S SEE. I WANT TO TRY TO MOVE THINGS ALONG FAIRLY QUICKLY.

SO LET'S SEE. ONE OTHER THING THAT I THOUGHT WE COULD PROBABLY AGREE ON IS THAT, IN ORDER TO DO ANY KIND OF AN ASSESSMENT OF WHETHER AN AGENT IS A CAUSE OF HARM, YOU HAVE TO KNOW THAT THE EXPOSURE TO THE AGENT

PRECEDES THE HARM; CORRECT?

A YES, I WOULD AGREE WITH THAT.

Q OKAY.

OKAY. AND I GATHER, IN YOUR WORK AS A SCIENTIST, YOU ALSO AGREE THAT STATISTICAL SIGNIFICANCE IS AN IMPORTANT CONCEPT?

A YES, I AGREE. I USE P VALUE OF .05 IN ALL OF MY STATISTICS. THAT'S A P VALUE THAT'S SET TO SIGNIFY STATISTICAL DIFFERENCE.

Q AND YOU SET OUT IN YOUR REPORT A BUNCH OF BASIC PRINCIPLES THAT WERE IMPORTANT TO TOXICOLOGY.

CAN I GET SLIDE 4, PLEASE?

AND I JUST TRIED TO SUMMARIZE THEM ON A SINGLE SLIDE, AND I THINK THIS WILL BE ANOTHER AREA WHERE WE CAN AGREE.

SO, AGAIN, SUMMARIZING FROM YOUR REPORT, DOCTOR, I THINK THAT YOU POINTED OUT THAT A TOXICOLOGIST HAS TO CONSIDER ROOT OF EXPOSURE, TIME AND DURATION OF EXPOSURE, THE AGE OR THE DEVELOPMENTAL STAGE IN WHICH THE EXPOSURE IS OCCURRING, THE FACT THAT CELLS OR TISSUES DO NOT MIMIC INVIVO, MEANING IN A HUMAN BEING, METABOLISM, THAT ANIMAL STUDIES, WHILE VERY USEFUL FOR THEIR OWN PURPOSE, ARE OFTEN POOR PREDICTORS OF HUMAN RESPONSES, AND THAT THE BODY HAS DEFENSE MECHANISMS TO PROTECT ITSELF FROM HARM SO THAT, EVEN IF AN AGENT CAUSES WHAT LOOKS LIKE AN ADVERSE EFFECT AT THE CELLULAR LEVEL, THAT DOESN'T NECESSARILY MEAN IT'S GOING TO TRANSLATE INTO A CLINICAL HARM.

SO THAT WAS MY SUMMARY.

I GUESS THE QUESTION AT THE END OF THAT LONG STATEMENT IS: DID I FAIRLY CAPTURE ITEMS THAT YOU ACKNOWLEDGE ARE IMPORTANT TO CONSIDER AS PART OF A TOXICOLOGIC ASSESSMENT?

A YES, MA'AM. SO IF I MAY, I'D LIKE TO GO OVER THEM BECAUSE, YOU KNOW, I DON'T AGREE WITH ALL THESE STATEMENTS AS THEY ARE NOTED.

SO I AGREE THAT TOXICITY DEPENDS ON THE ROUTE OF EXPOSURE.

Q OKAY.

A AND SOMETHING THAT'S INHALED MIGHT BEHAVE VERY DIFFERENTLY THAN SOMETHING THAT'S DIGESTED. THERE ARE OTHER IMPORTANT ISSUES WHICH IS NOT MENTIONED HERE. THE DOSE IS IMPORTANT. AND THE FORM. SOME OTHER THINGS THAT WE TALKED ABOUT, YOU KNOW, FREE IRONS VERSUS NANO PARTICLES. THESE ARE OTHER ISSUES THAT NEED TO BE CONSIDERED.

BUT GENERALLY, I AGREE WITH 1.

I AGREE WITH NUMBER 2, THAT THE TIMING AND THE DURATION ARE IMPORTANT. I THINK YOU'RE REFERRING WITH RESPECT TO TIME, YOU'RE NOT MAKING ANY DISTINCTION BETWEEN YOUNG OR OLD. YOU'RE JUST BASICALLY TALKING ABOUT ONE MONTH, THREE MONTHS, NOT TAKING INTO ACCOUNT WHAT LIFE STAGE THE INDIVIDUAL MIGHT BE, BUT THAT'S FINE.

AND TOXICITY MAY VARY BASED ON AGE, DEVELOPMENTAL AGE, YOU KNOW, OR STAGE. I WOULD AGREE

WITH THAT. AND WHAT I WOULD POINT OUT, ACTUALLY, THAT, IN MOST CASES, THE DEVELOPMENTAL STAGE IS A STAGE THAT'S MUCH MORE SENSITIVE.

IF YOU TAKE LEAD, FOR EXAMPLE. INDIVIDUALS ARE MUCH MORE SUSCEPTIBLE TO LEAD WHEN THEY ARE YOUNG THAN WHEN THEY ARE OLD, BECAUSE MANY OF THE PROCESSES THAT WE DISCUSSED TODAY, SUCH AS SYNAPTOGENESIS. WE HAVEN'T MENTIONED CELL DIFFERENTIATION, PRUNING OF CELLS.

ALL OF THESE ARE INHERENT TO THE DEVELOPING BRAIN, AND THEY ARE NOT INHERENT TO THE MATURE BRAIN. SO THE DEVELOPMENTAL STAGE, IN GENERAL, IS MUCH MORE SUSCEPTIBLE TO XENOBIOTICS. SO, AGAIN, I AGREE WITH WHAT YOU SAY, BUT I THINK WE HAVE TO MAKE THIS DISTINCTION.

I DON'T NECESSARILY AGREE WITH POINT NUMBER 4 BECAUSE I THINK IT IMPLIES THAT TISSUES OR CELLS CANNOT MIMIC NORMAL METABOLISM, WHICH IS NOT CORRECT, AND I WOULD SAY THAT CELLS, IN CULTURE, ARE A REDUCTIONIST APPROACH, BECAUSE SOMETIMES YOU DON'T HAVE ALL THE CELLS IN THE TISSUE CULTURE. IT MIGHT BE JUST ONE CELL TYPE, BUT THAT DOES NOT EXCLUDE THAT CELL TYPE FROM MIMICKING THE EFFECT OR HANDLING THE MATERIAL IN AN ANALOGOUS WAY THAT THE SAME CELL WOULD HANDLE THE METAL OR THE XENOBIOTICS INVIVO.

SO I THINK THIS HAS TO BE QUALIFIED. TO SAY THAT CELLS OR TISSUES CANNOT MIMIC NORMAL METABOLISM IS GENERALIZING. IT'S NOT CORRECT.

EXPERIMENTAL ANIMAL STUDIES ARE OFTEN POOR

PREDICTORS.

THERE ARE SOME EXAMPLES, I AGREE, AND YOU'LL PROBABLY KNOW THE CASE OF THALIDOMIDE. IT WAS NOT -- THAT THE RATS WERE NOT PREDICTED TO THE TERETOGENIC EFFECTS OF THE THALIDOMIDE. AND THERE'S OTHER CASES, I BELIEVE IT'S SACCHARIN, WHICH IS MUCH LESS TOXIC TO HUMANS THAN RATS BECAUSE RATS TEND TO METABOLIZE SACCHARIN IN A VERY DIFFERENT WAY USING P450S; P450S THAT ARE NOT INHERENT TO HUMANS.

SO THERE ARE SOME DIFFERENCES, BUT I WOULD NOT SAY THAT THEY ARE GENERALLY POOR PREDICTORS, NOT OFTEN. RARELY ARE THERE POOR PREDICTORS. IN MOST CASES THERE ARE VERY GOOD PREDICTORS OF HUMAN RESPONSES. THOUGH, AS WE SAID BEFORE, I WOULD NOT EXPECT A RAT TO SHOW A TREMOR OR TO SHOW ALL THE SYMPTOMS THAT YOU SEE IN ASD, AND I WOULDN'T EXPECT A WORM TO DEVELOP PARKINSON'S DISEASE AND HAVE PROBLEMS WITH SPEECH BECAUSE THEY DON'T VOCALIZE.

SO, AGAIN, THIS HAS TO BE QUALIFIED.

AND THE BODY HAS DEFENSE MECHANISMS TO PROTECT IT FROM HARM. YES, THAT'S A GIVEN. I WOULD AGREE WITH THAT, MA'AM.

Q OKAY.

SO I'LL TELL YOU WHAT, JUST TO SAVE TIME, YOU WROTE OUT IN YOUR OWN WORDS CONSIDERATIONS IN ASSESSING EXPERIMENTAL ANIMAL STUDIES AND CONSIDERATIONS IN ASSESSING INVITRO STUDIES, AND THOSE CONSIDERATIONS CAN BE FOUND AT PAGES 13 TO 16 OF YOUR EXPERT REPORT AND,

CERTAINLY, THE COURT CAN LOOK AT THOSE.

AND I ASSUME YOU STAND BY WHAT YOU WROTE IN YOUR REPORT?

A I FULLY STAND BY. I SAY THAT SOMETIMES THE ANIMAL STUDIES USE CONCENTRATIONS OR DOSES THAT ARE NOT RELEVANT TO THE HUMAN EXPOSURES. SO, YOU KNOW, THAT'S NOT A GOOD STUDY. AND PEOPLE USE ONE LITTER. YOU KNOW, YOU DON'T -- YOU CANNOT ACCOUNT FOR GENETIC DIFFERENCES, SO THEY DO HAVE LIMITATIONS.

Q OKAY. SO --

A BUT I DIDN'T SAY THAT THEY ARE POOR PREDICTORS. I DON'T THINK I DID. I ACTUALLY PROVIDED SOME EXAMPLES WHERE THEY ARE GOOD PREDICTORS, AND I POINTED OUT TO THOSE COUPLE CASES WHERE ANIMAL STUDIES HAVE NOT MIMICKED EXACTLY WHAT YOU'RE SEEING IN HUMANS.

I WOULD VENTURE TO SAY, THOUGH, THAT IN THE CASE OF LEAD AND MERCURY AND ARSENIC, ANIMALS ARE VERY GOOD PREDICTORS OF HUMAN TOXICITY.

Q SO WE'LL LET THE REPORT SPEAK FOR ITSELF.

AND, SIR, YOU DID POINT OUT THOSE, WHICH I WAS GOING TO ASK YOU ABOUT.

YOU HAVE NOTED CORRECTLY THE DOSE MAKES THE POISON. THAT'S A STATEMENT YOU AGREE WITH; CORRECT?

A I AGREE THE DOSE MAKES THE POISON. THERE IS OTHER THINGS THAT NEED TO BE TAKE IN ACCOUNT, BUT THE PRINCIPAL TOXICOLOGY -- I MEAN, WE TALKED ABOUT. IT'S NOT JUST THE DOSE, IT'S GENETICS, BUT GENERALLY, I WOULD AGREE WITH YOUR STATEMENT, MA'AM, YES.

Q OKAY. AND YOU TALKED WITH YOUR COUNSEL ABOUT THE CONCEPT OF A THRESHOLD DOSE.

AND YOU WOULD AGREE THAT THE STATEMENT THAT THERE IS NO KNOWN SAFE DOSE, WHICH IS USED FOR REGULATORY PURPOSES; IT'S USED FOR PURPOSES OF FIGURING OUT WHETHER THERE IS A FLOOR AT WHICH YOU CAN SAY THERE'S NO HARM, IS NOT THE SAME THING AS SAYING THAT THERE IS A HARM AT EVERY LEVEL?

A I WOULD AGREE WITH THAT STATEMENT. WE DON'T KNOW THE DOSE RESPONSE IN RELATIONSHIP TO LEAD AT VERY LOW DOSES. THAT DOES NOT INTIMATE THAT IT'S VERY TOXIC AT .1 MICROGRAM PER DECILITER, BUT IT ALSO DOESN'T INTIMATE THAT IT'S NOT. AND WHAT I'M BASING MY OPINION ON IS LEVELS THAT ARE SEEN IN AUTISTIC KIDS.

SO, YOU KNOW, I DON'T -- FOR -- TO MAKE THE CONCLUSION I DON'T HAVE TO INFER FROM THE LEFT OF THE CURVE. I DON'T EVEN KNOW THE SHAPE OF THE CURVE --

Q SO WHAT --

A -- WHEN I GO DOWN TO VERY LOW DOSES. SO, I MEAN, I KNOW WHAT HAPPENS AT 2 MICROGRAMS PER DECILITER AND 5 MICROGRAMS PER DECILITER AND HIGHER CONCENTRATIONS.

Q WHAT THE STATEMENT BASICALLY MEANS IS WE DON'T KNOW HOW LONG WE'RE GOING TO HAVE TO GO IN THE FUTURE BEFORE WE KNOW IF THERE'S REALLY AN ASSOCIATION BETWEEN LEAD EXPOSURE AND ASD AT LOW LEVELS?

A NO. WE KNOW -- WE ALREADY KNOW THAT THERE IS AN ASSOCIATION. I DON'T THINK WE CAN MAKE A STATEMENT

AS TO BLOOD LEVELS OF .001 MICROGRAMS PER DECILITER ARE ASSOCIATED WITH ASD. I DON'T THINK WE ARE AT THAT POINT. BUT WE CAN MAKE THAT STATEMENT, AT LEVELS OF LEAD AT 10 MICROGRAMS PER DECILITER OR EVEN LOWER THAN THAT.

MS. FREIWALD: SO CAN WE PULL UP THE TRANSCRIPT AT 166, PLEASE? AND PULL OUT -- I THINK IT'S STARTING AT LINE 11, MAYBE IT'S A LITTLE BEFORE.

Q SO YOU REMEMBER, SIR, I ASKED YOU:

"CAN WE ALSO -- DO YOU UNDERSTAND, OR WOULD YOU AGREE WITH ME THAT THE STATEMENT, THERE'S NO SAFE LEVEL OF LEAD WHICH IS MADE FOR A REGULARLY PURPOSE IS NOT THE SAME STATEMENT AS AT EVERY DOSE, NO MATTER HOW LOW, LEAD HAS BEEN PROVEN TO CAUSE A SPECIFIC OUTCOME LIKE ASD? THOSE ARE DIFFERENT STATEMENTS?"

AND YOUR ANSWER WAS, "WHAT THE STATEMENT BASICALLY SAYS THAT WE DON'T KNOW HOW LONG WE'RE GOING TO GO IN THE FUTURE BEFORE WE REALIZE THAT THERE'S AN ASSOCIATION BETWEEN LEAD EXPOSURE AND ASD. THE DATA MIGHT NOT BE AVAILABLE AT THE MOMENT, BUT THE LACK OF EVIDENCE OR THE ABSENCE OF EVIDENCE IS NOT EVIDENCE OF ABSENCE."

A AND I THINK IT'S EXACTLY WHAT I'M SAYING RIGHT NOW, THAT I KNOW THAT THERE IS EVIDENCE THAT'S AT 10 MICROGRAMS PER DECILITER, BUT YOU'RE ASKING ME AT THRESHOLDS APPROACHING ZERO MICROGRAMS OF LEAD PER

DECILITER. I CANNOT TELL YOU WHAT HAPPENS AT THOSE CONCENTRATIONS IN THE BLOOD.

Q OKAY.

A BUT I CAN TELL YOU AND THAT'S THE BASIS OF MY REPORT, THAT AT THE LEVELS THAT ARE DISCUSSED IN MY REPORT, THERE IS AN ASSOCIATION BETWEEN LEAD BLOOD LEVELS AND ASD.

Q SO WE TALKED EARLIER ABOUT THE FACT THAT LEAD LEVELS, AND OTHER METAL LEVELS, HAVE BEEN GOING DOWN IN THIS COUNTRY SIGNIFICANTLY OVER THE LAST SEVERAL DECADES.

BUT THAT WASN'T SOMETHING THAT YOU SPECIFICALLY LOOKED AT IN PREPARING YOUR REPORT; CORRECT?

A I ACTUALLY TEACH TOXICOLOGY, SO I DO HAVE A SLIDE THAT SHOWS THE LEVELS OF LEAD IN THE ENVIRONMENT IN RELATIONSHIP TO THE REMOVAL OF LEAD FROM GASOLINE AND FROM PAINT, AND THERE IS A VERY NICE PARALLEL LINE BETWEEN THE TWO. AS -- SINCE IT'S BEEN REMOVED FROM THESE SOURCES, THE LEVELS OF LEAD IN THE BLOOD OF KIDS HAS GONE DOWN. SO IT'S ABOUT 2 MICROGRAMS, IF NOT LESS AT THIS POINT.

Q SO, OKAY, SO YOU DON'T REMEMBER TELLING ME YOU DIDN'T ACTUALLY LOOK AT THIS IN PREPARATION FOR GIVING YOUR OPINION IN THIS CASE?

A ARE YOU ASKING ME IF I'M AWARE OF THE FACT THAT THE LEAD LEVELS ARE GOING DOWN?

Q NO. NO, I'M ASKING IF IT WAS PART OF YOUR METHODOLOGY TO CONSIDER THAT FACT BEFORE ISSUING YOUR

OPINIONS IN THIS CASE.

A NO. NO, I DON'T SEE HOW IT'S PERTINENT TO THIS.

Q SO CAN WE PUT UP SLIDE 8.

AND I THINK THIS IS CONSISTENT WITH WHAT YOU'VE SAID, DR. ASCHNER, THAT CONSISTENT WITH, FRANKLY, YOU KNOW, SOME BIG CHANGES, LEAD COMING OUT OF GAS LINE AS AN ADDITIVE, COMING OUT OF TIN CANS, WE'VE SEEN DRAMATIC DROPS.

SO THAT AS YOU -- I THINK YOU SAID THAT THE MEDIAN LEVEL IN THIS COUNTRY TODAY IS BELOW 2, AND EVEN THE 95TH PERCENTILE IS PROBABLY SOMEWHERE AROUND 2, AND THIS CHART -- IT'S THE MOST RECENT DATA I COULD GET MY HANDS ON. I'M SURE IF I WERE A MORE CLEVER RESEARCHER, THERE MIGHT BE A COUPLE OF MORE YEARS TO ADD, BUT I THINK IT'S PROBABLY A REASONABLE REPRESENTATION ENDING AROUND 2013, 2014, THAT 95 PLUS PERCENT OF CHILDREN ARE GOING TO BE BELOW 2 IN THIS COUNTRY TODAY; RIGHT?

A THAT'S CORRECT, MA'AM, YES.

Q OKAY.

SO WHEN WE READ THE LITERATURE AND WE HEAR THE TERM "LOW DOSE" USED, YOU WOULD AGREE WITH ME THAT THAT CAN ACTUALLY MEAN VERY DIFFERENT THINGS DEPENDING UPON WHEN THE PAPER WAS WRITTEN OR WHAT TIME PERIOD WAS BEING LOOKED AT, BECAUSE WHAT WAS LOW DOSE 10 OR 20 YEARS AGO IS NOT LOW TODAY; CORRECT?

A SO TRYING TO CONNECT THIS WITH WHAT WE'VE TALKED ABOUT BEFORE, YOU'RE ASKING ME QUESTIONS -- CAN

YOU HEAR ME? I'M SORRY. --

Q YES, SIR. I JUST -- I JUST WAS WONDERING IF YOU COULD ANSWER MY QUESTION.

AM I CORRECT THAT WHAT WAS -- MIGHT BE DESCRIBED AS LOW DOSE IN THE LITERATURE 10 OR 20 YEARS AGO, WOULD BE A -- COULD BE A MUCH HIGHER VALUE THAN WHAT WOULD BE CATEGORIZED AS LOW DOSE TODAY?

A NO, BECAUSE 10 MICROGRAMS PER DECILITER IN THE BLOOD TODAY IS THE SAME AS 10 MICROGRAMS PER DECILITER 20 YEARS AGO.

Q I'M SORRY. I MUST BE ASKING MY QUESTION BADLY.

WHAT I'M SAYING TO YOU IS: A STUDY MIGHT SAY, WE LOOKED AT LOW DOSE, AND THEN YOU GO AND READ THE PARENTHETICAL, AND YOU FIND OUT THAT WHAT THEY ARE CALLING LOW DOSE MIGHT BE 30 MICROGRAMS PER DECILITER. OR --

A THAT'S NOT THE DOSE. I'M SORRY. I'M SORRY TO DISTURB. BUT THE 10 MICROGRAMS PER DECILITER IS NOT THE DOSE. IT HAS NOTHING TO DO WITH THE LEVEL TO WHICH AN INDIVIDUAL WAS EXPOSED. THAT'S THE BLOOD LEVEL.

Q FAIR ENOUGH.

A THAT'S A TOTALLY DIFFERENT FACTOR. SO WHAT I'M SAYING IS, THE DOSE DOESN'T REALLY MATTER. WHAT'S IN THE BLOOD IS IS 30 MICROGRAMS PER DECILITER, WHETHER IT'S TODAY, YESTERDAY OR 30 YEARS AGO, IT'S 30 MICROGRAMS PER DECILITER.

Q I STAND CORRECTED. I'LL REPHRASE MY QUESTION.

IT MIGHT HAVE SAID: WE SAW LOW BLOOD LEVELS

AND IT WAS 30 MICROGRAMS PER DECILITER 10 OR 20 YEARS AGO, AND TODAY A PAPER WOULD BE TALKING ABOUT LOW BLOOD LEVELS AND IT WOULD BE TALKING ABOUT SOMETHING MUCH LOWER THAN THAT.

SO YOU JUST HAVE TO LOOK AT THE TIME PERIOD OF WHAT YOU'RE READING, AND BE CAREFUL AND NOT USE THE TERM "LOW LEVELS" AND ASSUME THAT IT MEANS THE SAME THING ACROSS ALL PAPERS?

A RIGHT. I DON'T THINK -- WELL, I CAN SPEAK ABOUT MYSELF. WHEN I LOOK AT A PAPER -- WHEN THEY SAY LOWS DOSE LEVEL, IT'S RELATIVE. SO IT DOESN'T REALLY MATTER IF THEY PUBLISHED THE PAPER 30 YEARS AGO OR YESTERDAY. I GO BACK AND REFER TO THE BLOOD CONCENTRATION OF LEAD.

Q OKAY.

A SO, YOU KNOW, I MEAN, IT'S IMPORTANT. PERHAPS PEOPLE SAID 30 YEARS AGO THAT A LOW DOSE IS 30 MICROGRAMS PER DECILITER, BUT THAT'S NOT THE CRITERION BY WHICH YOU SHOULD JUDGE WHETHER THE PAPER IS SOUND ON OR NOT. WHAT YOU JUDGE THE PAPER BASED ON IS THE CAUSATION BETWEEN A CERTAIN BLOOD LEVEL OF LEAD AND THE GIVEN BEHAVIOR THAT YOU MIGHT BE INTERESTED IN OR ANYTHING ELSE.

Q OKAY.

SO TO BE CLEAR, GOING BACK TO YOUR METHODOLOGY AND OPINIONS YOU'RE OFFERING, YOUR METHODOLOGY DOES NOT INCLUDE -- I DO NOT SEE IN YOUR REPORT ANY STATEMENT IDENTIFYING ANY DOSE OF ANY METAL THAT IS REQUIRED TO

CAUSE ASD.

A NO, I DID NOT TALK ABOUT DOSE. I -- WHAT I DID IS I SPECIFICALLY DISCUSSED, TO THE BEST OF MY MEMORY, THE RELATIONSHIP BETWEEN THE DIFFERENT BIOMARKERS THAT WE TALKED ABOUT BEFORE AND ASD.

Q AND IT DOESN'T INCLUDE --

A NOT ABOUT THE EXTERNAL DOSE.

Q OKAY.

A I DON'T THINK I TALKED ABOUT THE EXTERNAL DOSE BECAUSE, AS I SAID BEFORE, IN MOST CASES, PROBABLY, THAT KIND OF INFORMATION IS NOT AVAILABLE.

Q AND IT DOESN'T INCLUDE -- YOUR METHODOLOGY DID NOT INCLUDE PUTTING INTO YOUR REPORT ANY OPINIONS ABOUT THE DURATION OF EXPOSURE TO ANY METAL THAT'S REQUIRED TO CAUSE ASD?

A WELL, THIS KIND OF INFORMATION, IT'S NOT POSSIBLE TO PUT IT INTO THE METHODOLOGY BECAUSE YOU'RE ASKING ME TO PUT INFORMATION THAT DOESN'T EXIST.

Q AND YOUR REPORT DIDN'T INCLUDE -- IT WASN'T PART OF YOUR METHODOLOGY TO IDENTIFY ANY SPECIFIC SET OF KNOWN UNDERLYING GENETIC TRAITS OR VULNERABILITIES THAT ARE NEEDED FOR METALS TO PLAY A ROLE IN ASD; CORRECT?

A IF THAT INFORMATION WAS AVAILABLE, I WOULD HAVE INCLUDED IT, BUT I DON'T THINK THERE'S ANY LITERATURE THAT DISCUSSES THE RELATIONSHIP BETWEEN DMT 1 AS A METAL TRANSPORTER, AND -- THE MERE ABSENCE OF THIS INFORMATION REFLECTS THE ABSENCE OF INFORMATION. IT JUST DOESN'T EXIST.

SO, YEAH, WITH DUE RESPECT IT'S NOT INCLUDED BECAUSE IT DOESN'T EXIST.

Q ALL RIGHT. OKAY.

AND YOUR REPORT DID NOT PARSE PRENATAL VERSUS POST-NATAL EXPOSURE IN TERMS OF IMPACT ON ASD; CORRECT?

A I THINK I DISCUSS THEM BOTH. I DID NOT DIFFERENTIATE BETWEEN THEM AND, YOU KNOW, TO A CERTAIN EXTENT, THERE'S NO REASON TO DIFFERENTIATE BETWEEN THEM BECAUSE, AS I NOTED IN MY REPORT, THE HUMAN BRAIN DEVELOPS FOR TWO YEARS POST-NATALLY.

Q AND --

A SO MANY OF THE PROCESSES THAT WE HAVE DISCUSSED IN TERMS OF, AGAIN, SYNAPTOGENESIS. I DON'T WANT TO GO BACK TO IT. THEY ARE NOT JUST INHERENT TO THE DEVELOPING BRAIN, THEY ARE ALSO INHERENT TO A CHILD, A TODDLER -- WELL, NOT A TODDLER -- TO A CHILD UP TO THE AGE OF TWO, NEONATE.

Q AND IN DEVELOPING YOUR METHODOLOGY FOR THE OPINIONS YOU'RE GIVING HERE, YOU DID NOT GO AND DO ANY RESEARCH IN THE AUTISM LITERATURE TO LEARN WHAT IS THE CURRENT STATE OF THINKING OR THE DEVELOPING SCIENCE IN TERMS OF WHEN CHILDREN FIRST BEGIN TO MANIFEST ASD?

A SO I THINK I'M FAMILIAR WITH THIS LITERATURE. PERHAPS IT'S NOT INCLUDED IN MY REPORT, BUT I'M FAMILIAR WITH REGRESSIVE AUTISM. I KNOW MANY KIDS ARE BORN NORMALLY.

Q SO --

A AND THEY DEVELOP NORMALLY, THEY MAY REGRESS AT

THE AGE OF TWO. AND I MEAN, I DID NOT PUT EVERYTHING IN MY REPORT, BUT AGAIN, IT'S PROBABLY -- I WOULD HAVE TO WRITE AN ENCYCLOPEDIA TO INCLUDE EVERYTHING THAT I KNOW.

Q JUST TO BE CLEAR, YOU DIDN'T INCLUDE ANY STUDIES THAT ARE TALKING ABOUT WHAT ASD EXPERTS UNDERSTAND TODAY ABOUT WHAT REGRESS -- WHAT SO-CALLED "REGRESSIVE AUTISM" IS; CORRECT?

A NO, I DID NOT.

Q OKAY.

AND YOU DIDN'T INCLUDE IN YOUR METHODOLOGY ANY REVIEW OF, FOR EXAMPLE, MRI WORK THAT'S BEING DONE ON THE BRAINS OF YOUNG CHILDREN TO LEARN MORE ABOUT WHEN ASD DEVELOPS; CORRECT?

A SO, AGAIN, YOU'RE REFERRING TO AREAS OF EXPERTISE THAT I WASN'T ASKED TO OPINE ON.

Q AND YOU --

A I WAS ASKED TO OPINE ON THE TOXICOLOGY OF METALS AND HOW THE EFFECTS THAT ARE SEEN IN EXPERIMENTAL ANIMALS CAN RELATE TO ASD. THE TASK IN FRONT OF ME WAS NOT TO REVIEW THE ASD LITERATURE.

Q OKAY.

A SO THERE ARE MANY THINGS THAT I DIDN'T DO.

Q AND YOUR REPORT DOES NOT IDENTIFY ANY METHOD THAT A SCIENTIST COULD REPRODUCE THAT, AT A GENERAL POPULATION, IDENTIFIES METAL INDUCED ASD FROM NON-METAL INDUCED ASD; CORRECT?

A AGAIN, I'M NOT FAMILIAR WITH THESE TYPES OF STUDIES. WHAT IS BEING STUDIED IS IF THERE'S A

RELATIONSHIP BETWEEN ASD -- YOU DON'T HAVE THE CHOICE OF TAKING INDIVIDUALS AND SAYING, YOU KNOW, I'M GOING TO EXPOSE YOU TO LEAD AND SEE WHETHER YOU'RE GOING TO HAVE, PROSPECTIVELY, ASD OR NOT.

SO, AS WE TALKED BEFORE, BEFORE EXPOSURE LEVELS ARE SOMETIMES VERY HARD TO DEFINE, AND YOU HAVE TO WORK WITH INTERNAL MEASURES OF LEAD OR MERCURY OR ARSENIC WHEN YOU TRY TO FIND THE CAUSALITY BETWEEN THOSE METALS AND ASD.

Q OKAY.

A AND AGAIN, YOU'RE ASKING ME TO DISTINGUISH AND DETAIL STUDIES THAT ARE NOT AMENABLE TO HUMAN EXPERIMENTATION, IN MY OPINION.

Q AND IN FAIRNESS, SIR, YOU DIDN'T LOOK TO SEE WHERE FUNDING IS GOING TODAY OR HOW MUCH FUNDING IS GOING TO DIFFERENT LANES OF RESEARCH IN ASD; CORRECT?

A NO, BECAUSE --

Q THAT WAS NOT PART OF YOUR CHARGE?

A ABSOLUTELY NOT. MY CHARGE WAS TO WORK ON METALS AND, AS I SAID BEFORE -- AND, I MEAN, PROBABLY I'VE BEEN FUNDED TO WORK ON METHYLMERCURY FOR -- CONTINUOUSLY FOR 29 YEARS. I BELIEVE THAT ESTABLISHES MY EXPERTISE IN AT LEAST MERCURY TOXICITY. AND MY MANGANESE GRANT IS FUNDED IN ITS 23RD YEAR CONSECUTIVELY, AND I WOULD LIKE TO THINK THAT ALL OF THESE ISSUES PROVIDE SOME MERIT TO THE TYPE OF RESEARCH THAT I DO.

AND MY RESEARCH IS FOCUSED -- I WANT TO

EMPHASIZE IT AGAIN. I'M NOT A CLINICIAN. I'M NOT AN ASD NEUROLOGIST. I'M NOT AN EPIDEMIOLOGIST. AND I'M OPINING ON THE RELATIONSHIP BETWEEN THE MECHANISMS THAT ARE INHERENT TO ASD AND THE RELATIONSHIP THAT WE SEE BETWEEN THEM IN HUMANS AND IN ANIMALS, THOSE THAT CAN BE MIMICKED IN ANIMALS.

SO I THINK YOU NEED TO RECOGNIZE THAT PEOPLE WORK TODAY IN SILOS. AND, YOU KNOW, I CAN'T PRETEND TO BE ONE FOR ALL. I CAN'T DO EVERYTHING. I HAVE MY AREA OF EXPERTISE AND IT'S JUST -- I DON'T THINK YOU ARE A CONSTITUTIONAL LAWYER, BUT YOU'RE A LAWYER. YOU CAN PROBABLY READ A PAPER ON CONSTITUTIONAL LAW AND YOU COULD PROBABLY OPINE TO A CERTAIN EXTENT.

AND THIS IS WHAT YOU'RE SEEING RIGHT HERE. I'M NOT A DIVORCE LAWYER, AND I'M NOT A -- OR, YOU KNOW, IN YOUR CASE, I GUESS. I HAVE TO OPINE ON THE AREAS THAT I KNOW. BUT IT DOESN'T PRECLUDE ME FROM BEING ABLE TO RENDER SOME OPINION AND ASSESS SOMETHING THAT'S NOT DIRECTLY WITHIN THE DOMAIN OF MY RESEARCH.

SO, I MEAN, I THINK I'M HONEST WITH YOU AS BEST AS I CAN BE.

Q SO YOU DO KNOW THAT POTENTIAL EXPOSURE TO METALS FOR ALL OF US ACTUALLY PROBABLY STARTS PRE-CONCEPTION.

I THINK WE HAD THIS CONVERSATION AT YOUR DEPOSITION.

WHAT MOM IS EXPOSED TO POTENTIALLY HAS IMPLICATIONS FOR BABY EVEN BEFORE CONCEPTION; RIGHT?

A I WOULD AGREE WITH THAT, YES.

Q OKAY.

BECAUSE LEAD IN MOM'S BONES COULD GET OUT AND COULD BECOME PART OF THE ENVIRONMENT IN UTERO.

AND THEN YOU CERTAINLY AGREE THAT ALL OF THE SOURCES OF METALS THAT MOM IS EXPOSED TO DURING PREGNANCY ARE ALSO A SOURCE OF EXPOSURE; CORRECT?

A WELL, THE MOTHER AND THE FETUS, THEY SHARE THE BLOODSTREAM. YES. SO WHAT'S IN THE MOTHER'S BLOOD --

Q OKAY.

A THERE MIGHT BE DIFFERENCES. IT DOESN'T APPLY THAT IT'S A RATIO OF ONE-TO-ONE, AND -- BUT LET ME GIVE YOU AN EXAMPLE BECAUSE, AGAIN, I THINK YOU QUALIFY ALL THE QUESTIONS BY SAYING "YOU AGREE." SO, YOU KNOW, I DON'T WANT TO SAY YES AND I DON'T WANT TO SAY NO, BECAUSE WE CANNOT GENERALIZE.

SO LET ME GIVE YOU MERCURY AS AN EXAMPLE.

THE BABY IS A SINK. THE GROWING FETUS IS A SINK FOR MERCURY, OKAY? HUMAN STUDIES. THE CONCENTRATION OF MERCURY THAT ACCUMULATES IN THE FETUS IS ABOUT TEN TIMES HIGHER THAN THE CONCENTRATION THAT ACCUMULATES IN THE MOTHER.

SO THE FACT THAT THE BLOOD LEVELS OF THE FETUS AND THE BLOOD LEVELS OF THE MOTHER ARE IDENTICAL DOES NOT NECESSARILY MEAN THAT THE BRAIN LEVELS OF MERCURY IN THE FETUS ARE GOING TO BE THE SAME AS THE BRAIN LEVELS OF THE MOTHER. AND THE REASON FOR THAT IS THAT THE FETAL BRAIN IS DEVELOPING. YOU DON'T HAVE A BLOOD-BRAIN

BARRIER. YOU DON'T HAVE MECHANISMS TO COMBAT THE OXIDATIVE STRESS. SO YOU WOULD EXPECT, ACTUALLY, TO SEE A LOT MORE DAMAGE IN THE FETAL BRAIN COMPARED TO THE MATERNAL BRAIN.

SO GENERALLY, YES. BUT I THINK ALL THESE QUESTIONS NEED TO BE QUALIFIED AND, YOU KNOW, I CAN GO ON. IT'S THE SAME STORY WITH LEAD. IT'S THE SAME STORY WITH ARSENIC.

AND PRINCIPALLY, YOU'RE CORRECT, BUT TO SAY THAT IT'S EXACTLY THE SAME EFFECT, THAT'S NOT CORRECT. THE LEVELS MIGHT BE THE SAME, BUT THE EFFECT MIGHT BE COMPLETELY DIFFERENT.

Q AND I WASN'T GETTING INTO A FACTOR EVEN LEVELS. I WAS JUST TRYING TO MARK OUR TIME PERIODS.

SO WE AGREE BEFORE PREGNANCY IS RELEVANT. WE AGREE PREGNANCY IS RELEVANT. THEN THE BABY IS BORN, AND THE BABY CAN BE EXPOSED TO SOME METALS THROUGH BREAST MILK, YOU AGREE WITH THAT; CORRECT?

A SOME MORE THAN OTHERS. YES, I AGREE.

Q YEAH.

AND -- OR IF THE BABY IS FED FORMULA FROM WATER SOURCES, DEPENDING UPON WHERE THEY LIVE, COULD BE A SOURCE; CORRECT?

A IF THEY GET WELL WATER THAT'S MIXED WITH THE BABY FORMULA, FOR SOME REASON AND LEAD LEVELS ARE VERY HIGH, YES, THAT'S POTENTIALLY --

Q OKAY.

A -- WILL INCREASE LEAD LEVELS. YES.

Q AND THEN, OF COURSE, THE BABY LIVES IN THE WORLD AND IS EXPOSED TO THE WORLD, JUST LIKE THE REST OF US, RIGHT, AND THE METALS IN THE WORLD.

AND SO, YOU EVEN DID A STUDY IN 2015, REMEMBER THAT, CALLED -- FIRST AUTHOR, I THINK, WAS JERING, AND YOU LOOKED AT MERCURY LEVELS IN THE NICU IN BABIES WHO WERE BORN PREMATURE.

DO YOU REMEMBER THAT?

A VAGUE RECOLLECTION. IT'S HARD TO REMEMBER, OUT OF 860 PAPERS, ONE THAT WAS PUBLISHED TEN YEARS AGO, BUT I'M HAPPY TO LOOK AT THE ABSTRACT.

Q OKAY.

SO CAN WE PULL UP 713.

A I THINK I REMEMBER. I THINK THERE'S -- YEAH. THESE ARE LEVELS OF MERCURY. MAYBE THEY ARE LEAKING FROM --

Q SO JUST TO REFRESH YOU --

A YEAH.

Q -- THIS WAS A STUDY WHERE YOU AND A COLLEAGUE, DR. JERING, LOOKED AT BABIES WHO WERE BORN VERY PREMATURE. THEY WERE IN THE NICU FOR ABOUT 80 DAYS, AND YOU NOTED, IF WE GO DOWN TO THE NEXT PAGE, PAGE 3, THAT THE MERCURY LEVELS ACTUALLY WENT UP WHILE THE BABIES WERE IN THE HOSPITAL.

A YEAH, BECAUSE --

Q RIGHT?

IN THAT SHORT PERIOD OF 80 DAYS, THEIR MERCURY LEVELS WENT UP, AND YOU LOOKED AT WHETHER THERE WAS A

DIFFERENCE BETWEEN BREAST MILK AND FORMULA. YOU REMEMBER THAT?

BUT THE IMPORTANT THING IS, YOU THEN FOLLOWED THEM FOR TWO YEARS AND YOU DIDN'T FIND ANY ADVERSE EFFECTS.

YOU REMEMBER THAT, DOCTOR?

A AND I TAKE YOUR WORD. I DON'T REMEMBER. BUT I BELIEVE WHAT YOU SAY, YES.

Q OKAY. ALL RIGHT. SO LET'S --

A LET ME JUST -- WELL, GO AHEAD. YOU HAVE QUESTIONS FOR ME. I SHOULDN'T INTERRUPT.

Q SO I JUST WANT TO TALK ABOUT ALL YOUR MECHANISMS. AND IF WE COULD --

A SO CAN I REFER TO THIS PAPER? WOULD IT BE REASONABLE IF I...

Q I HAVE A -- IF I HAVE A QUESTION ON IT, THEN YOU CAN CERTAINLY REFER TO IT. IF NOT, THEN YOUR COUNSEL IS FREE TO ASK YOU QUESTIONS.

A OKAY. BECAUSE AGAIN, THIS IS --

Q SO I'M GOING TO GO INTO MECHANISMS.

THE COURT: DR. ASCHNER, THE PROTOCOL IS THAT MR. WISNER, OR OTHER COUNSEL FOR THE PLAINTIFF, CAN ASK YOU QUESTIONS TO BRING OUT THE POINTS YOU WANT TO MAKE OR THAT YOU THINK ARE IMPORTANT, BUT RIGHT NOW SHE HAS THE FLOOR AND SHE'S MOSTLY JUST TRYING TO HELP THE COURT UNDERSTAND WHAT MIGHT BE IN OR NOT IN YOUR STUDY. SHE'S NOT REALLY TO CRITICIZE YOU AS A SCIENTIFIC. I DON'T THINK ANY OF US WOULD DO THAT.

MS. FREIWALD: YEAH.

THE COURT: SO, ANYWAY, GO AHEAD, COUNSEL.

MS. FREIWALD: OKAY. THANK YOU, YOUR HONOR.

Q SO FOR -- JUST TO ASSIST THE COURT, AS I READ YOUR REPORT, YOU HAD STATEMENTS ABOUT THE MECHANISM THAT YOU BELIEVE ARE ASSOCIATED WITH ARSENIC AT PAGE 22, WITH MERCURY AT PAGE 38, AND WITH LEAD AT PAGE 26 -- SORRY, THAT'S OUT OF ORDER. THERE WERE SOME OTHER PLACES WHERE HAD YOU SHORT SUMMARY STATEMENTS. BUT THAT WAS WHERE, I THINK YOU, LISTED MOST OF YOUR MECHANISMS.

AND IF WE CAN PUT UP SLIDE 9.

I TRIED TO SUMMARIZE THEM. IT WAS A LOT OF WORDS. SOME OF THEM ARE VERY LONG AND DON'T EXACTLY DRIP OFF OF THE TONGUE, BUT I BASICALLY TRIED TO CAPTURE, FOR EACH METAL, THAT YOU HAVE SOMEWHERE TEN, A DOZEN, DIFFERENT MECHANISMS THAT YOU PROPOSE, AND I JUST WANT TO BE CLEAR ABOUT A COUPLE THINGS.

FIRST OF ALL, NONE OF THESE MECHANISMS, WHICH I UNDERSTAND YOU SAY YOU CAN SEE IN YOUR LABORATORY WORK, THAT THESE METALS AFFECT THESE MECHANISMS. I JUST WANT TO BE CLEAR. NONE OF THESE MECHANISMS HAVE BEEN PROVEN AS CAUSAL FOR ASD?

A SO MANY OF THESE MECHANISMS HAVE BEEN PROVEN IN ANIMAL STUDIES AS PART OF THE BEHAVIORAL DEFICITS THAT THESE ANIMALS MANIFEST. AGAIN, THERE IS NO MEANS TO PERFORM THE TYPES OF STUDIES THAT YOU'RE SUGGESTING BECAUSE IT WOULD BE IMPOSSIBLE TO GET A HUMAN BRAIN OF A CHILD THAT HAS ASD AND THEN TRY TO MEASURE PKC OR, I

DON'T KNOW, ENZYME ACTIVITY. IT'S IMPOSSIBLE TO DO.

SO WE HAVE TO RELY ON ANIMAL STUDIES, AND IT HAS BEEN PROVEN IN ANIMAL STUDIES THAT MANY OF THESE, IF NOT ALL OF THESE, PERTUBATION IN ALL OF THESE MECHANISMS ARE ASSOCIATED WITH BEHAVIORAL DEFICITS THAT ARE COMORBID TO ASD.

Q SO WHAT YOU HAVE IS YOU HAVE THINGS THAT YOU SEE THE METALS DO IN ANIMALS OR CELL LINES, C. ELEGANS, THAT YOU SAY ARE LIKE BEHAVIORS THAT ARE LIKE WHAT HUMANS MIGHT MANIFEST THAT WOULD BE LIKE WHAT YOU SEE IN ASD, BUT YOU'RE NOT CLAIMING THAT ANY OF THESE MECHANISMS HAVE BEEN DEMONSTRATED AS WITHIN THE CAUSAL PATHWAY FOR ASD IN HUMAN BEINGS?

A SO THESE -- SOME OF THESE MECHANISMS MAY LEAD TO REDUCED BRAIN VOLUME, FOR EXAMPLE, THE GRAY MATTER. IT'S BEEN DONE IN ANIMALS. WHAT I CAN RELATE IT, IS TO THE STUDY THAT I SHOWED IN THE BEGINNING THAT SHOWS THE BRAIN VOLUME IN AUTISTIC KIDS IS DECREASED. I CANNOT TELL YOU THAT IT'S EXACTLY THE SAME MECHANISM, BUT I CAN DEDUCE FROM THE ANIMAL STUDIES THAT, MORE LIKELY THAN NOT, THE SAME MECHANISMS -- BECAUSE WE KNOW THAT ALL THESE SIGNALLING PATHWAYS ARE INHERENT TO ANIMALS AND HUMANS.

SO YOU SEE END POINT A -- END POINT A IN KIDS. YOU SEE END POINT A IN ANIMALS. YOU KNOW WHAT'S LEADING TO THIS END POINT A IN ANIMAL STUDIES. SINCE YOU CANNOT DO IT IN HUMAN BEINGS, YOU HAVE TO POSIT, AT LEAST RAISE THE HYPOTHESIS, THAT THE SAME MECHANISMS ARE INVOLVED.

AS FAR AS A LOT OF THESE THINGS, ACTUALLY, THERE IS DATA BECAUSE WE CAN MEASURE NEUROTRANSMITTERS, AND THERE HAVE BEEN OTHER STUDIES THAT HAVE LOOKED AT OTHER COMPONENTS OF THE -- OF WHAT YOU'RE SHOWING HERE THE OXIDATIVE STRESS, FOR EXAMPLE, FROM DECEASED CHILDREN. WE KNOW THAT SOME OF THESE ARE OPERATIVE IN HUMANS. I CANNOT POINT TO EACH OF THEM AS BEING CAUSATIVE, BUT A LOT OF THEM ARE INHERENT TO THE HUMAN BRAINS AS WELL.

TO SAY THAT WE HAVE NO INFORMATION ABOUT ANY OF THIS IN THE HUMAN BRAIN WOULD BE INCORRECT.

Q CAN YOU PULL UP PAGE 59 OF THE DEPOSITION, PLEASE?

SO LET'S JUST START TO PULL IT OUT ENOUGH THAT EVERYBODY CAN SEE IT. I'M GOING TO READ FROM MY HARD COPY.

"I'M ASKING YOU IF, OF THE RANGE OF POSSIBLE MECHANISMS, MECHANISMS THAT HAVE BEEN INVESTIGATED SO FAR, AND YOU'VE NAMED MANY, RIGHT, IF THERE IS ANY ONE OR MORE OF THEM THAT HAS BEEN AGREED BY SCIENTISTS AS A CAUSE OF ASD AS OPPOSED TO A POSSIBLE CAUSE?"

AND YOUR ANSWER WAS "ALL OF THESE ARE POSSIBLE CAUSES OF ASD, YES."

A THEY ARE, AND THEY HAVE BEEN SOME OF THEM, AND --

Q OKAY.

A -- WE CAN GO INTO MY LITERATURE THAT SHOWS THAT

GLUTAMIC LEVELS ARE ALTERED. WE CAN LOOK AT GLUTAMATE RECEPTORS. THERE'S ALL KINDS OF THEORIES ABOUT WHY ASD IS MANIFEST.

SO, AGAIN, I THINK YOU'RE PULLING ONE LINE OUT OF MY DEPOSITION, AND IT'S JUST NOT FAIR TO CHARACTERIZE MY ANSWER AS SUCH.

Q AND IN YOUR OWN WRITING, YOU'VE SAID THAT, AND IT'S -- AGAIN, TO -- TO JUST ECHO THE COURT, IT'S NOT ABOUT CASTING ANY ASPERSIONS ON THE SCIENCE THAT YOU DO, BUT I THINK IT'S IMPORTANT THAT THE COURT -- OUR JOB HERE TODAY IS TO MAKE IT CLEAR WHAT THE STATE OF THE SCIENCE IS, HOW ADVANCED IT IS, AND WHERE IT HASN'T YET GOTTEN.

AND SO, IF WE COULD PULL UP EXHIBIT 26, PDF PAGE 6.

THAT IS A PAPER THAT YOU'RE A CO-AUTHOR ON FROM 2021. THE FIRST AUTHOR IS ALUKO, AND IT'S LOOKING AT ONE OF YOUR MECHANISMS, MAPK SIGNALLING IN ASD, AND AT THE CONCLUSION -- AND YOU HAVE A LOT OF INTERESTING SCIENCE IN IT, BUT AT THE CONCLUSION YOU SAY, "THE

> RELATIONSHIP BETWEEN THESE METALS AND ASD AND METAL EXPOSURE REMAINS CONTROVERSIAL AND REQUIRES FUTURE STUDIES. FURTHER RESEARCH IS NEEDED TO PROVIDE ADDITIONAL EVIDENCE ON THE RELATIONSHIP BETWEEN METAL EXPOSURE AND ASD AND ELUCIDATE OF THE ROLE OF METAL INDUCED PERTURBED MAPK IN THE ETIOPATHOGENESIS OF ASD."

DID I READ THAT CORRECTLY?

A AGAIN, I WOULD QUALIFY THIS.

YES, FUTURE STUDIES ARE ALWAYS NEEDED BECAUSE THERE'S A LOT MORE TO LEARN AND THE RELATIONSHIP BETWEEN THESE METALS AND ASD AND METAL EXPOSURES REMAINS CONTROVERSIAL. I POINTED OUT THAT 20 PERCENT OF THE STUDIES DO NOT SHOW THAT THERE'S AN ASSOCIATION. SO I'M CONSISTENT THROUGHOUT ALL MY REPORTS, AND IT DOES REMAIN CONTROVERSIAL. YOU DO NOT AGREE WITH ME. SO NOT EVERYBODY'S ONBOARD AND -- BUT I THINK THE CRITICAL MASS IS THERE AND --

Q AND --

A -- AND FURTHER RESEARCH IS NEEDED. I SAID SO.

MAP KINASE IS ONLY ONE MECHANISM AND THIS IS THE SPECIFIC FOCUS OF THIS PAPER. SO I'M NOT TALKING ABOUT ANY OTHER RESEARCH IN THIS PAPER THAT HAS CORRELATED WITH ASD. THIS IS SPECIFIC TO MAP KINASE, WHICH IS ONLY ONE OF THE MECHANISMS THAT IS ASSOCIATED WITH ASD.

Q WELL, WE DON'T HAVE TIME TO GO --

A SO THERE IS REALLY NOTHING INCONSISTENT WITH MY OPINION.

Q OKAY. WE DON'T HAVE TIME TO GO THROUGH ALL THE MECHANISMS, BUT IF I JUST PULL UP ONE OTHER PAPER, 712, PDF 2.

THAT'S A PAPER THAT YOU WROTE IN 2019, SO ALSO VERY RECENTLY. AND THAT'S A PAPER THAT IS LOOKING AT MICRO RNA EXPRESSION AS A POTENTIAL MECHANISM, AND IF WE CAN GO TO THE CONCLUSION --

IAN, CAN WE GO TO THE CONCLUSION? NO. PAGE 7. SORRY.

SORRY ABOUT THAT.

SO IF YOU JUST LOOK AT THE MIDDLE OF THAT PARAGRAPH, THE FIRST PARAGRAPH, "SOME ASSOCIATIONS WITH KNOWN MECHANISMS OF METHYLMERCURY TOXICITY CAN BE MADE, BUT ARE STILL LIMITED WITHOUT FURTHER INVESTIGATION."

AND THEN, GOING DOWN TO THE END, "MOREOVER, IT WOULD BE DIFFICULT TO DETERMINE A MECHANISTIC FOUNDATION FROM WHOLE ORGANISM INVESTIGATIONS, ALTHOUGH INCONSISTENCIES BETWEEN INVITRO DATA AND HUMAN STUDIES COULD BE DISCERNED AT THIS POINT IF THERE'S LIMITED EVIDENCE TO VALIDATE CONCERNS FOR SPECIES EXTRAPOLATION."

AND THAT BASICALLY MEANS YOU HAVEN'T DONE THE WORK ACROSS SPECIES YET; RIGHT?

A NO. THAT BASICALLY MEANS THAT THIS STUDY FOCUSES ON EPIGENETICS. AND I CAN DESCRIBE WHAT EPIGENETICS.

EPI GENETICS INVOLVES --

Q WELL, SIR --

A WELL, I THINK YOU NEED TO KNOW THE CONTEXT.

Q I'M JUST ASKING MY QUESTION.

MS. FREIWALD: YOUR HONOR, IF I COULD ASK THE WITNESS TO ANSWER MY QUESTION.

THE COURT: YES. I JUST NEED TO HIM YOUR QUESTION, PLEASE. THANK YOU.

THE WITNESS: OKAY. SO THIS PAPER FOCUSES ON THE EPIGENETICS AND -- MA'AM, EPIGENETICS IS ONLY ONE OF THE MECHANISMS BY WHICH -- WHICH IS RELATED TO THE ONSET OF ASD OR ADHD. I'VE DESCRIBED MULTIPLE MECHANISMS BY WHICH -- THIS IS SPECIFICALLY FOCUSING ON EPIGENETICS.

SO WHEN I MAKE THESE CONCLUSIONS, I'M SAYING THAT THERE'S MORE STUDY TO BE DONE IN TERMS OF HOW THE EFFECTS OF METHYLMERCURY ON EPIGENETICS AND DNA METHODLATION RELATES TO THESE BEHAVIORAL EFFECTS. IT DOESN'T TALK ABOUT MAPK KINASE. IT DOESN'T TALK ABOUT SYNAPTOGENESIS WHERE WE HAVE A MUCH BETTER PICTURE.

SO, AGAIN, OUT OF 100 MECHANISMS, WHAT'S BEING DONE HERE IS TRYING TO CHERRY-PICK ONE MECHANISM, IGNORING THE OTHER 99 MECHANISMS THAT ARE FACILITATING THE DEVELOPMENT OF THIS DISEASE.

Q AND IN YOUR REPORT YOU ALSO NOTE, IN YOUR DISCUSSION OF THE KIM STUDY, YOUR REPORT AT PAGE 46, IF WE COULD PULL THAT UP, YOU CITE KIM, ET AL., WHICH TALKS ABOUT MECHANISMS THAT ARE NOT YET KNOWN.

"LEAD EXPOSURE MIGHT AFFECT THE NERVOUS SYSTEM BY HINDERING NEUROTRANSMITTER RELEASE. LEAD MIGHT INFLUENCE THE NERVOUS SYSTEM BY INCREASING THE RISK OF CONDITIONS, SUCH AS HYPERTENSION, ET CETERA. THE PRESENCE OF LEAD MIGHT AFFECT THE NERVOUS SYSTEM BY INHIBITING FORMATION OF KEY MOLECULES DURING THE MATURE DIFFERENTIATION OF GLIAL CELLS."

AND THEN, IT ALSO GOES ON -- AND I'M SORRY. I

DON'T HAVE -- CAN WE PULL UP KIM?

WE'LL GET UP KIM IN A MINUTE.

BUT IN THE INTEREST OF TIME, THOSE AUTHORS GO ON TO SAY SOMETHING YOU DON'T CITE, WHICH IS: "SEVERAL MECHANISMS HAVE BEEN SUGGESTED TO EXPLAIN THE EFFECTS OF LEAD EXPOSURE ON THE NERVOUS SYSTEM. HOWEVER" -- IF WE COULD GO -- JUMP TO THE PAGE I THINK WE MARKED.

"HOWEVER, NO SPECIFIC PATHWAY IS KNOWN TO LEAD TO AUTISTIC BEHAVIORS, THEREFORE, FURTHER MECHANISTIC STUDIES OF THIS SUBJECT ARE WARRANTED."

THERE WE ARE.

SO I CAN'T COVER EVERY SINGLE ONE OF THEM, BUT I DID ACCURATELY READ WHAT'S IN YOUR REPORT; CORRECT? AND WHAT IS IN THE KIM PAPER; CORRECT?

A THAT'S CORRECT. OMITTING THE --

Q OKAY.

A -- 80 PERCENT OF THE PAPER THAT SUPPORT MY OPINION.

Q AND SOME OF YOUR MECHANISMS ARE --

A INCLUDING KIM.

Q -- SOME OF YOUR MECHANISMS ARE -- IMPLICATE A WHOLE RANGE OF DISEASES FROM PARKINSON'S TO ALZHEIMER'S TO CANCER TO RENAL DISEASE, CARDIOVASCULAR DISEASE; CONNECT?

A THAT'S BECAUSE -- THAT'S BECAUSE CELLS DIE IN VERY SPECIFIC MANNERS. IT'S LIKE A FUNNEL. YOU CAN

HAVE MANY, MANY EFFECTS AT THE TOP OF THE FUNNEL. AS YOU GO DOWNSTREAM OF THAT FUNNEL, THE EXECUTING MECHANISM OF CELL DEATH ARE VERY LIMITED.

Q OKAY.

A SO IT'S NOT SURPRISING THAT CANCER CELLS HAVE THE SAME KIND OF -- SAME KIND OF PHENOTYPE THAT DYING BRAIN CELLS HAVE. IT'S EXACTLY THE SAME THING.

SO --

Q AND --

A -- IT'S VERY CONSISTENT WITH WHAT I REPORTED, YES.

Q AND MANY OF THE MECHANISMS OR CELL PATHWAYS YOU IDENTIFIED ARE FOUND THROUGHOUT THE BODY. MITOCHONDRIA ARE IN ALL THE CELLS. BILE IS UBIQUITOUS.

CORRECT?

A BUT THE BRAIN IS MUCH MORE SENSITIVE AND IT TENDS TO ACCUMULATE A LOT MORE OF THE METALS, SO THE EFFECTS WOULD BE MUCH GREATER IN THE BRAIN VERSUS THE KIDNEY, FOR EXAMPLE.

Q BUT THERE'S NO DISCUSSION IN YOUR REPORT ABOUT HOW THESE ARE UBIQUITOUS MECHANISMS; CORRECT?

A I DON'T REALLY UNDERSTAND WHY IT WOULD BE NECESSARY FOR ME TO DISCUSS THAT THERE'S MITOCHONDRIA IN THE KIDNEY. PARDON ME, COUNSEL, BUT --

Q AND OXIDATIVE -- OXIDATIVE STRESS, THAT'S ANOTHER ONE.

WE ALL HEAR ABOUT OXIDATIVE STRESS WITH EATING ANTIOXIDANTS; RIGHT?

A RIGHT. BUT YOU MIGHT NOT GET ANY OXIDATIVE STRESS IN THE KIDNEY IF NOT VERY MUCH OF THE MERCURY ACCUMULATES THERE, AND YOU MIGHT GET A LOT OF OXIDATIVE STRESS IN THE BRAIN IF THERE'S A LOT OF LEAD THERE.

SO, AGAIN, COMPARING APPLES AND ORANGES DOESN'T SERVE MY REPORT, AND I DON'T SEE ANY RATIONALE -- NO SCIENTIST WOULD ACTUALLY DISCUSS THOSE KINDS OF CONCEPTS BECAUSE THEY DON'T HAVE SCIENTIFIC MERIT.

Q AND I ASKED YOU IF IT WAS YOUR TESTIMONY THAT LEAD, ARSENIC, AND MERCURY CAUSE OXIDATIVE STRESS IN DIFFERENT AREAS OF THE BRAIN, AND YOU SAID IT WASN'T, THAT IT -- IT COULD BE ONE AREA, IT COULD BE ANOTHER AREA, ALL DEPENDS; RIGHT?

A SO I SAID BEFORE THAT THESE METALS TEND TO ACCUMULATE AT THE SAME AMOUNT, PRETTY MUCH, HETEROGENOUSLY THROUGHOUT BRAIN, AND THAT'S CORRECT. THE LEVEL OF OXIDATIVE STRESS MIGHT BE DIFFERENT IN DIFFERENT REGIONS BECAUSE THE DEFENSE MECHANISMS TO COMBAT OXIDATIVE STRESS ARE NOT ANALOGOUS THROUGHOUT THE BRAIN.

Q RIGHT.

A THERE ARE CERTAIN CELLS, LIKE ASTROCYTES, FOR EXAMPLE, GLIAL CELLS, WHICH HAVE VERY HIGH LEVELS OF GLUTATHIONE, WHICH IS VERY IMPORTANT IN COMBATING OXIDATIVE STRESS.

ON THE OTHER HAND, NEURONS HAVE MUCH LOWER LEVELS OF ANTIOXIDANTS, SUCH AS GLUTATHIONE. SO THAT'S CORRECT. THE FACT THAT A CELL HAS THE SAME AMOUNT OF

MERCURY DOES NOT NECESSARILY MEAN THAT THE END POINT IS GOING TO BE THE SAME. IT'S GOING TO DEPEND ON A LOT OF DIFFERENT PARAMETERS, AS WE DISCUSSED BEFORE.

SO DIFFERENT REGIONS MIGHT BE DIFFERENTIALLY SUSCEPTIBLE TO OXIDATIVE STRESS. I STAND BY MY COMMENT. YES.

Q RIGHT.

AND THAT WASN'T -- THAT WASN'T DISCUSSED IN YOUR REPORT, ALL THE DIFFERENT PROTECTIVE MECHANISMS OR DIFFERENT REGIONS OR -- RIGHT? THAT'S JUST NOT IN YOUR REPORT?

A I'M GLAD I COULD TALK ABOUT IT NOW.

Q OKAY.

JUST -- I WANT TO GET THROUGH TWO THINGS REALLY QUICKLY.

YOU DID TALK ABOUT THAT CECIL PAPER THAT COUNSEL PUT UP, THE ONE THAT TALKS ABOUT SMALLER BRAIN VOLUMES -- I DON'T KNOW IF IT WAS CITED IN THE RECORD -- DECREASED BRAIN VOLUME IN ADULTS WITH CHILDHOOD LEAD EXPOSURE.

DO YOU REMEMBER TALKING WITH YOUR COUNSEL?

A I DON'T REMEMBER THE CITE.

Q OKAY. DO WE HAVE THAT? CAN WE THROW THAT UP REAL QUICKLY?

I JUST WANT TO BE CLEAR. YOU'RE AWARE, SIR, THAT THIS IS A STUDY, A LONG-TERM STUDY, THAT LOOKED AT A COHORT OF KIDS IN CINCINNATI WHO WERE EXPOSED TO HIGH LEVELS OF LEAD; RIGHT? DO YOU KNOW THAT? AND THEY

FOLLOWED THEM TO ADULTHOOD; RIGHT?

A I MENTIONED THAT THE MRI WAS DONE IN THE ADULTS, YES.

Q RIGHT.

AND THESE WERE -- NONE OF THESE KIDS HAD ASD -- OR NONE OF THESE ADULTS HAD ASD; RIGHT?

A THEY DID HAVE A LOT OF COMORBIDITIES ACTUALLY THAT HAD BEEN ASSOCIATED WITH --

Q THIS WAS --

A -- WITH ASD.

Q THIS WAS NOT AN ASD STUDY, AND THEY WEREN'T DIAGNOSED WITH ASD; RIGHT?

A THEY WERE DIAGNOSED WITH A LOT OF THE COMORBIDITIES THAT ARE PART OF ASD.

Q WHERE IS THAT IN THE STUDY?

A YOU CAN LOOK AT THE NEUROPSYCHOLOGICAL ASSESSMENT THAT'S DESCRIBED IN THE STUDY.

Q IF WE -- IF --

A SOME OF THE SYMPTOMS -- AND THEY HAVE ACTUALLY ALSO CORRECTED FOR THE LEAD LEVELS, AND WHEN YOU CORRECT FOR THE LEAD LEVELS, THOSE -- SOME OF THESE COMORBIDITIES DISAPPEAR.

Q RIGHT.

A AS IT'S STATED IN THE CONCLUSION. YEAH. IT'S NOT A ASD STUDY, I FULLY AGREE --

Q IT'S NOT --

A -- BUT A LOT OF THE BEHAVIORS THAT THESE INDIVIDUALS HAVE ARE INHERENT TO INDIVIDUALS WITH ASD.

THAT'S ALL I'M SAYING.

Q IT'S A STUDY IN ADULTS NOT WITH ASD, AND IT WILL BECOME PART OF THE RECORD, AND HER HONOR CAN LOOK AT IT MORE CLOSELY.

YOU DIDN'T ACTUALLY LOOK AT WHETHER ASD IS ASSOCIATED WITH LARGER OR SMALLER BRAINS. THAT'S NOT IN YOUR REPORT EITHER.

A NO, BUT IT'S LIKE --

Q OKAY.

A -- I KNOW THE SKY IS BLUE DURING THE DAY, MOST OF THE TIME, IF THERE'S NO CLOUDS.

Q LAST -- LAST THING.

YOU'VE SAID THAT YOU SEPARATE YOURSELF FROM THIMEROSAL, BUT YOU ACTUALLY CITE, AND CAN WE PULL UP SLIDE 10? YOU CITE TO SEVERAL AUTHORS WHO ARE STILL TALKING ABOUT THIMEROSAL IN VACCINES AS SUPPORT FOR YOUR OPINIONS IN THIS CASE, SIR, AND I PULLED OUT JUST A FEW OF THEM. THEY ARE IN YOUR REPORT.

THE OLSAK PAPER, THESE DATED DOCUMENT.

"THE EARLY POST-NATAL THIMEROSAL ADMINISTRATION CAUSES LASTING BEHAVIORAL IMPAIRMENT PLUS ETHYLMERCURY EXPOSURE FROM THIMEROSAL IN SOME VACCINES HAS BEEN ASSOCIATED WITH AUTISM," AND BJORLAND.

AND I DON'T HAVE TIME TO READ THEM ALL.

AND, IN FACT, YOU'VE ALSO EVEN WRITTEN ABOUT THIMEROSAL AND IT BEING AN AREA TO INVESTIGATE AS A POTENTIAL CAUSE OF NEUROLOGICAL HARMS; CORRECT?

A SO AGAIN, I'D HAVE TO READ THIS PAPER AGAIN, BUT IT LOOKS LIKE MY PAPER. YES.

Q OKAY.

MS. FREIWALD: THAT'S ALL I HAVE THANK YOU, SIR.

THE WITNESS: THANK YOU, MA'AM.

MR. ESFANDIARY: YOUR HONOR, IF YOU LIKE A SHORT BREAK, I DON'T MIND GOING -- IT'S ON REDIRECT, A VERY SHORT REDIRECT. IT SHOULDN'T MAKE MORE THAN FOUR OR FIVE MINUTES.

THE COURT: WELL, WHY DON'T WE PROCEED AND THEN WE CAN RELEASE THE WITNESS.

MR. ESFANDIARY: VERY GOOD, YOUR HONOR. THANK YOU.

REDIRECT EXAMINATION

MR. ESFANDIARY:

Q DR. ASCHNER, THANK YOU FOR YOUR TIME THIS AFTERNOON. I'M GOING TO PICK UP WHERE COUNSEL LEFT OFF.

DOCTOR, ISN'T IT TRUE THAT YOU HAVE IN FACT TESTIFIED FOR THE US GOVERNMENT AND VACCINE MANUFACTURERS THAT THERE IS NO ASSOCIATION BETWEEN THIMEROSAL AND ASD?

A THAT'S CORRECT.

Q OKAY.

THAT WAS A LITIGATION AGAINST THE DEPARTMENT OF HUMAN AND -- HUMAN SERVICES; CORRECT?

A I THINK -- IT'S PROBABLY A LONG STORY, BUT I

THINK THE GOVERNMENT HAS SOME FUNDS FOR VACCINE LITIGATION THAT THEY'VE SET ASIDE. SO I BELIEVE IT WAS THE GOVERNMENT, NOT THE PHARMACEUTICAL COMPANIES, THAT WERE SUED. YES.

Q AND IS THERE A DIFFERENCE, DOCTOR, BETWEEN ETHYLMERCURY AND METHYLMERCURY IN TERMS OF THEIR ABILITY TO CAUSE ASD?

A APPLES AND ORANGES, YES. ETHYLMERCURY TENDS TO BEHAVE A LOT MORE LIKE INORGANIC MERCURY BECAUSE THE ALKALINE CHAIN, THE CH GROUPS THAT ARE ATTACHED TO THE MERCURY. IT'S MUCH LONGER THAN METHYL, WHICH IS ONE SINGLE CH3 GROUP. SO THAT TENDS TO BE CLEANED IN THE LIVER, AND ETHYLMERCURY DOES NOT GET AS READILY INTO THE BRAIN AS METHYLMERCURY.

Q IS THERE ANY EVIDENCE THAT ETHYLMERCURY CAN CAUSE ASD?

A I'M NOT FAMILIAR WITH THAT. I MEAN, THERE ARE SOME PAPERS THAT I HAVE CITED IN MY REPORTS, BUT, YOU KNOW, I FOCUSED ON MERCURY IN GENERAL, PRIMARILY METHYLMERCURY.

Q DOCTOR, COUNSEL SHOWED YOU THE ALUKO PAPER AND SHE SHOWED YOU A SNIPPET OF PART OF YOUR DISCUSSION IN THAT PAPER. AND THAT'S A PAPER THAT YOU AUTHORED, ISN'T THAT CORRECT, DOCTOR, THIS ONE?

A YES.

Q ALL RIGHT. VERY GOOD.

I'D LIKE TO JUST -- AND YOU WERE TALKING ABOUT THIS WHEN COUNSEL WAS ASKING YOU ABOUT WHETHER SOME OF

THESE MECHANISMS HAVE BEEN PROVEN IN ASD.

I'D JUST LIKE TO TAKE A LOOK AT WHAT YOU SAID ABOUT THIS SPECIFIC MECHANISM, MAPK PATHWAY, AND THE ABILITY FOR METALS TO IMPACT THIS.

I JUST WANT TO PULL IT UP RIGHT HERE.

IT SAYS RIGHT HERE, "THE DEVELOPING BRAIN IS VULNERABLE TO TOXIC SUBSTANCES AND METAL, SUCH AS LEAD, MERCURY, NICKEL, MANGANESE, AND OTHERS, HAVE BEEN PROVEN TO INDUCE DISTURBANCES IN THE MAPK SIGNALLING PATHWAY."

DO YOU SEE THAT, DOCTOR?

A YES.

Q FAIR TO SAY THAT YOU CONCLUDE RIGHT HERE IN YOUR OWN PAPER THAT THIS PATHWAY HAS BEEN PROVEN TO BE DISTURBED BY METALS; CORRECT?

A YES. I THINK WHAT COUNSEL ASKED ME ON THE DEFENDANTS' SIDE WAS, THOUGH, IF THAT'S BEEN PROVEN IN HUMANS, IF I RECALL CORRECTLY.

SO I THINK I MADE THE POINT THAT IT'S BEEN PROVEN IN ANIMAL STUDIES. I MEAN, I'M NOT AWARE OF ANY SPECIFIC STUDY WHERE KIDS WITH AUTISM HAVE BEEN TESTED FOR THEIR MAP KINASE ACTIVITY, AGAIN, BECAUSE I DON'T THINK THAT WOULD BE ETHICAL.

Q AND IT SAYS HERE "FURTHERMORE, WE HIGHLIGHT THE ROLE OF METAL TOXICITY IN THE DEVELOPMENT OF ASD AND HOW PERTURBED MAPK SIGNALLING MAY RESULT IN ASD."

DO YOU SEE THAT, DOCTOR?

A YES.

Q IS THAT WHAT YOU WERE GETTING AT WHEN YOU WERE TALKING ABOUT THE WAY IN WHICH THIS METAL -- THIS PATHWAY PLAYS A ROLE IN ASD?

A SO ALL THE MECHANISMS THAT I DISCUSSED, OR MOST OF THE MECHANISMS THAT I'VE DISCUSSED BEFORE IN TERMS OF SYNAPTOGENESIS, IN TERMS RELEASE OF NEUROTRANSMITTERS, THEY ALL REQUIRE NORMAL MAP KINASE SIGNALLING, AND OXIDATIVE STRESS, COMBATTING OXIDATIVE STRESS, REQUIRES MAP KINASE ACTIVITY.

SO WHILE YOU MAY NOT LOOK NECESSARILY AT MAP KINASE, YOU KNOW THAT THESE OTHER EFFECTS ARE INHERENT TO THE AUTISTIC BRAIN. SO I THINK ALL YOU HAVE TO DO IS CONNECT A WITH B, JUST, YOU KNOW, JUST PUT A STRAIGHT LINE BETWEEN TWO DOTS.

Q DOCTOR, AT THE END OF THIS -- I'M JUST GOING TO CLEAR THIS -- I'M JUST GOING TO ASK YOU A QUESTION.

WHEN IT'S UNETHICAL TO DO THESE KIND OF EXPERIMENTS ON HUMAN, IS IT STANDARD PRACTICE IN THE SCIENTIFIC COMMUNITY TO THEN USE ANIMAL MODELS INSTEAD?

A YES. I MEAN, A STUDY LIKE THIS WOULD NOT BE AUTHORIZED BY IRB, THE INSTITUTIONAL REVIEW BOARDS. IT WOULD BE RECOGNIZED OR AUTHORIZED BY WHAT WE CALL THE IAUCC, THE INSTITUTIONAL ANIMAL USE AND CARE COMMITTEE.

SO, YOU KNOW, WE CAN ARGUE ABOUT ANIMALS IN RESEARCH AND WHETHER IT'S ETHICAL OR NOT, BUT THE CLOSEST YOU CAN GET TO GATHERING SOME INFORMATION ABOUT WHATEVER MECHANISM YOU MIGHT BE INTERESTED IN IS

PURSUING ANIMAL STUDIES.

Q DOCTOR, COUNSEL SHOWED YOU A PART OF THE ALUKO STUDY WHERE YOU TALK ABOUT HOW THE UNDERLYING PATHOGENESIS OF ASD REMAINS CONTROVERSIAL. I WANT TO SHOW THE NEXT SENTENCE THAT THEY DIDN'T SHOW YOU, OKAY.

LET'S JUST GO DOWN TO PAGE 4. IT SAYS HERE, "HOWEVER, A COMPREHENSIVE REPORT ON THE RELATIONSHIP BETWEEN MERCURY AND AUTISM SHOWS THAT A VAST MAJORITY, 74 PERCENT OF SUCH STUDIES, INDICATES BOTH DIRECT AND INDIRECT ASSOCIATION BETWEEN MERCURY AND ASD ONSET."

DO YOU SEE THAT, DOCTOR?

A I DO.

Q AND THIS IS IN YOUR PUBLICATION THAT YOU, IN FACT, PUBLISHED BEFORE EVER GETTING INVOLVED IN THIS LITIGATION, CORRECT, THIS CONCLUSION?

A THAT'S CORRECT.

Q AND HOW --

A AND I WOULD ACTUALLY EXPAND AND SAY THAT THIS IS VERY CONSISTENT WITH WHAT I'VE DONE BY MYSELF COUNTING ALL THESE STUDIES AND DETERMINING THAT UPWARDS OF 80 PERCENT OF ALL THE STUDIES ARE SHOWING POSITIVE ASSOCIATION BETWEEN THOSE METALS AND ASD. SO I WOULD LIKE TO THINK THAT THE 80 PERCENT THAT SHOW THAT THERE'S A RELATIONSHIP ARE JUST AS SOUNDLY PERFORMED AS THE OTHER 20 PERCENT THAT DO NOT SHOW THE ASSOCIATION. I DON'T KNOW WHY WE WOULD PREFER ONE OVER THE OTHER.

Q THAT CONCLUSION THAT YOU PUT IN THAT PAPER,

THAT WAS SUBJECT TO PEER-REVIEW, CORRECT, BEFORE BEING PUBLISHED IN THE ACADEMIC FIELD?

A THE PAPER THAT YOU REFERRED TO?

Q YES.

A ALL MY -- I CAN'T SAY ALL, BUT 99 PERCENT OF ALL MY PAPERS ARE PEER-REVIEWED, YES.

MR. ESFANDIARY: OKAY. THANK YOU, DOCTOR, I HAVE NO FURTHER QUESTIONS.

THE WITNESS: THANK YOU.

THE COURT: MAY WE EXCUSE THE WITNESS THEN?

MR. ESFANDIARY: YES, WE MAY EXCUSE THE WITNESS. THANK YOU.

THE COURT: THANK YOU. THANKS, DR. ASCHNER. THANK YOU FOR YOUR PATIENCE.

THE WITNESS: THANK YOU, YOUR HONOR. THANK YOU, COUNSEL, FOR BOTH SIDES, AND HAVE FUN.

MS. FREIWALD: GOOD TO SEE YOU, DR. ASCHNER. THANK YOU.

THE WITNESS: THANK YOU. BYE BYE.

THE COURT: SO IS DR. RITZ ON OUR AGENDA NEXT?

MR. ESFANDIARY: YES, YOUR HONOR. SHE'LL BE -- SHE'LL TESTIFYING NEXT.

THE COURT: OKAY. SO WHY DON'T WE TAKE ABOUT A TEN-MINUTE BREAK, PLEASE?

MR. ESFANDIARY: VERY GOOD, YOUR HONOR. THANK YOU.

(RECESS)

THE COURT: DR. RITZ, WELCOME BACK. JUDGE

HOGUE SPEAKING. IT LOOKS LIKE OUR INTERROGATORS ARE READY TO GO. I THINK WE'RE STARTING WITH THE DEFENSE SIDE, MR. PETROSINELLI, RIGHT?

MR. PETROSINELLI: YES, YOUR HONOR. THANK YOU. I'LL NOT TO BE TOO MUCH OF AN INTERROGATOR. BUT I THINK, LIKE I TOLD YOU, YOUR HONOR, THE OTHER DAY, HOPEFULLY, WE CAN GET DONE WITHIN ABOUT 30 MINUTES AND THAT PUT ME AT ABOUT EVEN TIME WITH MR. WISNER. SO I'LL DO THE BEST I CAN.

CROSS EXAMINATION (RESUMED)

MR. PETROSINELLI:

Q DR. RITZ, GOOD AFTERNOON. SORRY WE COULDN'T FINISH YOU THE OTHER DAY, BUT THANK YOU FOR COMING BACK.

I JUST WANTED TO COVER REALLY TWO GENERAL TOPICS WITH YOU IN THE REMAINDER OF MY EXAMINATION. I WANTED TO ASK YOU ABOUT SOME EPIDEMIOLOGICAL CONCEPTS YOU COVERED IN YOUR DIRECT EXAMINATION AND HOW THEY RELATE TO YOUR BRADFORD HILL ANALYSIS, AND THEN I WANT TO ASK YOU ABOUT YOUR OPINION ON LEAD AND ADHD, OKAY?

A UM-HMM, YES.

Q LET'S PUT UP EXHIBIT 140, WHICH IS DEMONSTRATIVE THAT YOU USED DURING THE DIRECT EXAMINATION. THE LAST -- IT'S THE LAST PAGE OF THAT DEMONSTRATIVE, BECAUSE I THOUGHT IT WAS USEFUL TO TALK ABOUT SOME OF THESE CONCEPTS.

DO YOU REMEMBER TALKING ABOUT THIS WITH MR. WISNER?

A YES.
Q OKAY.
ONE OF THE THINGS YOU TALKED ABOUT WAS THE CONCEPT OF RELATIVE RISK IN EPIDEMIOLOGY.
AND ON THIS CHART, THE RELATIVE RISK NUMBER IN THE STUDIES IS THE THING THAT'S REPRESENTED BY THE RED CIRCLE; IS THAT CORRECT?
A NO. THE RELATIVE RISK IS ACTUALLY REPRESENTED IN ENTIRETY BY THE CIRCLE IN THESE WHISKERS. THE DOT IN THE MIDDLE IS REALLY ONLY THE POINT ESTIMATE, BUT IT'S REALLY IMPORTANT TO LOOK AT THE WHOLE DATA IN THE SENSE THAT, YOU KNOW, THE RELATIVE RISK COULD BE VARYING FROM THE UPPERMOST TO THE LOWER MOST, RISK -- RELATIVE RISK IN THIS WHOLE -- YEAH.
Q YEAH. THAT'S A GREAT CLARIFICATION. THANK YOU.
AND SO, YOU TESTIFIED, AND I JUST WANT TO MAKE SURE THIS IS RIGHT, THAT THE RELATIVE RISK IS THE RISK OF A DISEASE IN AN EXPOSED POPULATION DIVIDED BY THE RISK OF A DISEASE IN AN UNEXPOSED POPULATION; CORRECT?
A THAT'S CORRECT.
Q AND SO, JUST -- IF YOU LOOK AT THESE TWO -- THE TOP TWO STUDIES HERE THAT ARE IN THIS -- JUST -- I UNDERSTAND THESE ARE JUST HYPOTHETICAL STUDIES, BUT IT LOOKS LIKE THE POINT ESTIMATE IS ABOUT 1.3 OR SOMETHING LIKE THAT; IS THAT RIGHT?
A YES.
Q AND SO, THAT WOULD MEAN THAT THE RELATIVE RISK,

THAT IS THE RISK IN THE EXPOSED POPULATION DIVIDED BY THE RISK IN THE UNEXPOSED POPULATION, IN THESE STUDIES, IS 1.3; CORRECT?

A YES.

Q ALL RIGHT.

LET ME ASK YOU TO LOOK AT A QUOTE FROM THE REFERENCE MANUAL ON SCIENTIFIC EVIDENCE ABOUT THE STRENGTH OF ASSOCIATION BRADFORD HILL FACTOR.

IT'S EXHIBIT 677, WHICH WILL COME UP IN A SECOND. PAGE 602.

A YES, I SEE THAT.

Q OKAY. HOLD ON ONE SECOND. OKAY. WE'LL BLOW THIS UP A LITTLE BIT, THIS IS SECTION B.

JUST BEFORE I ASK YOU ABOUT THIS, STRENGTH OF ASSOCIATION IS INDEED ONE OF THE BRADFORD HILL FACTORS; CORRECT?

A YES.

Q AND THIS -- AND THE REFERENCE MANUAL, WHEN THEY DESCRIBE STRENGTH OF ASSOCIATION, THEY SAY, "THE RELATIVE RISK IS ONE THE CORNERSTONES FOR CAUSAL INFERENCES. RELATIVE RISK MEASURES THE STRENGTH OF THE ASSOCIATION. THE HIGHER THE RELATIVE RISK, THE GREATER THE LIKELIHOOD THAT THE RELATIONSHIP IS CAUSAL."

DO YOU SEE THAT?

A YES, I DO.

Q OKAY. LET ME -- LET'S LOOK AT YOUR STRENGTH OF ASSOCIATION ANALYSIS FOR LEAD AND ASD IN YOUR REPORT,

WHICH IS EXHIBIT 4 AT PAGE 30.

OKAY. DOCTOR, WE'RE LOOKING AT THE SECTION OF YOUR REPORT THAT IS ON LEAD AND ASD, AND YOUR BRADFORD HILL CRITERIA EVALUATION, AND THE FIRST ONE THAT WAS LISTED IS THE STRENGTH OF THE ASSOCIATION.

DO YOU SEE THAT?

A YES.

Q ALL RIGHT.

AND AM I CORRECT THAT YOU DID NOT PROVIDE A RELATIVE RISK NUMBER, A RISK RATIO, THAT RATIO WE JUST TALKED ABOUT, FOR LEAD AND ASD; CORRECT?

A THAT'S CORRECT. MAY I EXPLAIN WHY?

Q WELL, I WAS GOING TO ASK YOU WHY.

YOU SAY THERE THAT MOST STUDIES DID NOT ESTIMATE EFFECT SIZES.

DO YOU SEE THAT?

A YES.

Q OKAY. AND THAT MEANS THAT MOST OF THE STUDIES ON LEAD AND ASD THAT YOU RELIED ON DID NOT CALCULATE AND PUBLISH IN THE ARTICLE A RELATIVE RISK; CORRECT?

A THAT'S CORRECT. BUT YOU CAN DO THAT IN -- YOU KNOW, YOU CAN DO THAT FROM THE DATA THAT THEY GIVE YOU WITH THE MEANS.

Q RIGHT.

BUT IN THE -- IN YOUR REPORT YOU DID NOT CALCULATE -- WE'RE LOOKING AT IT HERE. THERE IS NO RELATIVE RISK NUMBER; TRUE?

A IN THIS -- IN THIS ONE NOTE, NO.

Q LET'S GO BACK TO EXHIBIT 140, THAT DIAGRAM THAT WE WERE LOOKING AT. I WANTED TO ASK YOU ONE MORE THING ABOUT IT.

YOU MENTIONED THE WHISKERS. I LOVE THAT PHRASE THAT YOU USED. THOSE ARE THE CONFIDENCE INTERVALS AROUND THAT RED CIRCLE, THE POINT ESTIMATE, THOSE ARE CALLED CONFIDENCE INTERVALS; CORRECT?

A YES.

Q AND USUALLY IN EPIDEMIOLOGY, THEY USE 95 PERCENT -- I THINK YOU TESTIFIED ON YOUR DIRECT EXAMINATION, USUALLY THEY USE 95 PERCENT CONFIDENCE INTERVALS; TRUE?

A YEAH. THAT'S A WAY THAT MOST STUDIES USE, BUT YOU SEE SOME STUDIES THAT USE 90 PERCENT CONFIDENCE INTERVALS, BUT MOSTLY IT'S 95, YES.

Q OKAY.

A SOME USE 99.

Q YEAH.

A SO --

Q YEAH, I THINK YOU TESTIFIED, WHICH I FOUND HELPFUL TO UNDERSTAND THAT, I THINK YOU TESTIFIED THAT WHAT THAT MEANT IS, IF YOU RAN -- LIKE, IF WE LOOK AT THESE TWO STUDIES, THE TOP TWO LET'S SAY, IF YOU RAN THE EXPERIMENT, OR THE RESEARCH, A HUNDRED TIMES, 95 OF THOSE TIMES, THE RELATIVE RISK WOULD BE BETWEEN THE LOWER AND UPPER CONFIDENCE INTERVAL; TRUE?

A THAT'S CORRECT.

Q AND IF ANY PART OF THE CONFIDENCE INTERVAL,

LIKE WE SEE HERE IN THIS DEMONSTRATIVE YOU USED, IF ANY OF THE PART OF THE CONFIDENCE INTERVAL CROSSES ONE, IN EPIDEMIOLOGY WHAT THAT MEANS IS, THE EPIDEMIOLOGIST WOULD SAY IT'S NOT STATISTICALLY SIGNIFICANT; CORRECT?

A AT THE POINT PO -- P VALUE OF 0.05. SO THE 5 PERCENT CONFIDENCE LIMIT, BUT THAT'S -- YOU KNOW, THAT'S VERY ARBITRARY. I MEAN, THAT'S A DECISION-MAKING TOOL. IT'S NOT AN INFORMATION UNDERSTANDING TOOL.

IF YOU HAVE TO DO A YES/NO -- GIVE A YES/NO ANSWER, STATISTICAL SIGNIFICANT HELPS YOU SAY YES/NO, BUT IT DOESN'T HELP YOU UNDERSTAND THE DATA VERY WELL.

Q I WAS JUST -- SO YOU'VE ANTICIPATED MY NEXT QUESTION, WHICH IS: SO IF WE LOOK AT THESE TWO STUDIES, AGAIN IN THIS GRAPH THAT YOU USED, THE TOP TWO --

A UM-HMM.

Q -- YOU WOULD SAY THE STUDY NUMBER -- I THINK YOU DID SAY STUDY NUMBER 1 AND STUDY NUMBER 2 WOULD BE VIEWED AS NOT STATISTICALLY SIGNIFICANT; CORRECT?

A THAT'S CORRECT.

Q AND STUDY NUMBER 3 ACTUALLY WOULD BE VIEWED AS STATISTICALLY SIGNIFICANT BECAUSE THE CONFIDENCE INTERVALS DO NOT CROSS 1; CORRECT?

A CORRECT.

Q ALL RIGHT. AND THE TOP TWO, THE ONES THAT AREN'T STATISTICALLY SIGNIFICANT, EVEN THOUGH THAT POINT ESTIMATE IS ABOUT 1.3, IS ABOVE 1, THAT WOULD MEAN THAT ONE, FROM LOOKING AT THOSE RESULTS, ONE CAN'T EXCLUDE THAT THERE'S NO ASSOCIATION; TRUE?

A THAT'S CORRECT. ONE CAN NEVER REALLY EXCLUDE THAT, BUT WHAT YOU CAN SAY IS THAT BOTH STUDIES ARE NOT LARGE ENOUGH, DON'T HAVE ENOUGH SAMPLE SIZE, TO SHORTEN THE WHISKERS.

IF BOTH STUDIES WERE LARGER AND, YOU KNOW, THE POINT ESTIMATE REMAINS WHERE IT IS, THE WHISKERS WOULD SHRINK, AND EVENTUALLY, THEY WOULD LOOK LIKE STUDY 3, IF THAT POINT ESTIMATE IS THE TRUE ESTIMATE.

Q RIGHT.

A SO IT DEPENDS ON THE STRENGTHS OF THE ASSOCIATION AND THE SIZE OF THE STUDY IN TERMS OF STATISTICAL POWER WHETHER WE CAN ACTUALLY SHOW THAT A 1.3 IS STATISTICALLY SIGNIFICANT WITH THIS CRITERIA OF, YOU KNOW, P VALUE LESS THAN .05.

Q AND IN YOUR DEPOSITION YOU MAY REMEMBER, WHEN I ASKED YOU WHAT ROLE STATISTICAL SIGNIFICANCE PLAYED AS YOU EVALUATED THE STUDIES IN TERMS OF THE STRENGTH OF ASSOCIATION BRADFORD HILL CRITERIA, YOU TOLD ME IT PLAYED VERY LITTLE ROLE.

DO YOU REMEMBER THAT?

A WELL, I DO NOT LOOK AT STATISTICAL SIGNIFICANCE. I LOOK AT THE DATA AS A WHOLE. SO I WOULD LOOK AT STUDY 1 AND 2 IN TERMS OF WHAT'S THE STRENGTHS OF THE ASSOCIATION, MEANING WHAT IS THE POINT ESTIMATE, BUT I WOULD, OF COURSE, CONSIDERED WHETHER THESE WHISKERS INCLUDE THE NULL OR NOT.

HOWEVER, IF YOU GIVE ME 20 STUDIES LIKE STUDY 1 AND 2, AND THEY ALL INDIVIDUALLY HAVE BEEN TOO SMALL TO

SHOW STATISTICAL SIGNIFICANCE, IT WOULD, HOWEVER, TELL ME THAT IF I RAN A META ANALYSIS, THERE IS A GOOD CHANCE THAT THE ESTIMATES ARE ABOVE 1 AND I CAN RUN THE META ANALYSIS, AND THEN I HAVE MORE INFORMATION. I HAVE MORE SAMPLE SIZE. I HAVE MORE DATA, AND THOSE WHISKERS WOULD JUST REALLY SHRINK SO THAT YOU HAVE YOUR STATISTICAL SIGNIFICANCE. THAT'S WHY WE DO META ANALYSIS.

Q LET ME -- LET'S LOOK AT YOUR DEPOSITION. IT'S PAGE 113 OF YOUR DEPOSITION TESTIMONY. THIS IS EXHIBIT 7, I BELIEVE.

AND ASK YOU TO LOOK AT THE QUESTION THAT STARTS AT LINE 18.

I ASKED YOU, "WHEN YOU'RE EVALUATING THE STRENGTH OF ASSOCIATION FACTOR, WHAT ROLE DOES STATISTICAL SIGNIFICANCE PLAY?"

AND YOU SAID, "VERY LITTLE."

DO YOU SEE THAT?

A YES.

Q AND THEN I ASKED YOU WHY.

AND YOU SAID WHAT YOU SAID THERE, INCLUDING THAT, "STATISTICAL SIGNIFICANCE IS NOTHING BUT ABUSED IN MEDICAL LITERATURE AND IN THE WAY THAT PEOPLE THINK ABOUT EVIDENCE AND DATA FROM SCIENTIFIC STUDIES."

DO YOU SEE THAT?

A YES. AND I SAID A LOT MORE ABOUT IT AS WELL.

Q LET ME LOOK -- LET'S LOOK AT A COUPLE OF YOUR STUDIES THAT RELATE TO AUTISM AND OTHER CHILDHOOD

CONDITIONS.

I WANT TO ASK YOU TO LOOK AT A STUDY WHERE THE LEAD AUTHOR'S NAME IS VON EHRENSTEIN FROM 2014.

DO YOU REMEMBER THAT STUDY?

A YOU NEED TO SHOW IT TO ME BECAUSE THAT'S A JUNIOR COLLEAGUE OF MINE.

Q OKAY.

A AND HE TAKES FULL RESPONSIBILITY FOR THE WRITING THAT SHE DOES.

Q THIS IS EXHIBIT -- WELL, WE CAN LOOK AT THE STUDY FIRST, EXHIBIT 7 -- LET'S GO TO EXHIBIT 704 -- THAT'S 703. LET'S DO THIS. SO THIS IS -- IT'S ENTITLED, "IN UTERO EXPOSURE TO TOXIC AIR POLLUTANTS AND RISK OF CHILDHOOD AUTISM." THE FIRST AUTHOR LISTED IS VON EHRENSTEIN.

DO YOU SEE THAT?

A YES.

Q AND YOU WERE -- YOU WERE THE SENIOR AUTHOR ON THIS STUDY, WERE YOU NOT?

A YES, BECAUSE I ASSEMBLED THE DATA. HOWEVER, AS I SAID, THIS IS NOT A POST-DOC. THIS IS ACTUALLY A PROFESSOR OF EPIDEMIOLOGY. SO THE FIRST AUTHOR IN THIS CASE IS A COLLEAGUE TAKING FULL RESPONSIBILITY FOR ITS CONTENT.

Q OKAY.

AND THIS STUDY YOU -- WHAT YOU AND YOUR COAUTHORS DID WAS -- WE CAN SEE FROM THE TITLE, YOU LOOKED AT IN UTERO EXPOSURE TO AIR POLLUTANTS AND HOW

THAT RELATED TO RISK OF AUTISM; TRUE?

A YES.

Q AND WHAT YOU DID WAS, YOU STUDIED MOTHERS WHO, WHEN THEY WERE PREGNANT, LIVED NEAR BUFFER ZONES AROUND AIR POLLUTANT MONITORING STATIONS, I THINK, IN LOS ANGELES; IS THAT RIGHT?

A THAT'S CORRECT.

Q AND YOU EXAMINED A NUMBER OF DIFFERENT AIR POLLUTANTS; TRUE?

A YES, ALL THE ONES THAT WERE MONITORED AT THE TIME.

Q AND YOU CONCLUDED THAT SOME OF THE AIR POLLUTANTS SHOWED AN INCREASED RISK OF AUTISM IN THE CHILDREN THAT WERE BORN TO THOSE MOTHERS AND SOME OF THEM DID NOT.

DO YOU REMEMBER THAT?

A YEAH, PROBABLY.

Q OKAY. LET'S LOOK AT EXHIBIT 704, WHICH IS JUST A CALL OUT FROM THIS STUDY.

AND LET'S -- ONE OF THE METALS -- ONE OF THE POLLUTANTS YOU STUDIED WAS COPPER.

DO YOU REMEMBER THAT?

A NO.

Q OKAY.

LET'S LOOK AT -- THIS IS FROM TABLE 2 AND THIS SHOWS, FOR COPPER, THE ODDS RATIO OF DEVELOPING OF A LINK BETWEEN THE COPPER AND AUTISM IN THE CHILDREN WAS 1.09 WITH A CONFIDENCE INTERVAL 1.02 TO 1.16.

DO YOU SEE THAT?

A YES.

Q AND THAT MEANS THAT'S A STATISTICALLY SIGNIFICANT POSITIVE ASSOCIATION; TRUE?

A YES, THAT'S WHAT YOU WOULD CALL THIS.

Q BUT THEN AT 3 --

A THERE'S A P VALUE OF .05 AS A CRITERIA.

Q RIGHT.

A UM-HMM.

Q RIGHT.

AND THEN -- BUT AT 3.35 KILOMETERS, THE ODDS RATIO WAS ABOUT THE SAME, 1.05, BUT THE 95 PERCENT CONFIDENCE INTERVALS WERE .94 TO 1.18.

SO THAT'S NOT STATISTICALLY SIGNIFICANT; TRUE?

A NOT ACCORDING TO THIS CRITERION.

AND IF I MAY POINT OUT, THE PROBLEM IS THAT, THE CLOSER YOU GO INTO THE AIR MONITORING STATION, THE LESS KIDS YOU HAVE. SO YOU SEE THAT THE SAMPLE SIZE HERE REDUCED BY HALF. AND WHEN THE SAMPLE SIZE REDUCES BY HALF, THEN THIS IS WHAT YOU WOULD EXPECT TO HAPPEN, EVEN IF THE ODDS RATIO STAYED EXACTLY THE SAME.

Q EXACTLY.

AND LET'S LOOK AT THE CONCLUSION THAT YOU AND YOUR CO-AUTHORS DREW ABOUT THIS DATA.

"AMONG POLLUTANTS NOT LOADING ON A FACTOR, TRICHLOROETHYLENE," WHICH IS ANOTHER THING THAT WAS STUDIED, "AND COPPER, SLIGHTLY INCREASED RISKS IN THE 5 KILOMETER, BUT NOT IN THE 3.5

KILOMETER BUFFER."

DO YOU SEE THAT?

A YES.

Q AND SO WHEN -- AND FOR THE STATISTICALLY SIGNIFICANT RESULT, THAT IS THE 5 KILOMETER BUFFER, YOU AND YOUR CO-AUTHORS CONCLUDED THERE WAS A SLIGHT INCREASED RISK, BUT WITH THE NON-STATISTICALLY SIGNIFICANT RESULT IN THE 3.5 KILOMETER BUFFER, YOU DIDN'T CONCLUDE THERE WAS AN INCREASED RISK; CORRECT?

A IT WASN'T ME. THIS WAS THE FIRST AUTHOR WHO IS A ASSOCIATE PROFESSOR OF EPIDEMIOLOGY, AND I CANNOT CORRECT EVERY SINGLE WORD SHE WRITES BECAUSE SHE'S A COLLEAGUE. WITH A STUDENT, I WOULD HAVE CORRECTED THIS.

Q DR. RITZ, YOU'RE LISTED AS AN AUTHOR ON THE PUBLICATION. YOU REVIEWED THE MANUSCRIPT BEFORE IT WAS SUBMITTED TO THE JOURNAL; DID YOU NOT?

A YES, OF COURSE.

Q OKAY.

AND LET'S LOOK AT ONE MORE OF YOUR STUDIES.

THIS IS A STUDY, ACTUALLY, THAT WAS PUBLISHED IN THE LAST TWO WEEKS. IT'S THE -- LEAD AUTHOR, THE FIRST LISTED AUTHOR, IS NAMED YEH, Y-E-H. I'M NOT SURE EXACTLY HOW TO PRONOUNCE THAT. DO YOU KNOW HOW TO PRONOUNCE THAT NAME?

A NO, BECAUSE SHE'S NOT MY STUDENT.

Q OKAY.

AND THIS IS A PUBLICATION IN CANCER EPIDEMIOLOGY 2022 THAT JUST CAME OUT A COUPLE OF WEEKS

AGO, AND YOU'RE ONE OF THE AUTHORS ON IT.

DO YOU SEE THAT?

A I'M A CO-AUTHOR, YES.

Q AND IN THIS STUDY, YOU AND YOUR CO-AUTHORS EXAMINED THE RISK OF, AS IT SAYS, CHILDHOOD BRAIN TUMORS ASSOCIATED WITH DELIVERY INTERVENTIONS, SPECIFICALLY FORCEPS DELIVERY AND VACUUM DELIVERY.

DO YOU REMEMBER THAT?

A YES.

Q OKAY.

AND IF WE COULD LOOK AT THE RESULTS OF THE STUDY, WHICH IS A CALL OUT ON EXHIBIT 706.

LET'S LOOK AT THE RESULTS.

THE CONCLUSION WAS, "WE DID NOT OBSERVE AN OVERALL INCREASE IN ALL CENTRAL NERVOUS SYSTEM TUMORS COMBINED WITH EITHER VACUUM DELIVERY OR FORCEPS DELIVERY."

DO YOU SEE THAT?

A YES.

Q AND LOOKING AT THE FORCEPS DELIVERY, THE ODDS RATIO IS ACTUALLY 1.26, BUT THE CONFIDENCE INTERVAL .78 TO 2.03.

DO YOU SEE THAT?

A YES.

Q AND SO THAT'S NOT A -- ALTHOUGH THE CONFIDENCE INTERVAL -- I MEAN, ALTHOUGH THE ODDS RATIO WOULD SUGGEST A 26 PERCENT INCREASED RISK, THAT'S NOT STATISTICALLY SIGNIFICANT; CORRECT?

A NOT ACCORDING TO THE .05 CRITERIA, YES.

Q AND SO YOU AND YOUR CO-AUTHORS CONCLUDED THAT THERE WAS -- YOU DID NOT OBSERVE AN OVERALL INCREASE IN TUMORS FOR WITH FORCEPS DELIVERY; TRUE?

A THAT'S WHAT MY COLLEAGUES CONCLUDED.

AGAIN, THIS IS NOT A PAPER I WROTE OR WAS REALLY THE FINAL CALL ON. THIS WAS A STUDENT IN DENMARK WHO WAS SUPERVISED BY DR. HECK, WHO WAS AN ASSOCIATE PROFESSOR AND NOW THE DEAN FOR RESEARCH AT ANOTHER SCHOOL, I DIDN'T EVEN SEE THE FINAL MANUSCRIPT. SO IT'S NOT MY WORDING.

Q LET'S LOOK AT -- LET'S GO BACK TO THE ACTUAL STUDY, EXHIBIT 705. LET'S GO TO THE FIFTH PAGE OF THE PDF. DO YOU SEE THERE'S A PARAGRAPH AT THE BOTTOM, CREDIT AUTHORSHIP CONTRIBUTION STATEMENT.

A YES.

Q DO YOU SEE THAT?

A YES.

Q AN LET'S SEE WHAT DID YOU ON THE STUDY.

DO YOU SEE IT SAYS, "BEATE RITZ WRITING REVIEW AND EDITING."

DO YOU SEE THAT?

A CORRECT, YES.

Q AND DID YOU, IN FACT, REVIEW AND EDIT THIS MANUSCRIPT?

A YES. BUT NOT THE FINAL FINAL, BECAUSE THAT'S THE JOB OF THE LAST AUTHOR WHO IS RESPONSIBLE FOR THE STUDENT, AND THAT'S DR. HECK. OF COURSE, I WRITE AND

REVIEW WHILE WE WRITE THIS. I ALSO REVIEW THE RESULTS WITH EVERYONE, BUT THE FINAL SAY ON THE WORDING IN THIS CASE IS DR. HECK.

Q OKAY. LET'S TAKE THAT DOWN.

THANK YOU, DOCTOR.

LET ME ASK YOU, DOCTOR, BUT MOVE TO MY SECOND TOPIC, YOUR OPINION ON LEAD AND ADHD.

YOU -- WITH RESPECT TO THE STUDIES ON LEAD AND ADHD, DO YOU AGREE WITH ME THAT MOST OF THE STUDIES DO NOT INVOLVE CHILDREN WITH THE SPECIFIC CLINICAL DIAGNOSIS OF ADHD?

A WELL, THERE ARE LOTS OF COHORT STUDIES DIFFERENT FROM THE AUTISM FIELD, AND GENERALLY, IT IS HARDER IN COHORT STUDY TO GET THE NUMBERS IF YOU HAVE A CLINICAL DEFINED SYNDROME. SO WHAT THESE STUDIES ACTUALLY DO IS THEY USE TOOLS, QUESTIONNAIRES, ASK TEACHERS, ASK PARENTS, TO ASSESS SYMPTOMOLOGY, BUT THAT'S PERFECTLY FINE TO GET A -- TO A DIAGNOSIS OF ADHD.

Q RIGHT.

THEY USE THESE QUESTIONNAIRES AND SO ON, AS YOU SAY, FROM TEACHERS AND PARENTS, BUT IN MOST OF THE STUDIES, THERE'S NO DOCTOR WHO HAS CLINICALLY DIAGNOSED THE CHILDREN WITH ADHD; CORRECT?

A WELL, THESE INSTRUMENTS HAVE BEEN SHOWN TO HAVE VERY HIGH VALIDITY WHEN YOU COMPARE THEM TO CLINICAL ASSESSMENTS. YES, YOU CANNOT HAVE A CLINICIAN ASSESS 10,000 CHILDREN OR 5,000 CHILDREN. THE WAY YOU DO IT IS

YOU ASK THE PEOPLE WHO ARE AROUND THESE CHILDREN TO REPORT THEIR BEHAVIORS.

BASICALLY, IT'S THE SAME AS WHAT THE PARENTS WOULD BE DOING IN A CLINICIAN'S OFFICE. THEY COME AND THE CLINICIAN AND THE NURSE ASK ABOUT THESE KIND OF BEHAVIORS, AND IT IS THAT KIND AMERISTIC REVIEW THAT USUALLY HELPS MAKE THE DIAGNOSE. SO THESE INSTRUMENTS ARE PERFECTLY FINE TO USE.

Q OKAY. LET'S LOOK AT A META -- I'M SORRY. LET'S LOOK A SYSTEMATIC REVIEW ON THE LITERATURE ON LEAD AND ADHD. THIS IS THE DONZELLI STUDY, EXHIBIT 627.

SO JUST LOOKING AT THE STUDY, THIS IS A STUDY DONE IN 2019, SO A QUITE RECENT STUDY OR -- AND, AS THE TITLE INDICATES, IT'S A SYSTEMATIC REVIEW OF THE ASSOCIATION BETWEEN LEAD AND ADHD; CORRECT?

A THAT'S WHAT IT SAYS, YES.

Q AND YOU REVIEWED THIS STUDY AS PART OF RENDERING YOUR OPINIONS; TRUE?

A YES.

Q ALL RIGHT. LET'S LOOK AT WHAT THE AUTHORS -- BY THE WAY, A SYSTEMATIC REVIEW, WE JUST ACTUALLY HEARD DR. ASCHNER TESTIFY ABOUT ONE OF HIS SYSTEMATIC REVIEWS. THAT'S WHAT IT SOUNDS LIKE, WHICH IS, BASICALLY, THE AUTHORS SYSTEMATICALLY REVIEW THE LITERATURE ABOUT WHATEVER TOPIC THEY ARE INTERESTED IN, AND THEN THEY TRY TO SYNTHESIZE IT AND SUMMARIZE IT.

THAT'S GENERALLY WHAT A SYSTEMATIC REVIEW IS; TRUE?

A WELL, A SYSTEMATIC REVIEW, YES, IN A WAY, IT'S TRUE, BUT YOU HAVE TO, KIND OF, DISCLOSE THE CRITERIA YOU ARE USING AND, YOU KNOW, THERE ARE SYSTEMATIC REVIEWS THAT USE ONE TYPE OF CRITERIA, AND THEN THERE ARE OTHERS THAT USE OTHERS. AND SYSTEMATIC REVIEWS ARE ALSO DIFFERENT FROM META ANALYSES WHERE YOU'RE TRYING TO COME UP WITH A NUMBER IN THE END THAT REFLECTS THE OVERALL EFFECT SIZE OF THE STUDIES THAT YOU'VE CONSIDERED VALID. SO, YEAH.

Q YOU'VE AGAIN ANTICIPATED MY NEXT QUESTION. YOU'RE GETTING GOOD AT THIS, DOCTOR.

LET'S LOOK AT PAGE 3 OF THE STUDY TO SEE WHAT THESE AUTHORS DID, THAT IS THE METHODOLOGY THEY FOLLOWED. AND IF WE LOOK AT THE PARAGRAPH THAT BEGINS WITH "MOREOVER."

SO WHAT THESE AUTHORS DID IS THEY LOOKED AT THE LITERATURE THAT EXISTED FOR THE PAST FIVE YEARS BEFORE THIS STUDY, AND THEY ISOLATED THE STUDIES WHERE THE LEAD LEVELS WERE MEASURED DURING PREGNANCY OR EARLY CHILDHOOD.

DO YOU SEE THAT UNDER CRITERIA NUMBER 2?

A YES.

Q AND SO, IN THESE STUDIES, THAT FACTOR OF TEMPORALITY WHICH WE'VE TALKED ABOUT WOULD BE SATISFIED BECAUSE THE EXPOSURE ASSESSMENT HAPPENED DURING PREGNANCY OR EARLY CHILDHOOD AND THAT WOULD BE BEFORE ADHD WAS DIAGNOSED; CORRECT?

A ASSUMING THAT IT WASN'T DIAGNOSED AT THE SAME

TIME THEY TOOK THE BLOOD SAMPLE.

Q RIGHT.

AND THEY FOUND, IN ALL THE LITERATURE THEY REVIEWED -- YOU SEE IN THE TOP PARAGRAPH, THEY REVIEWED 829 ARTICLES -- OR IDENTIFIED 829 ARTICLES, AND 17 MET THESE THREE INCLUSION CRITERIA.

DO YOU SEE THAT?

A YEAH.

Q ALL RIGHT. LET'S LOOK AT THE CONCLUSIONS AFTER THE AUTHORS ANALYZED THE STUDIES, AND LET'S SEE WHAT THEIR CONCLUSIONS WERE. I WANT TO ASK YOU ABOUT THEM.

THEIR CONCLUSIONS, AFTER REVIEWING THESE 17 STUDIES THAT ISOLATED THE TEMPORALITY OF THE LEAD IN THE ADHD, WAS "BASED ON THE RESULTS OF THIS REVIEW,

ADDITIONAL DATA IS NEEDED TO FULLY ASCERTAIN THE NATURE OF THE RELATIONSHIP BETWEEN LEAD EXPOSURE AND ADHD."

DO YOU SEE THAT?

A YES.

Q AND THEN, THEY SAID "FUTURE RESEARCH SHOULD CONSIDER THE INFLUENCE OF ALL POTENTIALLY CONFOUNDING VARIABLES AND ALSO USE A STANDARDIZED METHOD OF ADHD DIAGNOSIS."

CORRECT?

A YES.

Q AND THEN THE FINAL SENTENCE SAYS, "THE COMBINED EXPOSURE TO MULTIPLE CHEMICALS OR RISK FACTORS SHOULD ALSO BE EVALUATED, TOGETHER WITH THE

INFLUENCE OF GENETIC FACTORS."

DO YOU SEE THAT?

A YES.

Q LET'S LOOK, DOCTOR, AT THE -- I WANT TO LOOK AT ONE MORE STUDY ON LEAD AND ADHD. THE SKOGHEIM STUDY. WE'VE TALKED ABOUT THE SKOGHEIM STUDY IN A NUMBER OF SITUATIONS.

A DO YOU HAVE -- I'M SORRY. WHAT WAS THE PURPOSE OF THIS -- SHOWING ME THIS CONCLUSION?

Q DOCTOR, I DON'T -- I DON'T KNOW THAT YOU NEED TO WORRY ABOUT THE PURPOSE. I'M JUST TRYING TO GET THROUGH THIS QUICKLY AND ASKING YOU QUESTIONS.

THE SKOGHEIM STUDY IS EXHIBIT 629.

NOW, THIS IS A STUDY -- TWO THINGS ABOUT THIS STUDY I WANTED TO ASK YOU ABOUT.

FIRST OF ALL, THIS IS A STUDY -- IF WE COULD BLOW UP THE TITLE PAGE WHERE THE DATE IS.

THIS IS A STUDY FROM 2021. SO THIS IS AFTER THE DONZELLI SYSTEMATIC REVIEW THAT WE JUST LOOKED AT; CORRECT?

A YES.

Q AND THIS IS A STUDY WHERE THEY ACTUALLY LOOKED AT CLINICALLY DIAGNOSED ADHD AS THE END POINT THEY WERE MEASURING; CORRECT?

A YES, BUT IT'S FROM THE HEALTH SYSTEMS. SO YOU DON'T REALLY KNOW HOW IT WAS DIAGNOSED. YOU JUST KNOW IT ENDED UP WITH SOME KIND OF ICD CODE IN A MEDICAL RECORD.

Q RIGHT.

AND THEY LOOKED AT THE ASSOCIATIONS BETWEEN -- OR POTENTIAL ASSOCIATIONS BETWEEN VARIOUS METALS, INCLUDING LEAD AND ADHD; CORRECT?

A YES.

Q LET'S LOOK AT THEIR RESULTS.

THIS WOULD BE IN SUPPLEMENTAL FIGURE S3, WHICH WE'VE LOOKED AT BEFORE, I THINK, IN A DIFFERENT CONTEXT.

WE'LL PULL THAT UP IN A SECOND.

THIS WAS FROM SUPPLEMENTAL FIGURE S3, AND YOU SEE "PB" ALONG THE LEFT, THAT MEANS LEAD; CORRECT?

A YES.

Q AND THESE ARE THESE QUARTILES WE'VE LOOKED AT BEFORE.

THAT IS AN INCREASING EXPOSURE TO -- OF THE MOTHER TO LEAD; CORRECT?

A YES.

Q AND THEN, TO THE RIGHT IS THE ADHD VERSUS THE CONTROLS, AND YOU SEE FOR -- THE ODDS RATIOS ARE WHAT THEY ARE THERE, AND THERE'S THE 95 PERCENT CONFIDENCE INTERVAL.

THERE'S NO STATISTICALLY SIGNIFICANT DIFFERENCE; CORRECT?

A NO. BUT THE AUTHORS, AS FAR AS I REMEMBER, INTERPRET THEIR RESULTS AS SHOWING A U-SHAPED RELATIONSHIP.

Q OKAY. FINAL QUESTION, DOCTOR.

WE CAN TAKE THAT DOWN.

YOU REFERRED TO, IN YOUR DIRECT EXAMINATION, A PUBLICATION FROM PROJECT TENDR THAT YOU WERE A SIGNATORY TO.

DO YOU REMEMBER THAT TESTIMONY?

A YES.

Q LET'S PULL THAT UP. THAT'S EXHIBIT 32, I BELIEVE.

OKAY. THIS WAS THIS 2016 STATEMENT CONSENSUS -- OR POSITION PAPER BY PROJECT TENDR.

DO YOU REMEMBER DISCUSSING THIS IN YOUR DIRECT EXAMINATION?

A YES.

Q ALL RIGHT.

AND ONE OF THE THINGS -- LET'S GO TO PAGE A121 OF THE STUDY. I DON'T KNOW EXACTLY WHAT PAGE IN THE PDF THAT IS, BUT WE'LL FIND IT IN A SECOND. IT'S PAGE 4 IN THE PDF.

ONE OF THE THINGS YOU HAD POINTED OUT IN YOUR DIRECT EXAMINATION, AMONG THE ORGANIZATIONS THAT ENDORSE OR SUPPORT THE TENDR STATEMENT WAS THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGIST, OTHERWISE KNOWN AS ACOG, WHICH YOU POINTED OUT SUPPORTED THE VALUE OF THE DOCUMENT AS A EDUCATIONAL TOOL.

DO YOU SEE THAT?

A YES.

Q OKAY.

LET'S TAKE THAT DOWN.

LET'S LOOK AT WHAT ACOG HAS TO SAY TODAY ABOUT

HEAVY METALS AND ASD.

THIS IS EXHIBIT 678.

DOCTOR, I'M SHOWING YOU WHAT'S BEEN MARKED AS EXHIBIT 678. A ACOG PUBLICATION ENTITLED "LABOR INDUCTION OR AUGMENTATION AND AUTISM," WHICH ORIGINALLY WAS ISSUED IN MAY OF 2014. THAT WOULD HAVE BEEN BEFORE THE PROJECT TENDR STATEMENT, AND YOU SEE IT'S BEEN REAFFIRMED IN 2022, JUST THIS PAST MONTH.

A YES.

Q AND LET'S GO TO THE SECOND PAGE OF THE DOCUMENT TO SEE WHAT THEIR CONCLUSION IS.

DO YOU SEE, IT'S BEEN HIGHLIGHTED, "ALTHOUGH THE CAUSE OF ASD IS UNCLEAR, IT DEMONSTRATES A STRONG GENETIC PREDISPOSITION AND MULTI-FACTORIAL INFLUENCES. A WIDE VARIETY OF EXPOSURES, INCLUDING MANY PERINATAL FACTORS HAVE BEEN LINKED TO ASD, BUT THE SUGGESTED ASSOCIATIONS IN MANY CASES ARE WEAK, INCONSISTENT, OR BOTH, AMONG STUDIES AND CANNOT BE EQUATED WITH A CAUSE-AND-EFFECT RELATIONSHIP."

DO YOU SEE WHAT I JUST READ?

A YES.

MR. PETROSINELLI: THANK YOU, DOCTOR. I DON'T HAVE ANY FURTHER QUESTIONS.

THE WITNESS: THAT WASN'T A QUESTION.

MR. PETROSINELLI: YOUR HONOR, I THINK I MADE MY 30-MINUTE PROMISE. SO TRYING TO GET US OUT OF HERE

EARLY TODAY. THANK YOU.

THE COURT: OKAY. THANK YOU.

MR. WISNER: YOUR HONOR, MAY I PROCEED WITH REDIRECT?

THE COURT: YEAH. COULD I JUST SEE THE LAST SLIDE FOR A MINUTE, BECAUSE I GOT A LITTLE BEHIND IN MY NOTETAKING?

MR. PETROSINELLI: I'M SORRY, YOUR HONOR, YES.

AND, YOUR HONOR, THIS IS -- THIS WILL BE EXHIBIT -- THIS IS EXHIBIT -- I'M SORRY -- 678.

MR. WISNER: AND IF -- YOUR HONOR, IF IT'S OKAY WITH THE COURT, I'D LIKE TO KEEP IT ON THE SCREEN JUST FOR A COUPLE SECONDS, SO I COULD ASK SOME QUESTIONS ABOUT IT.

THE COURT: SURE. YOU MAY PROCEED.

MR. WISNER: THANK YOU, YOUR HONOR.

REDIRECT EXAMINATION

MR. WISNER:

Q DR. RITZ, MR. PETROSINELLI JUST KIND OF READ YOU SOME STATEMENTS FROM THIS DOCUMENT. LET ME ASK YOU SOME QUESTIONS ABOUT IT.

WELL, FIRST OF ALL, DO YOU AGREE WITH THIS SENTENCE HERE THAT WAS WRITTEN IN 2014?

A THE SENTENCE OBVIOUSLY HASN'T BEEN UPDATED. I'M NOT TOO SURPRISED BECAUSE I'M PRETTY SURE THAT THE PEOPLE WHO ARE WRITING THIS STATEMENT ARE NOT EXACTLY THE SAME PEOPLE WHO ARE IN THE TENDR GROUP, WHO ARE MUCH

MORE INFORMED.

BUT I DO AGREE THERE'S A GENETIC DISPOSITION, AND THERE ARE MULTI-FACTORIAL INFLUENCES. WHERE THEY GET THEIR KNOWLEDGE ABOUT, YOU KNOW, WEAK, INCONSISTENT, ET CETERA, THEY ARE NOT EPIDEMIOLOGISTS, SO I DON'T KNOW WHERE THEY -- WHAT THEY BASE THEIR INFORMATION ON TO MAKE THIS KIND OF STATEMENT.

BUT, YES, WE ALL WISH WE HAD DONE A LOT MORE STUDIES, EPIDEMIOLOGIC STUDIES, STRONG STUDIES, OVER THE LAST 20 YEARS, BUT YOU HAVE TO INVEST IN THESE STUDIES, AND THEY ARE COSTLY. AND THE MORE WE DO RESEARCH, THE MORE WE FIND OUT. UNFORTUNATELY, YOU KNOW, WE HAVEN'T FOUND EVERY FACTOR THAT CONTRIBUTES TO ASD, AND I THINK BECAUSE WE DIDN'T LOOK.

Q AND I'M JUST LOOKING AT THIS SLIDE THAT WAS READ TO YOU.

DO YOU SEE ANY SORT OF BRADFORD HILL ANALYSIS BEING CONDUCTED HERE?

A NO.

Q OKAY.

IF WE COULD TAKE THAT DOWN, I'D APPRECIATE IT. THANK YOU.

WELL, DR. RITZ, I'M GOING TO JUST, SORT OF, KIND OF WORK BACKWARD FROM SOME OF THE THINGS THAT MR. PETROSINELLI SHOWED YOU AND READ TO YOU AND SHOW YOU OTHER PORTIONS THAT WERE NOT SHOWN, OKAY?

LET'S START OFF WITH THE DONZELLI PAPER THAT WAS JUST SHOWN TO YOU.

OKAY. DO YOU SEE THAT DOCUMENT IN FRONT OF YOU, DOCTOR?

A YEAH, BUT IT'S TINY.

Q YEAH. GIVE IT A SECOND.

ALL RIGHT. YOU SEE THIS -- THIS IS THAT PAPER THAT HE SHOWED YOU, THE ASSOCIATION BETWEEN LEAD AND ATTENTION DEFICIT HYPERACTIVITY DISORDER, A SYSTEMAT REVIEW?

A YES, I SEE THAT.

Q OKAY.

SO RIGHT HERE ON THE PAGE -- I'M GOING TO CALL OUT WHAT THEY SAY IN THE CONCLUSION.

IT SAYS, "TO CONCLUDE, THE EVIDENCE FROM STUDIES ALLOWED US TO ESTABLISH THAT THERE IS AN ASSOCIATION BETWEEN LEAD AND ADHD AND THAT EVEN LOW LEVELS OF LEAD RAISE THE RISK."

DO YOU SEE THAT?

A YES, I DO.

Q IT GOES ON TO SAY, "HOWEVER, THERE'S STILL A LACK OF LONGITUDICAL STUDIES ABOUT THE RELATIONSHIP BETWEEN LEAD EXPOSURE AND THE DEVELOPMENT OF ADHD."

DO YOU SEE THAT?

A YES.

Q AND THEN IT SAYS, "GIVEN THE IMPORTANCE" -- LET ME PULL CALL IT OUT FULLY. ALL RIGHT.

"GIVEN THE IMPORTANCE FOR PUBLIC HEALTH, FURTHER RESEARCH THAT INCLUDES THE ENTIRE

POTENTIAL RISK FACTORS FOR ADHD IN CHILDREN, MUST BE ENCOURAGED."

DO YOU SEE THAT?

A YES.

Q DO YOU GENERALLY ENCOURAGE FURTHER RESEARCH INTO THE CONNECTION BETWEEN LEAD EXPOSURE AND ADHD?

A ABSOLUTELY.

Q AND --

A YOU ALWAYS WANT TO KNOW MORE. YOU WANT TO KNOW MECHANISMS. YOU WANT TO KNOW LEVELS. YOU WANT TO KNOW INTERACTIONS WITH OTHER FACTORS. YOU WANT TO KNOW MORE ABOUT THE MOST VULNERABLE PERIODS. EACH STUDY CAN JUST TELL YOU ABOUT A SMALL PIECE OF THE PUZZLE, ALL OF THEM COME TOGETHER, AND CAN YOU ALWAYS WISH YOU WOULD KNOW MORE, BUT, AS A PUBLIC HEALTH PERSON, YOU HAVE TO START ACTING AT SOME POINT.

Q COUNSEL ALSO ASKED YOU ABOUT THESE 17 STUDIES.

AGAIN, RIGHT HERE ON THE FIRST PAGE, IT TALKS ABOUT THEM.

IT SAYS, "17 STUDIES MET THE INCLUSION CRITERIA. FIVE OF THESE STUDIES FOUND NO ASSOCIATION BETWEEN LEAD EXPOSURE AND ADHD, WHEREAS, THE REMAINING 12 STUDIES SHOWED POSITIVE ASSOCIATIONS, EVEN THOUGH NOT ALL OF THEM WERE HOMOGENEOUS IN TERMS OF EXPOSURE PERIODS CONSIDERED OR ADHD DIAGNOSIS."

DO YOU SEE THAT?

A YES.

Q AGAIN, THIS VERY LOPSIDED NUMBER OF STATISTICALLY SIGNIFICANT POSITIVE STUDIES RELATIVE TO NULL STUDIES, AND THE FACT THAT THEY ARE SEEN IN NOT HOMOGENEOUS STUDIES, WHAT DOES THAT TELL YOU AS AN EPIDEMIOLOGIST?

A WELL, IT TELLS ME THAT A PREPONDERANCE OF STUDIES ACTUALLY SHOWED POSITIVE ASSOCIATIONS IN DIFFERENT POPULATIONS WITH DIFFERENT INSTRUMENTS, AND DIFFERENT EXPOSURE PERIODS. SO THAT'S ALL CONTRIBUTING TO BRADFORD HILL CRITERIA OF, YOU KNOW, BEING CONSISTENT, BUT ALSO BEING DONE IN DIFFERENT ENVIRONMENTS AND WITH DIFFERENT METHODS, AND THAT'S ACTUALLY A STRENGTH.

Q NOW, I WANT TO SHOW YOU ONE OF THE PUBLICATIONS THAT YOU PUBLISHED THAT WAS SHOWN TO YOU ON YOUR CROSS JUST A MINUTE AGO. THIS IS THE IN UTERO EXPOSURE TO TOXIC AIR POLLUTANTS AND RISK OF CHILDHOOD AUTISM.

DO YOU SEE THAT?

A YES.

Q AND YOU RECALL MR. PETROSINELLI, HE ASKED YOU QUESTIONS AND SHOWED YOU SOME RESULTS REGARDING COPPER; DIDN'T HE?

A YES.

Q DID HE SHOW YOU ANY OF THE RESULTS ABOUT ONE OF THE METALS THAT'S ACTUALLY AT ISSUE HERE, SPECIFICALLY LEAD?

A NO.

Q LET'S TAKE A LOOK.

SO DOWN HERE ON PAGE 15 OF THE DOCUMENT, THIS IS WHERE YOU HAVE THAT COOPER RESULT.

DO YOU SEE THAT?

A YES.

Q OKAY. THAT'S WHAT YOU DISCUSSED.

NOW, LET'S GO TO THE NEXT PAGE, AND DOWN HERE WE HAVE -- I'LL DO THE HEADER FIRST.

A RIGHT.

Q AND THEN YOU HAVE THE DATA FOR LEAD.

A YES.

Q DO YOU SEE THAT?

A YES.

Q I KNOW IT'S KIND OF SMALL, BUT IF YOU CAN -- HOPEFULLY, YOU CAN READ IT.

A YES.

Q WHAT I SEE HERE IS AN ODDS RATIO FOR IMPAIRED EXPRESSIVE LANGUAGE OF 1.58.

THAT'S STATISTICALLY SIGNIFICANT; IS THAT RIGHT?

A YES.

Q AND THEN, I ALSO SEE ANOTHER ODDS RATIO OF 1.64 FOR LESS IMPAIRED EXPRESSIVE LANGUAGE THAT'S ALSO SIGNIFICANTLY SIGNIFICANT.

A YES.

Q DO YOU SEE THAT?

A YES.

Q THIS STUDY REGARDING LEAD POLLUTION BEING EXPOSED TO CHILDREN AND THEIR DEVELOPING OF THESE

CHARACTERISTICS ASSOCIATED WITH ASD, THIS IS FROM 2014.

IS THIS CONSISTENT WITH THE OPINIONS YOU'VE REACHED IN THIS CASE?

A ABSOLUTELY. YES.

Q AND WHAT, IF ANY, STRENGTH IS THERE IN LOOKING AT A SORT OF STUDY THAT LOOKS AT AIR POLLUTION IN THIS CONTEXT?

A WELL, AIR POLLUTION IS ACTUALLY NOT DEPENDENT ON THESE CHILDREN HAVING, YOU KNOW -- THE TIMING IS CORRECT BECAUSE WE ARE MEASURING THE TIMING OF THE AIR POLLUTION AT RIGHT TIME. WE ARE USING BIRTH RECORDS TO IDENTIFY THE LOCATION OF THE MOTHER'S HOME AT TIME OF BIRTH AND EARLY LIFE. SO THE TIMING IS DEFINITELY PRIOR TO THE DIAGNOSIS.

AND AIR POLLUTION CHANGES. SO -- AND THIS IS CONTINUOUS AIR POLLUTION. SO WE HAVE THE TIMING RIGHT BECAUSE WE HAVE THAT TIME DEFINED MEASURE OF LEAD, BUT IT'S ALSO LESS CONFOUNDED BY ALL SORTS OF BEHAVIORAL FACTORS, BECAUSE THE MOTHERS LIVE THERE AT DIFFERENT POINTS IN TIME. THEY HAVE THEIR PREGNANCIES IN DIFFERENT POINTS IN TIME, AND, YOU KNOW, ONLY FACTORS THAT CHANGE OVER TIME WOULD BE CONSIDERED CONFOUNDERS, WHILE PERSONAL BEHAVIORS THAT ARE, KIND OF, STABLE WOULD NOT INFLUENCE THESE ANALYSES AT ALL.

SO DIET OF THE CHILD WOULDN'T INFLUENCE WHAT THE AIR POLLUTION METAL IS, AND, YOU KNOW, LOTS OF OTHER FACTORS WOULDN'T EITHER.

Q ALL RIGHT. DOCTOR, I'D LIKE TO NOW GO OVER

ANOTHER CHART THAT WAS SHOWN TO YOU. IT WASN'T JUST SHOWN TO YOU. THIS WAS A CHART THAT WAS SHOWN TO YOU ON, I THINK, TUESDAY. I'M TRYING TO REMEMBER ALL THESE DAYS. THEY ALL BLEND TOGETHER. BUT I WANT TO POP UP HERE, THIS WAS SHOWN TO YOU DURING YOUR TESTIMONY.

DO YOU SEE IT, DOCTOR?

A YES.

Q AND THIS WAS A LIST OF STUDIES THAT COUNSEL HAD REPRESENTED AS REFLECTING TEMPORAL STUDIES, TEMPORALITY STUDIES. MEANING, IN THESE STUDIES, THE MEASUREMENT OF THE EXPOSURE TO THE LEAD PRECEDED THE DIAGNOSIS.

DO YOU SEE THAT?

A YES.

Q OKAY.

SO IN THIS CHART, THERE IS A SORT OF REPRESENTATION OF THESE THINGS, AND THEN THERE'S THIS SORT OF YES/NO, BINARY SORT OF THING ON THE RIGHT, REGARDING A SIGNIFICANT ASSOCIATION.

DO YOU SEE THAT?

A YES.

Q AND YOU WERE ACTUALLY JUST TALKING ABOUT HOW DANGEROUS IT TO SORT OF ENGAGE IN THAT SORT OF BINARY YES/NO, WHEN IT COMES TO SIGNIFICANCE.

DO YOU RECALL THAT?

A YES.

Q ALL RIGHT. WHAT I'D LIKE TO DO IS, I'D ACTUALLY JUST LIKE TO SORT OF LOOK AT WHAT HAPPENS WHEN YOU DIG A LITTLE DEEPER INTO THESE STUDIES AND WHAT THE

AUTHORS THEMSELVES ARE SAYING.

DO LET'S START OFF WITH SKOGHEIM.

THIS IS -- OH, THERE WE GO. LET'S START OFF WITH SKOGHEIM.

SO THIS IS EXHIBIT 119 IN THE RECORD.

AND, AS YOU CAN, DOCTOR, THIS IS THE STUDY, "METAL AND ESSENTIAL ELEMENT CONCENTRATIONS DURING PREGNANCY AND ASSOCIATIONS WITH AUTISM SPECTRUM DISORDER AND ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN."

DO YOU SEE THAT?

A YES.

Q ALL RIGHT. SO WE'VE GONE OVER THIS. WE DISCUSSED THIS BEFORE, THAT THERE WAS THIS U-SHAPED CURVE ASSOCIATION.

AND I JUST WANT TO SHOW YOU WHAT THE AUTHORS THEMSELVES SAID. THIS IS ON PAGE 10 OF THE STUDY. HOPEFULLY YOU CAN SEE IT.

A YES, I SEE IT.

Q IT READS, "WE IDENTIFIED A NON-LINEAR U-SHAPED ASSOCIATION WITH PRENATAL LEAD EXPOSURE IN ASD. WHILE THERE WAS NO SUCH FINDINGS FOR ADHD DIAGNOSIS IN CHILDREN, THE NON-LINEAR U-SHAPED OBSERVED IN THE STUDY INDICATE THAT BOTH LOW LEVEL AND HIGHER PRENATAL EXPOSURES TO LEAD ARE ASSOCIATED WITH INCREASED RISK OF ASD IN CHILDREN."

DO YOU SEE THAT?

A YES.
Q AND IT EVEN GOES ON TO EXPLAIN THAT "NON-LINEAR DOSE RELATIONSHIPS HAVE BEEN SHOWN IN SEVERAL STUDIES OF LEAD EXPOSURE IN CHILDHOOD AND NEURODEVELOPMENTAL OUTCOMES, SUCH AS IQ."
DO YOU SEE THAT?
A YES.
Q AND THEN THEY GO ON TO SAY, JUST LOWER DOWN HERE, "WE ALSO DETECTED INCREASED RISK OF HIGHER LEVELS OF LEAD," WHICH IS IN LINE WITH THE LITERATURE.
DO YOU SEE THAT?
A YES.
Q NOW, DOCTOR, I GUESS MY QUESTION IS, GOING BACK TO THIS CHART: WHEN YOU REVIEWED THE SKOGHEIM STUDY, IN YOUR MIND, DID IT SUPPORT YOUR CONSIDERATION OF WHETHER OR NOT THERE WAS TEMPORALITY OR NOT?
A YES, IT DID.
Q AND WHY IS THAT?
A WELL, BECAUSE I TRUST THE AUTHORS IN THE WAY THAT THEY DESCRIBE THEIR RESULTS BECAUSE IT'S PUBLISHED IN A GOOD JOURNAL, THERE WAS PEER-REVIEW, AND THEY KNOW A LOT MORE ABOUT THEIR DATA AND THE QUALITY OF THEIR DATA, BUT I ALSO AM ABLE TO LOOK AT WHAT THEY PRESENT, AND IT WAS A NON-LINEAR RELATIONSHIP.
Q OKAY.
WHAT IF WE LOOK AT THIS NEXT STUDY, THE FRYE 2020 STUDY.
LET ME POP IT UP HERE.

DO YOU SEE THIS IS A STUDY BY RICHARD FRYE AND HIS COLLEAGUES, DOCTOR, DO YOU SEE THAT?

A YES, I SEE IT.

Q AND IT'S TITLED "EARLY LIFE METAL EXPOSURE DYSREGULATES CELLULAR BIO" --

A BIOENERGETICS.

Q -- "BIOENERGETICS IN CHILDREN WITH REGRESSIVE AUTISM SPECTRUM DISORDER,"?

AND, AS I CAN HERE, THE LAST AUTHOR ON HERE IS ACTUALLY DR. ARORA.

DO YOU SEE THAT?

A YES.

Q OKAY. THIS IS ONE OF THOSE STUDIES THAT I DO BELIEVE YOU DISCUSS IN YOUR REPORT; IS THAT RIGHT?

A YES.

Q AND RIGHT HERE IN THE ABSTRACT, IT KIND OF EXPLAINS WHAT THEY ARE DOING.

THEY HYPOTHESIZE, THEY SAY "EARLY LIFE DYSREGULATION AND NUTRITIONAL METALS AND/OR EXPOSURE TO TOXIC METALS HAVE BEEN ASSOCIATED WITH ASD, BUT THE UNDERLYING BIOLOGICAL MECHANISMS BY WHICH METALS INFLUENCE NEURODEVELOPMENT REMAIN UNCLEAR. WE HYPOTHESIZE THAT METALS INFLUENCE NEURODEVELOPMENT THROUGH DYSREGULATION OF BIOENERGETICS."

DO YOU SEE THAT?

A YES.

Q BIOENERGETICS. SORRY.

AND THEN DOWN HERE, THEY, KIND OF, REPORT BRIEFLY THE RESULT ON LEAD.

"GLYCOLYSIS DECREASED WITH INCREASED EXPOSURE TO PRENATAL MANGANESE AND LEAD AND POST-NATAL MANGANESE."

DO YOU SEE THAT?

A YES.

Q ALL RIGHT. AND I JUST WANT TO GO INTO THE STUDY. I WILL AGAIN SHOW YOU THE PARAGRAPH THEY HAVE HERE ABOUT LEAD.

THEY SAY "REGARDLESS OF THE -- OH, THE SOURCES OF LEAD EXPOSURE ARE UBIQUITOUS IN THE ENVIRONMENT FROM OLD MINE PEELINGS, LEGACY OF LEADED GASOLINE, PAINT DEPOSITS TO SOILS AND AIR POLLUTION. REGARDLESS OF THE SOURCE OF LEAD, A PREVIOUS TWIN STUDY SUGGESTS THAT ENVIRONMENTAL LEAD DEPOSITED INTO DECIDUOUS TEETH DURING FETAL LIFE IS HIGHER IN INDIVIDUALS WITH ASD."

DO YOU SEE THAT?

A YES.

Q AND THAT'S ACTUALLY REFERRING TO THE ARORA STUDY THAT WE TALKED ABOUT ALREADY?

A CORRECT.

Q IT SAYS "AND THE CURRENT STUDY SUGGESTS THAT IT CAN RESULT IN LONG-TERM CHANGES THAT DEGREASE GLUCOSE METABOLISM IN INDIVIDUALS WITH ASD AND

NDR."

DO YOU SEE THAT?

A YES.

Q ALL RIGHT. CAN YOU JUST EXPLAIN TO THE COURT WHAT THIS STUDY IS AND WHAT YOU UNDERSTOOD IT TO BE SHOWING?

A RIGHT. THIS IS A MECHANISTIC STUDY, NOT AN EPIDEMIOLOGIC STUDY. MECHANISTIC IN A SENSE THAT THEY ARE USING TISSUE -- TISSUE ANALYSES, IN THIS CASE GLUCOSE METABOLISM, TO ASSESS WHAT METALS DO.

WHY GLYCOLYSIS, WHY BIOENERGETICS, BECAUSE WE KNOW THAT THERE IS AN ORGANISM IN THE CELLS THAT'S CALLED MITOCHONDRIAL THAT ACTUALLY ARE THE POWERHOUSES. THEY PRODUCE ENERGY FOR THE CELL, AND THEY ARE LIKE LITTLE BACTERIA. THERE PROBABLY HAVE BEEN BACTERIA BEFORE THEY GOT INTO THE CELLS OF MULTICELLULAR AND SINGLE-CELLULAR ORGANISMS.

BUT ALL THEY DO NOW, THESE MITOCHONDRIALS, IS PRODUCE ENERGY FOR THE CELL, AND THEY USE GLUCOSE FOR PRODUCING ENERGY ADP, BUT THEY CAN ALSO USE FAT. SO, YOU KNOW, THEY CAN TURN AND USE FAT INSTEAD.

AND HERE IS A HYPOTHESIS, WE KNOW THAT MITOCHONDRIA ACTUALLY SYNCS FOR METALS. SO A LOT OF THE METALS IN THE CELL GO INTO THE MITOCHONDRIA, AND IF ENOUGH METALS GO INTO MITOCHONDRIA THAT ARE TOXIC, WE SEE THAT THE MITOCHONDRIA SWELL UP AND, EVENTUALLY, GET DESTROYED.

AND LEAD IS ONE OF THESE AGENTS THAT, IF

THERE'S TOO MUCH OF IT, THE MITOCHONDRIA FIRST START NOT FUNCTIONING ANYMORE, AND ONE OF THEIR FUNCTION IS GLYCOLYSIS, GLUCOSE METABOLISM, AND THEN, WHEN IT GETS WORSE, EVENTUALLY, THE MITOCHONDRIA WILL NOT BE FUNCTIONING AT ALL, AND PROBABLY HAVE THIS PHENOTYPE WHERE THEY SWELL UP AND DISSOLVE.

THAT, IN THE END, MEANS THAT THE CELL IS NOT ABLE TO SURVIVE ANYMORE BECAUSE THERE'S NOT ENOUGH ENERGY IN THE CELL IF ENOUGH MITOCHONDRIA ARE HARMED.

AND THAT'S THE WHOLE HYPOTHESIS OF THIS PAPER, IS TO FIGURE OUT WHAT ARE THE MECHANISM ACTUALLY THAT METALS USE IN ORDER TO DESTROY CELLS.

AND WE KNOW THAT THE BRAIN, FOR EXAMPLE, USES MOST OF THE ENERGY, MOST OF THE GLUCOSE, IN THE BODY. SO THE CELLS OF THE BRAIN NEED THIS TYPE OF METABOLISM VERY MUCH AND THAT'S POSSIBLY ONE REASON WHY LEAD IS SO TOXIC.

Q GOING BACK TO THIS CHART, THE FRYE STUDY, I MEAN, DOES THAT SUPPORT TEMPORALITY OR DOES IT REFUTE IT?

A IT ACTUALLY SUPPORTS IT.

Q OKAY. GREAT.

YOU KNOW, IT'S FUNNY, I'VE PRE-WRITTEN THESE REPORTS. SO IF YOU ACTUALLY DISAGREE WITH ME, I'M GOING TO HAVE TO CHANGE THE SLIDE, BUT HOPEFULLY, I'VE PREDICTED YOUR TESTIMONY.

A YES.

Q OKAY.

LET'S TAKE A LOOK AT THE LONG STUDY FROM 2019.

THIS WAS A STUDY, IT'S EXHIBIT 92, FROM 2019. IT'S TITLED "AUTISM SPECTRUM DISORDERS, ENDOCRINE DISRUPTING COMPOUNDS AND HEAVY METALS IN AMNIOTIC FLUID, A CASE CONTROL STUDY."

DO YOU SEE THAT?

A YES.

Q AND, DOCTOR, THIS IS A CASE CONTROL STUDY.

HOW CAN IT POSSIBLY NOT SUFFER FROM A TEMPORALITY ISSUE OF MEASUREMENT?

A BECAUSE YOU HAVE SAMPLES TAKEN AT A TIME POINT PRIOR TO CASE IDENTIFICATION. SO SOMEBODY'S STORED BODY FLUIDS FOR YOU SO YOU CAN GO BACK IN TIME TO ACTUALLY MEASURE SOMETHING THAT HAPPENED PRIOR TO ONSET OF DISEASE.

Q IS THIS ONE OF THOSE INSTANCES WHERE A CASE CONTROL CAN ACTUALLY HAVE A, SORT OF, PROSPECTIVE DESIGN BUILT INTO IT BECAUSE OF WHEN IT WAS MEASURED?

A YEAH. PROSPECTIVE IN A SENSE OF -- IT'S STILL RETROSPECT BECAUSE WE START FROM THE CASE, BUT WHEN YOU, KIND OF, WALK BACK IN TIME TO THE TIME WHEN THE SAMPLE WAS TAKEN IN WHICH THE EXPOSURE IS MEASURED, AND YOU KNOW THE SAMPLE WAS TAKEN DURING PREGNANCY OR EARLY CHILDHOOD AND IT WAS PUT IN A FREEZER AND THEN SOMEBODY CAME AROUND, DIAGNOSED THE CASES, FOUND CONTROLS FOR THE CASES, AND THEN WENT BACK TO THE FREEZER TO ACTUALLY FIND THESE SAMPLES AND MEASURE THE EXPOSURES.

SO DEFINITELY, THE EXPOSURES WOULD HAVE

HAPPENED PRIOR TO THE ONSET.

Q SO IF WE GO INTO THE STUDY, THERE'S A DISCUSSION HERE ABOUT METALS AND, SPECIFICALLY, LEAD.

THEY WRITE "EXISTING STUDIES OF AUTISM SUGGEST THAT PRENATAL METAL EXPOSURE MAY BE RELATED TO AUTISM. EXPOSURE TO LEAD DURING NEURODEVELOPMENT HAS SIGNIFICANT EFFECTS ON NEUROBEHAVIORAL AND INTELLECTUAL PERFORMANCE, ALSO RESULTING IN ATTENTION HYPERACTIVITY AND LEARNING DISORDERS. LEAD POISONING HAS BEEN SUGGESTED AS A POSSIBLE RISK FACTOR FOR AUTISM, AS BLOOD LEVELS OF AUTISTIC CHILDREN HAVE BEEN REPORTED TO BE SIGNIFICANTLY HIGHER THAN THOSE OF HEALTHY CHILDREN. PREVIOUS STUDIES HAVE SHOWN THAT PERINATAL EXPOSURE TO MANGANESE, LEAD AND CADMIUM, FROM AIR POLLUTION INCREASED ASD RISK. IN THE PRESENT STUDY WE OBSERVED THAT ARSENIC AND LEAD LEVELS IN AF TEND TO BE POSITIVELY ASSOCIATED WITH ASD RISK SUGGESTING THE POSSIBLE ROLE OF PRENATAL EXPOSURE TO TOXIC METALS IN ASD DEVELOPMENT."

DO YOU SEE THAT?

A YES. AND AF IS AMNIOTIC FLUID. SO THAT'S TAKEN DURING PREGNANCY.

Q OKAY. GOOD.

SO AGAIN, IT LOOKS LIKE THESE AUTHORS IN THE LONG STUDY ARE ACTUALLY REPORTING A POSITIVE ASSOCIATION BETWEEN AT LEAST ARSENIC AND LEAD EXPOSURES AND ASD

RISK.

A YES, THAT'S WHAT THEY ARE SAYING. THAT'S HOW THEY INTERPRET THEIR RESULTS.

Q IT DOES SAY, HOWEVER, "GIVEN THAT THESE METALS WERE DETECTABLE IN LESS THAN 34 PERCENT OF THE AMNIOTIC FLUID SAMPLES, MORE STUDIES ARE NEEDED TO EXPLORE THE ROLE OF PRENATAL HEAVY METAL EXPOSURE ON THE RISK OF ASD."

DO YOU SEE THAT?

A YES.

Q AGAIN, DO YOU AGREE THAT IT'S A GOOD IDEA TO GET MORE STUDIES AND LOOK AT MORE DATA?

A ABSOLUTELY.

Q SO GOING BACK TO THE CHART HERE, WE HAVE THE LONG STUDY FROM 2019.

I GUESS THE QUESTION IS, DOCTOR: DO YOU BELIEVE THAT IT SUPPORTS TEMPORALITY OR REFUTES IT?

A ABSOLUTELY, IT SUPPORTS IT.

Q OKAY.

A AMNIOTIC FLUID IS PRENATAL.

Q OKAY.

BY THE NEXT STUDY ARORA, I THINK WE'VE DISCUSSED THAT ONE QUITE A BIT.

WOULD IT BE FAIR TO SAY THAT YOU BELIEVE IT SUPPORTS TEMPORALITY?

A YES.

Q OR, IN FACT, MAYBE EVEN ESTABLISHES IT?

A YES, IT DOES.

Q OKAY. COOL.

NOW, THE ABDULLAH STUDY, WE HAVEN'T SPEND TOO MUCH TIME ON IT, BUT THAT'S A STUDY THAT INVOLVED LOOKING AT THE HEAVY METALS OF CHILDREN'S TEETH COMPARED TO CONTROLS; RIGHT?

A YES.

Q AND UNLIKE THE ARORA STUDY, THE ABDULLAH STUDY DIDN'T -- IT WASN'T ABLE TO USE TWIN PAIRS, SO IT DIDN'T CONTROL FOR GENETICS; IS THAT RIGHT?

A THAT'S CORRECT.

Q ALL RIGHT. AND YOU WOULD AGREE WITH ME THE ABDULLAH STUDY IS DEFINITELY NULL?

A YES.

Q OKAY. YOU WOULD NOT SAY THE ABDULLAH STUDY, BECAUSE IT'S NULL, SUPPORTS TEMPORALITY; RIGHT?

A NO.

Q BUT WOULD YOU SAY THAT IT REFUTES TEMPORALITY?

A NO. FOR THAT WE NEED A LOT MORE EVIDENCE.

Q OKAY. ALL RIGHT.

LET'S LOOK AT THE NEXT STUDY THAT DEFENSE COUNSEL PUT ON THIS CHART, THE ALAMPI 2021 STUDY.

THIS IS EXHIBIT 24. AND LET'S POP IT UP RIGHT HERE.

THIS IS A STUDY TITLED "THE ASSOCIATION BETWEEN GESTATIONAL EXPOSURE TO TOXICANTS AND AUTISTIC BEHAVIORS USING BAYESIAN QUANTILE REGRESSION."

DO YOU SEE THAT?

A YES.

Q AND I'M WORRIED TO ASK YOU THIS QUESTION, BUT I NEED TO.

IN AS FEW WORDS AND AS QUICKLY AS POSSIBLE, WHAT IS A BAYESIAN REGRESSION?

A IT'S A BAYESIAN QUANTILE REGRESSION, WHICH IS A -- THE LATEST METHOD USED TO ANALYZE MIXED EXPOSURES AS -- LIKE A CONGLOMERATE OF EXPOSURES, RATHER THAN ONE EXPOSURE AT A TIME.

Q OKAY.

AND YOU SEE HERE, THERE'S AN AUTHOR, ACTUALLY, BRUCE LANPHEAR.

DO YOU SEE THAT?

A YES.

Q HE'S ACTUALLY ONE THE GUYS WITH YOU -- WHO WORKS WITH YOU IN TENDR; IS THAT RIGHT?

A THAT'S CORRECT.

Q ALL RIGHT.

SO THEY SAY HERE, "THAT ALTHOUGH PRENATAL EXPOSURE TO TOXICANTS HAS BEEN ASSOCIATED WITH AUTISTIC BEHAVIORS, MOST STUDIES HAVE BEEN FOCUSED ON SHIFTS IN MEAN BEHAVIOR SCORES. WE USED BAYESIAN QUANTILE REGRESSION TO ASSESS THE ASSOCIATIONS BETWEEN LOG2-TRANSFORMED TOXICANT CONCENTRATIONS AND AUTISTIC BEHAVIORS ACROSS THE DISTRIBUTION OF BEHAVIORS."

DO YOU SEE THAT?

A YES.

Q AND IS THIS THE CLEAN WAY OF -- EASIER WAY OF

SAYING THIS IS -- THEY'RE USING THIS FANCY STATISTICAL MODELLING TO SEE IF THEY CAN DIFFERENTIATE HOW THESE METALS ARE AFFECTING DIFFERENT ASPECTS OF BEHAVIORS?

A YES.

Q OKAY. ALL RIGHT.

LET'S LOOK WHAT THEY SAY.

SO AT FIRST THEY DO A LINEAR REGRESSION ANALYSIS.

DO YOU SEE THAT, DOCTOR?

A YES.

Q AND A LINEAR REGRESSION, THAT'S MORE OF A TRADITIONAL STATISTICAL REVIEW; IS THAT RIGHT?

A YES. YES. THEY CALL IT FREQUENTATIVE. THAT'S EXACTLY WHAT THAT IS.

Q OKAY.

A YEAH, ONE SIDE IS BAYESIAN, THE ONE IS FREQUENTATIVE.

Q OKAY. AND FREQUENTATIVE, THAT'S BASICALLY ODDS RATIO AND THE RISK RATIOS THAT WE SEE MOST OF THE TIME IN THESE STUDIES; IS THAT RIGHT?

A THAT'S -- YEAH, THAT'S MORE SIMPLE P VALUE IS 95 PERCENT CONFIDENCE INTERVALS, ET CETERA, ET CETERA.

WHILE THE BAYESIANS ARE ALLOWING FOR PRIOR KNOWLEDGE AND THEY SET THEIR -- THEY MORE CLEARLY STATE THEIR ASSUMPTIONS, AND EVEN SOMETIMES, INCLUDE PRIOR DATA INTO THEIR ANALYSES.

Q I SEE.

ALL RIGHT. WELL, WHAT THEY SAY HERE IN THE

MORE COMMON LINEAR REGRESSION ANALYSIS IS THAT HIGHER GESTATIONAL LEVELS OF LEAD, CADMIUM, DYSPANOL A, MONO 3 CARBOECIDEPROPYL PHTHALATE--

A PHTHALATE. YEAH. IT'S PHTHALATE, UM-HMM.

Q OKAY.

ALL THOSE CHEMICALS WERE ASSOCIATED WITH HIGHER MEAN SRS SCORES.

DO YOU SEE THAT?

A YES.

Q AND THOSE AT HIGHER MEAN SRS SCORES, THOSE ARE SCORES THAT HAVE IDENTIFIED AUTISTIC BEHAVIORS; RIGHT?

A YES.

Q OKAY.

AND THEN LATER ON, THEY MENTION THAT ARSENIC, CADMIUM, LEAD, AND A BUNCH OF OTHER STUFF, HAD SIGNIFICANTLY SIGNIFICANT DEVIATIONS FROM HOMOSCEDASTICITY AFTER ADJUSTING FOR CONFOUNDERS.

DO YOU SEE THAT?

A YES.

Q WOULD IT BE FAIR TO SAY, THEN, THAT USING THE TRADITIONAL, SORT OF, REGRESSION ANALYSIS THAT ARE USED ROUTINELY, THEY FOUND THAT THERE WAS A HIGHER -- THERE WAS AN ASSOCIATION BETWEEN LEAD AND ASD BEHAVIORS?

A YES.

Q OKAY.

AND THEN ON THE DISCUSSION SECTION, I FOUND THIS PARTICULARLY INTERESTING, THEY SAID, "WE DISCUSSED

A RELATIONSHIP BETWEEN GESTATIONAL EXPOSURE TO

VARIOUS TOXICANTS AND AUTISTIC BEHAVIORS MEASURED WITH SRS AND PRESCHOOL AGED COMMUNITY AND CHILDREN USING BAYESIAN QUANTILE REGRESSION. WE FOUND THAT ASSOCIATIONS BETWEEN SRS SCORES AND MATERNAL CONCENTRATIONS OF CADMIUM LEAD AND SOME" --

A PHTHALATE.

Q YEAH, THANK YOU.

"-- METABOLIZED IN BLOOD OR URINE WERE THE STRONGEST, THE HIGH END, OF THAT SRS DISTRIBUTION."

DO YOU SEE THAT?

A YES.

Q AND THEN THEY FINISH IT OFF WITH, "IN OTHER WORDS, OUR RESULTS SUGGEST THAT CHILDREN WITH THE MOST AUTISTIC-LIKE BEHAVIORS WHO ARE OF GREATER CLINICAL INTEREST, APPEAR TO BE PARTICULARLY SUSCEPTIBLE TO THESE TOXICANTS."

DO YOU SEE THAT?

A YES.

Q CAN YOU JUST EXPLAIN WHAT WE JUST READ AND WHAT THESE AUTHORS ARE TELLING US?

A SO WHAT THEY ARE DOING IS, THEY ARE USING A MUCH MORE ADVANCED STATISTICAL METHOD TO NOT ONLY SUMMARIZE ACROSS SO THAT THEY ARE ABLE TO PUT MULTIPLE TOXINS INTO THE SAME MODELS, AND AT THE SAME TIME, DISTINGUISH, IN THEIR ANALYSIS, BETWEEN DIFFERENT LEVELS OF THE OUTCOME. BECAUSE WE HAVE A CONTINUOUS MEASURE

FOR THE OUTCOME, THERE'S SOCIAL RESPONSIVENESS SCORE. SO YOU CAN BE VERY HIGH ON THE NOT-SO-GOOD RESPONSE TO SOCIAL CUES, AND YOU CAN BE VERY LOW.

AND WHAT THEY ARE SAYING IS, THE RELATIONSHIP IS NON-LINEAR IN A SENSE THAT YOU GET MUCH HIGHER ASSOCIATIONS WITH WORSE OUTCOMES AT THE HIGHER END.

Q AND AS AN EPIDEMIOLOGIST, WHEN YOU SEE SUCH A TARGETED EFFECT OF METALS IN MAKING A PARTICULARLY DISTINCT OUTCOME, LIKE WORSE SCORES, WHAT DOES THAT TELL YOU ABOUT THE STRENGTH OF ASSOCIATION?

A WELL, THIS STUDY SPECIFICALLY SAYS THAT THERE IS AN ASSOCIATION AND IT'S STRONGER FOR THE PEOPLE WITH THE WORST OUTCOME. BUT MORE IMPORTANTLY, THEY ARE ACTUALLY TAKING INTO ACCOUNT A LOT OF OTHER EXPOSURES THAT ALSO MAY BE NEUROTOXIC, AND THAT'S REALLY IMPORTANT AS WELL IN THIS STUDY.

Q SO AGAIN, GOING BACK TO THIS CHART, BEING THAT THIS STUDY DID LOOK AT MATERNAL BLOOD, SO IT PREDATES ANY DIAGNOSIS OR CHARACTERISTICS OR BEHAVIORS; DOES THIS SUPPORT TEMPORALITY?

A YES.

Q ALL RIGHT.

LET'S TAKE A LOOK AT DOHERTY.

NOW, THE DOHERTY STUDY IS FROM 2020, AND THIS WAS PUBLISHED IN THE ISEE.

DO YOU SEE THAT?

A YES.

Q DO YOU KNOW WHAT THE ISEE IS?

A YES, I'VE BEEN THE PRESIDENT OF IT FOR A FEW YEARS. THAT'S THE INTERNATIONAL SOCIETY FOR ENVIRONMENTAL EPIDEMIOLOGY, AND THIS IS ONE OF OUR PRIME JOURNALS THAT'S ALLOWED TO USE OUR LOGO.

Q OKAY.

AND THE TITLE HERE IS "PERI-CONCEPTIONAL AND PRENATAL EXPOSURE TO METAL MIXTURES IN RELATION TO BEHAVIORAL DEVELOPMENT AT THREE YEARS OF AGE."

DO YOU SEE THAT?

A YES.

Q NOW, WE'VE GONE OVER THIS STUDY. THE DEFENDANTS COVERED IT.

THIS STUDY DID NOT SHOW ANY ASSOCIATION -- DID NOT SHOW A POSITIVE -- OR A SIGNIFICANT ASSOCIATION BETWEEN LEAD AND ASD; RIGHT?

A CORRECT. ACCORDING TO THE TOENAIL METAL CONCENTRATIONS.

Q THAT'S RIGHT.

NOW, LET ME JUST GET TO THE CONCLUSION. ALL RIGHT. SOMETIMES IT DOES THIS.

CAN YOU SEE IT NOW?

A YES.

Q OKAY. SO HERE, AFTER REFLECTING THAT THERE WAS NO ANALYSIS, THE AUTHORS COMMENT ON IT.

THEY SAY "IN ADDITION TO THESE FINDINGS, WE ALSO OBSERVED ASSOCIATIONS THAT ARE NOT SUPPORTED BY THE PRIOR LITERATURE, INCLUDING THE LACK OF ADVERSE ASSOCIATIONS OF LEAD."

DO YOU SEE THAT, DOCTOR?

A YES.

Q WHAT ARE THEY SAYING HERE?

A WELL, THEY ARE SAYING THEY ARE VERY SURPRISED THAT IN THIS STUDY THEY ARE NOT SEEING THE EXPECTED ASSOCIATION, WHICH THEY EXPECT AS POSITIVE, BETWEEN LEAD AND THE OUTCOME.

Q SO THE AUTHORS THEMSELVES ARE SAYING, THIS IS INCONSISTENT WITH WHAT WE'RE SEEING IN THE LITERATURE?

A YES. AND THEY ACTUALLY KEEP GOING AND THEY ARE TRYING TO GIVE YOU SOME REASON WHY THAT'S THE CASE.

Q PRECISELY.

AND I'M ACTUALLY GOING TO GO THROUGH THAT.

THEY SAY "THE EXPLANATION FOR THESE UNEXPECTED FINDINGS IS UNCLEAR, THOUGH, THEY MAY BE PARTIALLY ATTRIBUTABLE TO RESIDUAL CONFOUNDING BY, FOR EXAMPLE, UNMEASURED LIFESTYLE FACTORS. ADDITIONALLY, SUCH RESULTS MAY BE OWING TO CHANCE, AS WE DID NOT CORRECT FOR MULTIPLE TESTING, OWING TO DEPENDENCE AMONGST OUTCOMES, AND POTENTIAL LEAD EXPOSURES, AND BECAUSE THIS WAS AN EXPLORATORY ANALYSIS."

DO YOU SEE THAT?

A YES.

Q SO, I MEAN, DOCTOR, THIS NULL FINDING, WHEN THE AUTHORS GO OUT OF THEIR WAY TO TRY TO EXPLAIN WHY IT'S INCONSISTENT WITH THE REST OF THE LITERATURE, WHAT DOES THAT TELL YOU AS A RESEARCHER?

A WELL, IT TELLS ME TO TAKE THIS WITH A GRAIN OF SALT BECAUSE THAT'S WHAT THE AUTHORS ARE TELLING ME.

Q OKAY.

SO I'M GOING TO PUT IN NULL HERE FOR DOHERTY.

IS THAT APPROPRIATE?

A YES.

Q OKAY.

FINALLY, WE HAVE THE KIM STUDY FROM 2016, AND I DON'T -- WE'VE TALKED ABOUT IT, SO I DON'T NEED TO GO THROUGH IT WITH YOU IN DETAIL.

I GUESS THE QUESTION, DOCTOR, IS: DOES THE KIM STUDY SUPPORT TEMPORALITY OR REFUTE IT OR IS IT NULL?

A IT ABSOLUTELY SUPPORTS IT.

Q AND WHY IS THAT, BRIEFLY?

A THE EXPOSURE MEASUREMENTS WERE PRIOR TO THE OUTCOME ASSESSMENT, AND THEY CLEARLY HAD ENOUGH LAG TIME BETWEEN THE AGE OF 7 AND THE AGE OF 12, AND IT'S A LARGE COHORT AND IT WAS REALLY WELL DONE. IT WAS DONE IN TEN DIFFERENT CITIES IN KOREA, AND I KNOW THE PEOPLE WHO DID THIS STUDY. THEY ARE EXTREMELY GOOD SCIENTISTS AND MEMBERS OF THAT INTERNATIONAL SOCIETY.

Q SO, DOCTOR, WHEN YOU TAKE ALL OF THESE ALL THESE STUDIES THAT THE DEFENDANTS SPECIFICALLY IDENTIFIED AS RELATING TO THE TEMPORALITY ASPECT OF LEAD AND ASD, WHEN YOU LOOK AT ALL THIS, DOES THIS CORPUS OF DATA SUPPORT TEMPORALITY OR UNDERMINE IT?

A WELL, IT OVERALL SUPPORTS IT.

Q OKAY.

NOW, DOCTOR, I'D LIKE TO BRIEFLY -- I'M ABOUT TO WRAP UP HERE. I KNOW WE'VE BEEN GOING FOR A BIT.

I'D LIKE TO SORT OF WALK THROUGH CONCEPTUALLY HOW YOU DID THIS SO THERE'S NO AMBIGUITY BECAUSE THIS IS POTENTIALLY THE LAST TIME I GET TO TALK TO YOU ON THIS RECORD.

SO YOU SEE A BLACK SCREEN IN FRONT OF YOU?

A YES.

Q OKAY. GREAT.

SO I'M GOING TO -- HERE'S WHAT WE'RE GOING TO DO. WE'RE GOING TO TALK ABOUT TEMPORALITY, OKAY.

AND WE'RE GOING TO -- WE HAVE A LITTLE TIMELINE HERE.

AND THE IDEA HERE IS THAT, AT SOME POINT, SOMEBODY WILL GET ASD.

DO YOU SEE THAT, DOCTOR?

A YES.

Q AND THEN, FOR SOME OF THESE STUDIES AND, OBVIOUSLY, WE JUST WENT THROUGH A BUNCH OF THEM WHERE THAT WASN'T THE CASE, BUT FOR SOME OF THESE STUDIES, THERE WAS A MEASUREMENT OF THE BIOMARKER THAT WAS, AT SOME POINT, AFTER THE ASD, AND IT COULD BE EVEN SOME YEARS; RIGHT?

A YES.

Q OKAY.

NOW, THE QUESTION OF TEMPORALITY, RIGHT, IS WHETHER OR NOT THIS BIOMARKER IS GETTING YOU AN IDEA OF WHAT THE EXPOSURES WERE BEFOREHAND; RIGHT?

A YES.

Q AND IN EPIDEMIOLOGICAL TERMS, THIS IS OFTEN CALLED A PROXY; RIGHT?

A YES.

Q AND SO YOU HAVE TO DECIDE, AS A EPIDEMIOLOGIST, IS: ARE THESE BIOMARKERS THAT WE'RE SEEING SHOWING THAT CHILDREN WITH ASD HAVE LARGE AMOUNTS OF LEAD IN THEIR URINE AND BRAINS AND, YOU KNOW, TEETH AND WHATEVER, RIGHT? IS THIS GETTING ME TO WHETHER OR NOT THAT EXPOSURE IS A REFLEXION OF PRIOR EXPOSURES; RIGHT?

A CORRECT. YES. CORRECT.

Q AND IN TRYING TO ASSESS THAT, THE FIRST PLACE YOU WOULD PROBABLY LOOK IS PRECISELY AT THESE STUDIES WHERE THERE WAS AN ASSESSMENT AT THE BEGINNING; RIGHT?

A YES, PRIOR TO ONSET.

Q THAT'S RIGHT.

AND THERE WE HAVE ALL THE STUDIES THAT WE JUST LOOKED AT; SKOGHEIM --

A KIM.

Q -- FRYE. I'LL DO KIM IN A SECOND BECAUSE KIM COMES LATER.

A OKAY.

Q WE HAVE ARORA, LONG, DOHERTY, ABDULLAH, AND OBVIOUSLY, NOT ALL OF THESE ARE SUPPORTED; SOME OF THEM ARE NULL.

BUT WE HAVE ALL THESE STUDIES THAT HAVE PRENATAL EXPOSURES, AND AS WE JUST WENT THROUGH, ALL OF THEM ACTUALLY VERY MUCH DO SUPPORT TEMPORALITY; RIGHT?

A YES.
Q OKAY.
WE ALSO, IF I RECALL, WE HAVE A STUDY CALLED KIM; RIGHT?
A YES.
Q AND KIM LOOKED AT BIOMARKERS LATER ON IN LIFE AND THEN, LATER ON IN LIFE, AND FOUND ASD BEHAVIORS; RIGHT?
A YES.
Q OKAY.
SO WHEN YOU HAVE ALL THIS DATA, YOU HAVE ALL THESE STUDIES THAT PREDATE EXPOSURE, YOU HAVE ALL THE STUDIES THAT HAVE THIS BIOMARKER LATER ON IN TIME, AND YOU HAVE EVEN A LATER STUDY SHOWING, PROSPECTIVELY, THE EFFECT OF LEAD ON ASD BEHAVIORS, DOES IT TAKE, IN YOUR MIND, A LEAP OF LOGIC OR CONJECTURE TO GET TO YOUR CONCLUSION ABOUT TEMPORALITY?
A NO.
Q WHY IS THAT?
A BECAUSE NOW MY PROXY BIOMARKER TELLS ME SOMETHING ABOUT EXPOSURES IN THE LONG-TERM, AND THE ONLY REASON WHY IT WOULDN'T IS IF I PRESUME THAT IT'S NOT A LONG-TERM MARKER AND THAT EVERY ASD KID IN EVERY COUNTRY AROUND THE GLOBE WOULD BE PRONE TO DO THINGS THAT WOULD INCREASE THEIR LEAD LEVEL WHILE ALL THE OTHER KIDS DON'T.
Q AND IN YOUR REVIEW AND CONSIDERATION OF THIS ISSUE AND YOU LOOK AT THE PROSPECTIVE DATA, DOES IT MAKE

SENSE THAT ALL THIS IS EXPLAINED BY SOME BEHAVIOR, OR IS IT MORE LIKELY A CAUSAL AGENT?

A IT'S NOT THE -- IT CANNOT BE EXPLAINED JUST BY BEHAVIOR BECAUSE THE SOURCES OF LEAD IN EVERY COUNTRY, IN EVERY STUDY, ARE DIFFERENT. WE DON'T ALWAYS HAVE THE SAME SOURCES.

IF WE HAVE WATER AS THE SOURCE THEN, YOU KNOW, IT DOESN'T MATTER WHETHER THE CHILD HAS HAND-MOUTH BEHAVIOR. WE EVEN SAW ONE STUDY IN ARIZONA THAT CLEARLY SHOWED THAT CHILDREN WHO HAD PICA BEHAVIOR, HAND-MOUTH BEHAVIOR, WITH PICA DID NOT HAVE HIGHER LEAD LEVELS THAN THE KIDS WHO DIDN'T HAVE IT.

SO CLEARLY, THE SOURCE OF LEAD WAS SOMETHING DIFFERENT FROM THE PICA. AND THAT'S -- YOU KNOW, IN SOME PLACES PICA MIGHT BE IT, HAND-MOUTH BEHAVIOR MIGHT BE IT, I AGREE, BUT NOT IN EVERY PART OF THE WORLD WITH SO MANY DIFFERENT STUDIES.

Q THANK YOU, DOCTOR.

MR. WISNER: NO FURTHER QUESTIONS AT THIS TIME.

MR. PETROSINELLI: YOUR HONOR, MAY I HAVE A COUPLE OF QUESTIONS?

THE COURT: I WAS MUTING NOT TO SNEEZE.

MR. PETROSINELLI: JUST TO FOLLOW-UP ON A COUPLE OF THE THINGS MR. WISNER JUST DID.

COULD WE PUT UP EXHIBIT 682.

NO. 682, THE CHART.

RE-CROSS EXAMINATION

MR. PETROSINELLI:

Q DOCTOR, I JUST WANTED TO ASK YOU SINCE MR. WISNER JUST ASKED YOU ABOUT THIS, BUT THEN HE WROTE ALL OVER MY CHART, WHICH MADE ME FEEL VERY BAD.

JUST TO BE CLEAR, IN THE RIGHT COLUMN, WHICH IS WHETHER OR NOT THERE'S A STATISTICALLY SIGNIFICANT ASSOCIATION BETWEEN THE EXPOSURE BEING MEASURED AND EITHER THE ASD DIAGNOSIS OR THE ASD BEHAVIOR, THAT -- WHAT'S LISTED IN THAT COLUMN IS CORRECT, THAT IS SIX OF THE EIGHT STUDIES DO NOT HAVE A STATISTICALLY SIGNIFICANT ASSOCIATION BETWEEN THE LEAD EXPOSURE AND THE DIAGNOSIS; CORRECT?

A THIS IS NOT THE RIGHT WAY TO LOOK AT DATA. I NEVER JUST COUNT STUDIES AND SAY IT'S A DECISION-MAKING TOOL YES/NO. SCIENCE IS NOT DECISION-MAKING. SCIENCE MEANS, IN OUR FIELD, THAT YOU'RE ESTIMATING EFFECT SIZES AND, YES, YOU GIVE CONFIDENCE INTERVALS.

I CAN LIST A HUNDRED STUDIES THAT ARE NON-SIGNIFICANT, EACH AND EVERY ONE OF THEM. IF I THEN DO A POOLED OR A META ANALYSIS, I MAY ACTUALLY COME UP WITH THE EXACT SAME OVERALL POINT ESTIMATE THAT NOW, BECAUSE I HAVE ACTUALLY SUFFICIENT SAMPLE SIZE, IS STATISTICALLY SIGNIFICANT.

DO THE TWO THINGS TELL ME TWO DIFFERENT THINGS? NO.

Q DOCTOR -- DOCTOR, I APPRECIATE YOUR POSITION ON THAT AND I UNDERSTAND IT. I JUST WANT YOU TO CONFIRM

FOR ME THAT IT IS IN FACT ACCURATE THAT THOSE -- THE SIX OF THOSE EIGHT STUDIES DO NOT SHOW A STATISTICALLY SIGNIFICANT ASSOCIATION; CORRECT?

A YOU NEED TO SHOW ME THOSE STUDIES AND SHOW ME WHAT YOU'RE REFERRING TO BECAUSE THIS IS JUST NOT SCIENCE.

Q OKAY. WELL, I DON'T HAVE TIME TO SHOW YOU SIX STUDIES, BUT I'LL SHOW YOU ONE OF THEM, BECAUSE YOU JUST TALKED ABOUT IT WITH MR. WISNER JUST AS AN EXAMPLE OF WHAT'S ON THIS CHART.

FRYE, 2020, WHICH IS FROM THE ARORA GROUP THAT YOU JUST WALKED WITH MR. WISNER. THAT'S EXHIBIT 628. LET'S JUST LOOK AT THAT AS ONE EXAMPLE.

YOU SAID, WITH MR. WISNER JUST NOW, THAT SUPPORTED YOUR VIEW ON TEMPORALITY; CORRECT?

A YES.

Q OKAY.

LET'S LOOK AT THE RESULTS OF THE STUDY, WHICH IS ON PAGE 5 UNDER THE TITLE "RESULTS."

AND THE FIRST PARAGRAPH UNDER RESULTS -- CAN WE BLOW THAT UP. NO?

THEY COMPARED THE CONCENTRATION OF METALS IN THE TEETH. WE TALKED ABOUT THE TEETH STUDY.

"THERE WERE NO DIFFERENCES IN TOOTH METAL CONCENTRATIONS IN THE PRENATAL OR POST-NATAL PERIOD BETWEEN THOSE WITH AND WITHOUT THE DISEASE."

A NDR.

Q AND IT -- RIGHT. THAT'S ONE RESULT. THAT'S CORRECT; RIGHT? THAT'S WHAT THEY SAY?

A YES.

Q AND THEN LET'S LOOK AT THE LEAD IN ASD RESULTS, WHICH ARE IN SUPPLEMENTARY TABLE S2.

LET'S BLOW UP THAT CHART AT THE TOP BECAUSE IT'S VERY HARD TO READ. BUT THESE ARE, IN FACT, THEIR RESULTS.

"THE METAL CONCENTRATIONS COMPARING CHILDREN WITH ASD CHILDREN, CHILDREN WITHOUT ASD, CHILDREN WITH DEVELOPMENTAL REGRESSION, AND THE CONTROLS."

DO YOU SEE THAT'S -- THIS IS THEIR RESULTS; CORRECT?

A YES, IT LOOKS LIKE IT.

Q OKAY. AND THEN LET'S HIGHLIGHT THE COLUMN TO THE RIGHT, WHICH IS LEAD PB; RIGHT?

A YES.

Q THAT'S LEAD.

AND YOU SEE IN THE HEADER TO THE CHART AT THE LAST SENTENCE, SAYS "SIGNIFICANT DIFFERENCES ARE BOLDED AND UNDERLINED."

DO YOU SEE THAT?

A YES. BUT THEY ARE USING THAT .50 CRITERIA. THEY ARE NOT GIVING YOU THE CONFIDENCE INTERVAL. YOU DON'T KNOW WHAT IS WHAT. I CAN'T TELL FROM THIS.

Q OKAY. YOU CAN'T -- WHEN THEY SAY "SIGNIFICANT DIFFERENCES ARE BOLDED AND UNDERLINED," YOU CAN'T TELL

WHETHER THAT MEANS STATISTICAL SIGNIFICANCE; IS THAT WHAT YOU'RE SAYING?

A YES.

Q OKAY.

WHATEVER THEY MEAN BY THAT, WE CAN LOOK THE WHAT THE AUTHORS SAID, THEY DIDN'T BOLD OR UNDERLINE ANY OF THE LEAD RESULTS; CORRECT?

A THAT MAKES NO DIFFERENCE BECAUSE USING A STATISTICALLY SIGNIFICANT ONLY CRITERION IS NOT SCIENCE, AND THEY ARE NOT TRYING HERE TO DO WHAT THEY DID IN THE OTHER STUDY, WHICH IS TO DETERMINE, YOU KNOW, LEAD EXPOSURES IN CHILDREN BEING HIGHER OR LOWER WHO ARE GENETICALLY RELATED.

HERE THEY ARE GOING AFTER MECHANISMS. SO THEY ARE TRYING TO FIGURE OUT WHETHER THERE IS BIOENERGETIC DIFFERENCES, NOT WHETHER OR NOT THERE ARE DIFFERENCES IN LEAD, BUT WHETHER LEAD CONTRIBUTES TO THOSE BIOENERGETIC DIFFERENCES.

Q OKAY. DOCTOR, THANK YOU VERY MUCH. I DON'T HAVE ANYTHING FURTHER.

THE COURT: ALL RIGHT. ARE WE READY TO RELEASE THE WITNESS, THEN?

MR. WISNER: YES, YOUR HONOR, PLEASE. THANK YOU.

THE COURT: ALL RIGHT. THANKS AGAIN, DR. RITZ. AGAIN, THANKS FOR YOUR PATIENCE.

THE WITNESS: NO PROBLEM.

THE COURT: YOU'RE EXCUSED.

THE WITNESS: THANK YOU. THANK YOU. HAVE A GOOD WEEKEND.

MR. PETROSINELLI: YOU TOO.

THE COURT: THANK YOU.

SO WHAT'S NEXT?

MR. PETROSINELLI: I THINK, YOUR HONOR, WHAT WE WERE GOING TO ADDRESS IS THE ISSUE OF THE DEFENSE EXPERTS AND THE DAY WE HAVE SET ASIDE ON MARCH 4TH. ACTUALLY, MS. FREIWALD IS GOING TO ADDRESS THAT FOR US. SO I'M GOING TO SLIDE OUT OF THE CHAIR, I'M HERE WITH HER, AND LET HER COME INTO THE CHAIR. AND ALSO, HER SCARF IS A LOT PRETTIER THAN MY TIE, I'LL TELL YOU THAT.

MS. FREIWALD: GOOD AFTERNOON AGAIN, YOUR HONOR.

THE COURT: HI. THANKS.

MS. FREIWALD: SO WE UNDERSTAND THAT MR. WISNER WOULD LIKE TO REVISIT THIS ISSUE. I THINK THERE'S BASICALLY TWO THINGS I WANT TO ADDRESS TO THE COURT.

I MEAN, THE FIRST ISSUE IS JUST KIND OF A FUNDAMENTAL FAIRNESS ONE.

WE HAVE BEEN EXPECTING SINCE I, YOU KNOW, FOR QUITE SOMETIME NOW, THAT WE WOULD HAVE AN OPPORTUNITY TO HAVE THE COURT HEAR FROM OUR EXPERTS. WE AGREED TO, YOU KNOW, VERY TIGHT EXAMINATIONS, EXPECTING THAT THERE WOULD BE THINGS THAT OUR EXPERTS COULD FILL OUT BECAUSE, FRANKLY, YOU KNOW, TO DO EXAMINATIONS OF THE PLAINTIFF'S EXPERTS WHERE YOU PUT A WHOLE LOT OF STUDIES IN FRONT OF THEM THAT THEY HAVEN'T SEEN, THEY HAVEN'T CONSIDERED,

THEY HAVEN'T USED AS PART THEIR METHODOLOGY, WOULD BE BOTH EXTRAORDINARILY TIME-CONSUMING AND PROBABLY EXTRAORDINARILY TEDIOUS AND PROBABLY NOT VERY HELPFUL TO THE COURT.

SO WHAT WE THOUGHT WE WOULD BE DOING IS, YOU KNOW, WHAT WE DID, WHICH IS ADDRESSING THE ISSUES THAT THEIR EXPERTS ARE ADDRESSING, TRYING TO ILLUMINATE THE ISSUES OF METHODOLOGY AND THE ANALYTICAL LEAPS.

AND WE WOULD LIKE THE OPPORTUNITY TO CONTINUE ON THAT PLAN SUBSTANTIVELY. ALSO, THE REASON WE THINK IT IS SO IMPORTANT IS NOT, AND I REALLY WANT TO EMPHASIZE THIS, BECAUSE WE HAVE A DESIRE TO BRING EXPERTS IN TO REHASH THE STUDIES THAT YOU'VE ALREADY HEARD ABOUT.

THE THING THAT IS SO, TO ME, EXTRAORDINARY, YOU KNOW, I THINK MOST OF US HAVE BEEN DOING THIS FOR A LONG TIME, EXTRAORDINARY ABOUT THIS LITIGATION, USUALLY THERE IS A FAIR BIT THAT IS UNDERSTOOD ABOUT THE UNDERLYING DISEASE AND YOU'RE, KIND OF -- YOU'RE WORKING ON SOME SCIENTIFIC LEVEL OF AGREEMENT ABOUT WHAT THE UNDERLYING SYNDROME IS AND WHAT ITS SPECIFIC CAUSES ARE, EVEN MECHANISTIC CAUSES, LIKE HEART ATTACKS, YOU KNOW, YOU HAVE CHOLESTEROL, IT BREAKS OFF, ET CETERA, YOU GET A CLOT.

AND HERE, WE HAVE A DISEASE STATE THAT IS REALLY POORLY UNDERSTOOD, AND TO SAY THAT THIS IS JUST A MATTER OF WHETHER YOU ALLOCATE X PERCENT TO GENETICS OR Y PERCENT TO ENVIRONMENT, ISN'T DOING IT JUSTICE.

AND THE COURT HAS HEARD FROM A CLINICAL ASD PRACTITIONER, BUT NOT SOMEBODY WHO IS STEEPED IN RESEARCH, HEARD FROM TWO EPI'S WHO ARE NOT ASD EXPERTS. I MEAN, DR. RITZ IS A GENERAL PHYSICIAN. SHE HASN'T PRACTICED MEDICINE FOR AS LONG AS SHE'S BEEN IN THIS COUNTRY BECAUSE SHE'S NOT LICENSED IN THIS COUNTRY. BUT EVEN AT THAT, SHE'S A GENERAL DOCTOR. AND A TOXICOLOGIST WHO, YOU KNOW, I THINK THE RECORD WILL REFLECT, HAS ADMITTED IS NOT AN ASD EXPERT.

WE HAVE TWO OF THE WORLD'S LEADING ASD EXPERTS; ONE IS IN THE L.A. AREA, ONE IS IN PORTLAND. AND IT SEEMS TO US EXTRAORDINARILY VALUABLE FOR THE SARGON QUESTIONS IS THERE SCIENTIFICALLY RELIABLE EVIDENCE, WHAT ARE THE ANALYTICAL LEAPS FOR THE COURT TO BE ABLE TO UNDERSTAND HOW AN ASD EXPERT WOULD INTEGRATE THIS DATA IN TERMS OF WHAT IT ALREADY KNOWS. WHAT DO WE REALLY KNOW ABOUT THE BRAIN SCIENCE? WHAT DO WE REALLY KNOW ABOUT LARGER OR SMALLER BRAINS? WHAT DO WE REALLY KNOW ABOUT AGE OF ONSET? WHAT ARE WE REALLY -- WHERE ARE WE REALLY HEADING ON GENETICS?

AND SO OUR ASK IS THAT WE STAY WITH THE PLAN. IT IS NOT TO CREATE A RECORD WHERE THERE'S ANY WEIGHING OF EVIDENCE. IT'S REALLY TO TRY TO ADDRESS THIS ANALYTICAL GAP ISSUE, AND WE WOULD LIKE TO DO IT WITH, YOU KNOW, SOME -- WE COULD DO IT WITH SOME VERY LIMITED TIME CONSTRAINTS WITH OUR EXPERTS, AND WE WOULD -- WE BELIEVE THAT IT WOULD BE VALUABLE TO THE COURT IN THE SARGON CONTEXT.

THE COURT: OKAY. THANK YOU.

DID YOU WANT TO RESPOND, MR. WISNER?

MR. WISNER: YES, YES, YOUR HONOR. I JUST WANT TO START OFF FIRST WITH THE ACTUAL RECORD.

SO WHEN WE DISCUSSED THIS ORIGINALLY, WE DID NOT AGREE THAT WE WOULD HEAR FROM THE EXPERTS. THE COURT SAID, AND I'LL QUOTE IT, BECAUSE I HAVE THE TRANSCRIPT IN FRONT OF ME. IT SAID, "LET ME HEAR THE PLAINTIFF'S EXPERTS AS WE PLANNED TO DO AND, AT THAT POINT, LET'S TALK ABOUT WHAT COMES NEXT. AND I MAY ASK THE DEFENDANTS TO GO FOR AN OFFER OF PROOF OR MAY JUST GO INTO EXPERT DISCOVERY OF THE DEFENSE EXPERTS IN FURTHER HEARING."

SO I JUST WANT TO MAKE IT CLEAR THAT ANY SORT OF ASSERTION THAT WE HAD AN AGREEMENT THAT THE DEFENDANTS WERE GOING TO TESTIFY IS NOT TRUE. WE ACTUALLY SPECIFICALLY SAID WE'D GET TO THIS DAY AND HAVE THIS EXACT CONVERSATION. SO I DON'T WANT TO -- DON'T LET MOMENTUM BE IT, BECAUSE THE MOMENTUM WAS, WE DON'T KNOW, AND THAT HAS BEEN THE CASE FROM THE BEGINNING.

BUT I THINK, MORE IMPORTANTLY, YOUR HONOR, IS YOU KNOW, WE'VE REALLY GONE VERY FAR OUTSIDE OF THE TEN YARD LINES OF WHAT IS SARGON, YOU KNOW.

SARGON IS ASKING: ARE THE CONCLUSIONS REACHED BY OUR EXPERTS BASED UPON CONJECTURE, LEAPS OF LOGIC, ARE THEY BASED ON PEER-REVIEWED LITERATURE, AND IS THERE A REASONABLE BASIS FOR THEM TO COME TO THE CONCLUSIONS THAT THEY DO?

WHAT THE DEFENDANTS HAVE DONE FOR ALMOST 90 PERCENT OF THEIR CROSS EXAMINATION, AND WHAT THEY INTEND TO DO BY CALLING THEIR EXPERTS, IS GO INTO THE WOLF AND WARP OF THE MERITS. TO GO INTO THE CONTROVERSY THAT DR. ASCHNER SO APTLY POINTED OUT TO THE COURT TODAY ON CROSS EXAMINATION. YES, THERE IS A CONTROVERSY.

AND THE SUPREME COURT OF CALIFORNIA HAS BEEN ABUNDANTLY CLEAR, THIS COURT DOES NOT DECIDE CONTROVERSIES. IT DOESN'T. THAT'S NOT -- IT'S NOT -- THAT'S NOT THE ROLE OF THE TRIAL COURT. THE TRIAL COURT HERE IS TO EXCLUDE, AS YOUR HONOR PUT IT ONCE, VOODOO SCIENCE.

AND I THINK WE HAVE A PRETTY CLEAR RECORD HERE ABOUT WHETHER OR NOT THE EXPERTS WHO ARE ON THE CHOPPING BLOCK, RIGHT, THE ONES WHO ARE UP FOR EXCLUSION, WHETHER OR NOT THE COURT CAN ASSESS WHETHER THEIR OPINIONS ON THE FOUR CORNERS OF THEIR REPORT, ON THE 40 HOURS OF DEPOSITION THAT HAVE HAPPENED, AND IN THE VERY LENGTHY HEARINGS THAT WE'VE HAD HERE, IS ENOUGH TO MAKE THAT CALL.

BY INVITING THE DEFENSE EXPERTS TO COME IN AND DISAGREE WITH OUR EXPERTS, IS EFFECTIVELY WHAT IT IS, IS INVITING THE COURT TO WEIGH IN ON A CONTROVERSY, TO SIT IN THE SEAT OF A TRIER-OF-FACT AND IT INVITES ERROR, AND I JUST DON'T THINK THAT'S THE RIGHT MOVE.

YOUR HONOR, HAS A HUNDRED-AND-SOMETHING PAGES OF BRIEFING, THOUSANDS OF PAGES OF EXHIBITS, I THINK YOU HAVE ENOUGH TO MAKE A DECISION ABOUT WHETHER OR NOT OUR

FOUR EXPERTS HAVE RENDERED THEIR OPINIONS BASED ON VOODOO SCIENCE OR NOT.

AND, YOU KNOW, MY CLIENT, YOUR HONOR, HAS WAITING NINE MONTHS TO ENGAGE IN DISCOVERY. WE'VE BEEN WAITING SIX MONTHS TO, IN YOUR COURT, FOR THIS SARGON HEARING. AND WHILE, SURE, WE CAN JUST KEEP TACKING ON MORE MONTHS, I WOULD RESPECTFULLY REQUEST THAT WE NOT DO THAT. I'VE BEEN EXCEPTIONALLY REASONABLE, YOUR HONOR. WE HAVEN'T MOVED FOR PREFERENCE. WE HAVE BEEN -- I CONSTANTLY AM TRYING TO BRING COMPROMISES TO THE COURT. WE HAVE SPENT ALL THIS MONEY AND TIME TO DO THIS. I THINK IT'S TIME TO LET US MOVE FORWARD WITH THIS CASE.

AND IF YOU'RE GOING TO EXCLUDE THEM, THEN WE HAVE NO MORE TO ADD TO THE RECORD AT THIS POINT. I THINK YOU CAN GO AHEAD AND ISSUE YOUR ORDER, AND THEN WE'LL TAKE IT UP ON APPEAL OR WHATEVER.

BUT I THINK THE RECORD IS WHERE IT IS AT THIS POINT, AND I THINK WE CAN MOVE FORWARD.

MS. FREIWALD: AND, YOUR HONOR, IF I MAY, I JUST WANT TO BE ABUNDANTLY CLEAR. THE PURPOSE IS NOT TO COME IN AND ASK YOU TO WEIGH, YOU KNOW, EVIDENCE OR TO HAVE EXPERTS DISAGREE.

THERE ARE, WE SAID THIS FROM THE BEGINNING, MAJOR LANES OF RESEARCH THAT THESE EXPERTS SIMPLY HAVE NOT ADDRESSED OR THEY ARE REALLY NOT CAPABLE OF ADDRESSING. I'M NOT SURE IF THIS IS A GREAT ANALOGY, BUT IT'S A LITTLE LIKE, YOU KNOW, YOU'RE AT YOUR FAMILY DOCTOR AND YOU HEAR WHAT IS AVAILABLE IN TREATMENT FOR

SOME DISEASE YOU HAVE, AND YOU THINK THAT IT'S THE WORLD. YOU'RE LOOKING AT IT THIS BIG. AND THEN YOU GO TO THE MAYO CLINIC AND YOU REALIZE THAT THE WORLD IS ACTUALLY THIS BIG OR THIS BIG.

AND WHAT WE HAVE HERE IS A PRESENTATION WHERE YOU'RE HEARING EXPERTS WHO ARE OPINING ON THE POSSIBLE WITHOUT THAT BASIC FLOOR, AND ALL WE WANT IS FOR EXPERTS WHO ARE THE WORLD LEADING EXPERTS IN AUTISM TO BE ABLE TO COME IN AND SAY, THIS IS WHY IT IS A HUGE ANALYTICAL LEAP FROM THE PERSPECTIVE OF WHAT WE KNOW TODAY IN AUTISM RESEARCH.

IF YOU WERE REALLY LOOKING AT WHAT WE KNOW ABOUT WHAT HAPPENS IN UTERO, IF YOU REALLY WERE AN EXPERT IN WHAT HAPPENS IN THE EARLY DEVELOPMENTAL PERIOD, IF YOU REALLY KNEW WHAT THE AREAS OF THE BRAIN WERE, AND THE CONCEPT OF THE SOCIAL BRAIN, AND NOT JUST GUESSING THAT THERE'S GOT TO BE SOMEPLACE ON THE BRAIN THAT MATTERS. IF YOU REALLY DID LOOK AT, YOU KNOW, WHAT THE EPI GENETIC STATE OF THE SCIENCE IS, AND WE THINK WE CAN DO THAT, PROBABLY, IN A COUPLE HOURS TOTAL, AND THAT IT WOULD BE VERY VALUABLE AND, FRANKLY, HELP THE COURT INTEGRATE WHAT YOU'RE HEARING ABOUT THIS MUCH MORE NARROW QUESTION OF, YOU KNOW, JUST LOOKING AT ESSENTIALLY TOXICOLOGY AND ENVIRONMENTAL SCIENCE.

THE COURT: OKAY. THANK YOU.

WELL, THIS IS MY FEELING ABOUT IT: MY FEELING ABOUT IT IS THAT IF YOU'RE OFFERING EXPERT TESTIMONY TO TELL THE COURT HERE ARE THE ANALYTICAL LEAPS OR THE

LEAPS OF LOGIC, THAT I SHOULD HEAR THAT, BECAUSE I'M NOT A SCIENTIST, AND I AM ABOUT 7/8THS THROUGH THINKING FAST AND SLOW, WHICH YOU PROBABLY READ WHEN IT CAME OUT, BUT I'M A LITTLE BEHIND. AND SO THE FRAMING THAT YOU REFERRED TO WAS RINGING A LOT OF BELLS. I'M ACTUALLY LISTENING TO IT ON TAPE, WHICH IS A LITTLE CHALLENGING.

MS. FREIWALD: I'M A BIG FAN OF BOOKS ON TAPE, YOUR HONOR.

THE COURT: ABOUT THE TABLE, YOU KNOW.

BUT ANYWAY, SO I THINK THAT IS FAIR. I THINK IT'S LIMITED IN SCOPE.

AND MY QUESTION, MR. WISNER, IS: DO YOU REALLY NEED TO TAKE THE DEPOSITION BEFOREHAND?

MR. WISNER: I MEAN, HOW CAN I NOT? I MEAN, IT'S REALLY TOUGH FOR ME TO, I MEAN, THEIR EXPERT REPORTS WERE -- YOU HAVE THEM, SO YOU KNOW WHAT THEY ARE GOING TO SAY.

THE COURT: NO. NO, I DON'T KNOW WHAT THEY ARE SAY BECAUSE THEIR ACTUAL REPORTS -- WHAT I'M LIMITING THIS TO IS, YOU KNOW, EXPERT NUMBER 1 SAYS ANALYTICAL GAP NUMBER 1 IS THIS, ANALYTICAL GAP NUMBER 2 IS THIS, LEAP OF LOGIC IS THIS. I DON'T THINK THAT'S IN THEIR REPORTS.

SO I THINK THAT'S WHY YOU NEED TO TAKE THEIR DEPOSITION, BECAUSE YOU WANT TO KNOW WHAT THEY ARE GOING TO SAY IN THIS HEARING, WHICH COULD BE ENTIRELY DIFFERENT THAN WHAT THEY SAY, YOU KNOW, ULTIMATELY IN TRIAL.

SO --

MR. WISNER: I DO ACKNOWLEDGE THAT, YOUR HONOR.

THEIR REPORTS ARE SPECIFICALLY -- OFFER NO AFFIRMATIVE OPINIONS; THEY'RE JUST CRITICISMS OF OUR EXPERTS.

AND SO -- AND THE PROBLEM HERE IS, IT'S GOING TO LEAD TO, OKAY, THEY RAISE SOME CRITICISM THAT I DIDN'T ANTICIPATE IN MY DIRECT.

THE COURT: YEAH.

MR. WISNER: AND THEN --

THE COURT: I --

MR. WISNER: -- AND THEN THEY CROSS THEM ON IT. SO I HAVE TO CALL THEM BACK. THIS IS TURNING INTO A BIT OF A CONGLOMERATION OF TIME. I THINK THEY --

THE COURT: NO, NO. LET'S WALK THROUGH IT, PLEASE.

MR. WISNER: SURE.

THE COURT: COUNSEL HAS OFFERED A TWO-HOUR HEARING. THAT MEANS ALL YOU NEED IS A TWO-HOUR DEPOSITION, OR MAYBE THREE. AND SO I DON'T THINK IT'S TERRIBLY BURDENSOME, AND I THINK IT CAN BE DONE FAIRLY QUICKLY.

AND AS I'VE SAID, I DON'T WANT TO HEAR CRITICISM, PER SE, OF THE STUDIES OR THE CONCLUSIONS THAT THESE EXPERTS HAVE TESTIFIED ABOUT THIS WEEK, BECAUSE YOU COULD -- YOU COULD CERTAINLY -- EXPERTS ARE VERY GOOD AT NITPICKING OTHER EXPERTS. WE ALL KNOW THAT.

WHAT I WANT TO HEAR IS: ARE THERE LEAPS OF LOGIC WHICH THESE EXPERTS THINK THAT I, AS A LAYPERSON, WOULD NOT RECOGNIZE. THAT'S WHAT I'M INTERESTED IN KNOWING. IF THERE ARE, THEN TELL ME, AND MAYBE I'LL UNDERSTAND IT. I FREELY ADMIT I'M A LAY PERSON.

MR. WISNER: YOUR HONOR, I HEAR YOU.

A COUPLE THINGS TO THINK ABOUT. THEY DEPOSED OUR EXPERTS FOR EIGHT, NINE HOURS AND CROSSED THEM FOR AN HOUR. SO THIS IDEA THAT I DON'T NEED TO DEPOSE THEM FOR MORE THAN THE AMOUNT OF TIME THEY ARE GOING TO TESTIFY TO IS JUST NOT HOW THIS WORKS.

THE COURT: I'M NOT SUGGESTING TO RESTRICT YOU. I'M JUST SUGGESTING --

MR. WISNER: I KNOW. I KNOW.

THE COURT: -- PRACTICAL TERMS. THIS IS A MUCH SHORTER HEARING THAN, YOU KNOW, I THINK, THAN THE OTHER HEARINGS WE'VE HAD, BUT.

MR. WISNER: FAIR ENOUGH.

I THINK THERE'S SOME OTHER CONSIDERATIONS, YOUR HONOR.

OKAY. SO THEY COME IN AND THEY SAY, DR. RITZ MADE AN ANALYTICAL LEAP OF LOGIC X, WHICH THEY, BY THE WAY, HAVE ALREADY PUT THIS THEIR BRIEF, IN THEIR CROSSES AND THEIR OPENINGS, AND POTENTIALLY, AT CLOSING ARGUMENT.

SO THE STATEMENT THAT THE COURT HASN'T BEEN SHOWN THOSE POTENTIALLY ANALYTICAL LEAPS OF LOGIC THAT THEY THINK EXIST, IN THIS INCREDIBLE RECORD, IS A BIT

FARFETCHED. THEY HAVE. THEY HAVE SHOWN YOU THEIR BEST HAND. THEY HAD A CHANCE TO WALK DR. RITZ THROUGH ALL OF HER THINGS, AND THEY WROTE A 45-PAGE BRIEF.

THE COURT: LET ME -- LET ME --

MR. WISNER: I'M SORRY.

THE COURT: -- LET ME SAY SOMETHING A LITTLE MORE.

MR. WISNER: OKAY.

THE COURT: MY TENTATIVE THINKING RIGHT NOW IS TO DENY THE MOTIONS TO EXCLUDE.

NOW, I HAVE TO GO THROUGH IN MUCH MORE DETAIL, BUT IF THAT IS THE WAY THE COURT IS LEANING, THEN I THINK I NEED TO ESPECIALLY LET THE EXPERTS ON THE OTHER SIDE TELL ME WHAT I'M MISSING BECAUSE I'M NOT A SCIENTIST. I'M A JUDGE.

MR. WISNER: YOUR THOROUGHNESS IS APPLAUDED. I CAN'T CRITICIZE THAT. SO, FAIR ENOUGH.

THE COURT: YES.

MR. WISNER: I WOULD ASK THIS, YOUR HONOR, THAT, YOU KNOW, AT LEAST IN THE INTERIM, COULD WE OPEN DISCOVERY?

THE COURT: WELL, LET'S TALK ABOUT TIMING.

DID WE -- YOU SAID WE SET ASIDE A DATE, MS. FREIWALD?

MS. FREIWALD: YES, WE DID. MARCH 4TH.

THE COURT: OKAY. SO THAT'S -- WE'RE IN FEBRUARY. SO THAT'S COMING RIGHT UP FROM MY POINT OF VIEW, AND I SEE A DAY BLOCKED OFF. YES. YES, I HAVE

SOME THINGS ON THAT DAY, BUT I CAN MOVE THEM. YES.

SO MY FEELING IS, WE KEEP THAT DAY. WE'VE GOT TO MAKE THE EXPERT AVAILABLE FOR A DAY OF A DEPOSITION OR -- THAT SHOULD BE ADEQUATE. MAYBE IT WILL GO SHORTER. AND I WANT THE WITNESS TO BE PREPARED TO IDENTIFY THE LEAPS OF LOGIC IN A LISTED SORT OF FASHION SO THAT WHEN HE OR SHE TESTIFIES, WE DON'T HAVE SURPRISE ON THE PLAINTIFF'S SIDE.

IS THAT DOABLE?

MR. WISNER: WE CAN OBVIOUSLY MAKE THAT WORK, YOUR HONOR. THAT SHOULDN'T BE A --

THE COURT: NO, I'M ASKING MS. FERWALD.

MS. FREIWALD: I CERTAINLY BELIEVE -- WE'LL HAVE TO KEEP IT TIGHT, OBVIOUSLY, BUT SURE, WE'LL IT WORK.

THE COURT: YEAH. I MEAN, BECAUSE HONESTLY I DID A LITTLE POKING AROUND IN WESTLAW OVER THE LAST COUPLE OF DAYS LOOKING AT -- BECAUSE THE FEDERAL COURTS, OF COURSE, MORE COMMONLY SEE THESE ISSUES THAN WE DO IN THE STATE COURTS. AND I DID -- I WAS PERSUADED THAT THE DISTRICT COURTS OFTEN HEAR FROM THE EXPERTS FOR BOTH SIDES. AND THE WAY YOU FRAMED IT WAS EXACTLY WHAT I HAD IN MIND AS WHAT I SHOULD HEAR AS A MATTER OF FAIRNESS, AND I'M CERTAINLY OPEN TO IT.

MS. FREIWALD: WE APPRECIATE THAT, YOUR HONOR. SO WE WILL -- WE ARE VERY MINDFUL OF WHAT THE CHARGE IS, AND WE'LL ACT ACCORDINGLY.

THE COURT: OKAY.

MR. WISNER: YOUR HONOR, I WOULD REQUEST --

MR. IMBROSCIO: OH, SORRY. GO AHEAD.

MR. WISNER: I WOULD REQUEST IF WE COULD, SINCE WE HAVE A MONTH BETWEEN NOW AND THEN, WE BE ALLOWED TO START SERVING DISCOVERY REQUESTS AND START THE PROCESS. IT WILL TAKE MONTHS TO GET THE DOCUMENTS, I KNOW, BUT AT LEAST START THE PROCESS OF HAVING THAT CONVERSATION AND GETTING RESPONSES GOING.

THE COURT: WELL, THIS IS NOT GOING TO BE A CASE WHERE IF THE PLAINTIFF UNILATERALLY SENDS OUT DISCOVERY REQUESTS AND -- WE'RE NOT IN THE CODE OF CIVIL PROCEDURE SO MUCH, WE'RE IN THE COURT OF COMPLEX LITIGATION IN LOS ANGELES. AND SO, EVEN BEFORE THAT PROCESS WOULD START, I NEED THE PARTIES TO MEET AND CONFER ABOUT THE MOST EFFICIENT WAY TO INITIATE DISCOVERY, AND MAYBE, WE START WITH A PMK DEPOSITION TO FIGURE OUT WHAT THERE IS TO DISCOVER BY WAY OF WRITTEN DISCOVERY.

OFTENTIMES, YOU KNOW, THE PLAINTIFF'S IN THE DARK ABOUT HOW THE DEFENDANT KEEP ITS RECORDS OR WHAT THERE MIGHT BE TO DISCOVER, AND IT'S VERY HARD TO PROPOUND DISCOVERY WHEN YOU DON'T REALLY KNOW WHAT'S THERE OR HOW THIS COMPANY WORKS.

SO THIS IS NOT GOING TO -- IT'S NOT A MATTER OF MY LIFTING THE STAY ON DISCOVERY AND YOU ISSUING HUNDREDS OF INTERROGATORIES OR REQUESTS. WE'RE NOT GOING TO WORK THAT WAY. WE'RE GOING TO WORK TOGETHER, AS I'M SURE YOU'RE VERY FINE LAWYERS ON THE OTHER SIDE,

AND WHO I'M SURE WILL DILIGENTLY WORK TO PULL RECORDS OUT OF THEIR CLIENTS AS APPROPRIATE. IT'S NOT AN EASY JOB WHEN YOU HAVE A BIG CORPORATION.

I'VE JUST BEEN THROUGH THIS IN A -- IT'S BEEN -- COME BACK TO ME HOW DIFFICULT IT IS WORKING THROUGH ONE OF THE CASES I HAVE PRESENTLY, WHICH IS A PREFERENCE CASE WITH A SIMILAR BODY OF EVIDENCE TO BE DISCOVERED. I MEAN, A PREFERENCE CASE WITH A CLOCK TICKING AND ACTUALLY, YOU KNOW, FOLKS WHO ARE OLDER AND DYING AS OPPOSED TO CHILDREN.

ANYWAY, SO I DON'T THINK SO.

BUT THE QUESTION IS: COULD WE START, PERHAPS, THAT MEET AND CONFER PROCESS, AND MY CONCERN IS, I DON'T THINK THE DEFENDANTS ARE GOING TO HAVE THEIR HEART IN IT UNTIL THEY HEAR FROM ME AND GET A RULING FROM ME. AND SO, I WONDER HOW PRODUCTIVE IT WOULD BE.

BUT, YEAH, I'M GOING TO ORDER THE PARTIES TO MEET AND CONFER JUST IN GENERAL ABOUT, YOU KNOW, HOW WOULD WE EVEN BEGIN TO APPROACH DISCOVERY IN THIS CASE.

AND THE PROBLEM YOU HAVE, MR. WISNER, IS YOU'VE GOT A LOT OF DIFFERENT DEFENDANTS WHO ALL OPERATE IN A DIFFERENT WAY, HAVE DIFFERENT WAYS OF KEEPING RECORDS, DIFFERENT PLACES THEY KEEP THEM. I MEAN, IT'S QUITE DAUNTING.

AND SO, YOU NEED TO TALK TO EACH OTHER ABOUT WHAT'S THE BEST WAY TO APPROACH THIS. I THINK IT'S PROBABLY EVERYBODY SITS AROUND A TABLE TOGETHER, ALL OF THE DEFENDANTS AND THE PLAINTIFF. IT MIGHT BE EVERYBODY

SITS AROUND THE TABLE, AND I SIT AT THE TABLE TOO, WHICH I'VE DONE ON OCCASION AND, YOU KNOW, TRY TO FIND THAT MIDDLE GROUND WHERE WE CAN MAKE PROGRESS WITHOUT TOO MUCH ANGST.

BUT I WILL ASK THE PARTIES TO MEET AND CONFER IN REALTIME, NOT IN PERSON, IN REALTIME, BETWEEN NOW AND MARCH 4 TO SEE WHETHER YOU CAN COME UP WITH A CASE MANAGEMENT PLAN, AND WHETHER THERE IS A REASON TO PHASE DISCOVERY, FOR EXAMPLE.

I WOULD SAY THAT THIS QUESTION OF CAUSATION IS NOT BY ANY MEANS PUT TO BED BY OUR INITIAL SET OF HEARINGS BECAUSE WE HAVEN'T ADDRESSED KEY ISSUES LIKE DOSE RESPONSE. I MEAN, IT HAS COME UP IN PASSING HERE AND THERE, BUT THAT'S ANOTHER ASPECT OF CAUSATION.

YOU KNOW, THE VERY NARROW QUESTION I FRAMED HERE: ARE THE METALS CAPABLE OF BEING A SUBSTANTIAL FACTOR CAUSING ASD IS ALL THAT WE'VE LOOKED AT AND IT DOESN'T, BY ANY MEANS, CLOSE THE DOOR ON GENERAL, LET ALONE, SPECIAL CAUSATION.

SO THE OTHER THING YOU PROBABLY OUGHT TO MEET AND CONFER ABOUT IS WHAT ELSE DOES THE PLAINTIFF HAVE TO PRESENT BY WAY OF A SARGON HEARING OR WHAT ELSE WOULD THE DEFENDANTS RAISE AS A REASON TO EXCLUDE, BESIDES THIS PRELIMINARY QUESTION: WHETHER THE HEAVY METALS ARE CAPABLE OF BEING A SUBSTANTIAL FACTOR CAUSING INJURY.

SO TALK TO AMONG YOURSELVES.

MR. WISNER: I WILL DO THAT. WE HAD PREVIOUS DISCUSSIONS. THEY TOLD US THEY WANTED TO PHASE EVERY

LITTLE POSSIBLE THING IN THE WORLD. THEY WANTED ONE-SIDED DISCOVERY. IT'S FINE. WELL, WE WILL DO THE MEET AND CONFER.

I WILL SAY THIS, YOUR HONOR, AND I REALLY THINK THIS IS IMPORTANT AND I -- YOU KNOW, I AM TRYING MY BEST NOT TO GET FRUSTRATED, BUT, YOU KNOW, NOAH, MY CLIENT, YOU KNOW, HE'S AT AN AGE IN HIS LIFE WHERE RESOURCES MAKE A DIFFERENCE TO HOW HE'S GOING TO BE TRAINED AND GROW UP AS A KID.

HIS AUTISM -- YOU KNOW, HAVING A JUDGMENT FOR HIM IS REAL MEANINGFUL AND WOULD BE REAL SUBSTANTIAL INTO HOW HIS LIFE DEVELOPS, AND IT'S NOT LIKE WE CAN JUST SIT HERE AND DO MULTIPLE SARGON HEARINGS AND NEVER LET US GET A DOCUMENT AND NEVER LET US CONDUCT DISCOVERY. I THINK THAT'S GOING TO BE VERY PREJUDICIAL TO MY CLIENT.

AND WE'VE TRIED OUR BEST TO BE VERY PATIENT. WE'VE SPENT SO MUCH MONEY AND TIME FOR THIS, YOUR HONOR, BUT AT SOME POINT THERE IS A PROCESS FOR DISCOVERY, AND I UNDERSTAND WE'RE IN THE COMPLEX COURT, BUT WE'RE ALSO IN THE STATE OF CALIFORNIA, AND MY CLIENTS HAVE A RIGHT TO GET DISCOVERY AND TO GET THEIR CASE TRIAL. AND I FEEL LIKE PUTTING UP MORE ROADBLOCKS IS REALLY NOT FAIR.

I'D JUST ASK THE COURT TO CONSIDER THAT AS WE THINK THROUGH THIS PROCESS OVER THE NEXT MONTH.

THE COURT: I DON'T THINK THE COURT IS PUTTING UP ROADBLOCKS. I'M VERY SENSITIVE TO YOUR CLIENT'S RIGHT TO TRIAL, AND AS YOU KNOW, I GET CASES TO TRIAL.

MR. WISNER: I KNOW.

THE COURT: AND THAT'S MUCH OF MY MISSION.

MR. WISNER: I KNOW.

THE COURT: SO YOU DON'T THINK YOU NEED TO BE OVERLY CONCERNED; BUT ON THE OTHER HAND, I THINK THIS COULD TURN INTO ABJECT CHAOS. WHAT DID I SAY THE OTHER DAY, A TRAIN WRECK. YOU KNOW, I'M JUST TRYING TO ORGANIZE AND MANAGE IN A WAY THAT YOU DON'T SPEND TOO MUCH MONEY THAT YOU DON'T HAVE TO. WE DON'T WASTE MONEY.

AND I AGREE THAT, YOU KNOW, YOU NEED TO GET TO TRIAL. I CAN GIVE YOU A TRIAL DATE, IF THAT WOULD MAKE YOU FEEL BETTER.

MR. WISNER: SURE. THAT WOULD BE GREAT.

MS. FREIWALD: YOUR HONOR, LOOK, WE WOULD CERTAINLY LIKE TO THINK THAT IF WE'RE GOING TO -- DOING THIS EXERCISE IN MARCH IS -- IS BECAUSE YOUR HONOR'S MIND IS STILL OPEN --

THE COURT: ABSOLUTELY.

MS. FREIWALD: -- TO UNDERSTANDING THE ISSUES, AND IT SEEMS TO US APPROPRIATE THAT WE SHOULD BE PROCEEDING WITH THAT. I MEAN, THAT'S WHY WE'RE DOING THIS, WITH THAT IN MIND; THAT YOUR HONOR IS STILL OPEN.

AND IT MAY ALSO BE THAT EVEN IF YOUR HONOR DECIDES TO RULE AGAINST US IN PART, OR EVEN IN WHOLE, THAT IT IS WITH A MUCH MORE REFINED SENSE OF WHAT THE ISSUES AND CHALLENGES ARE IN THE CASE, AND THAT MAY CREATE A MUCH BETTER MANAGEMENT PROCESS BECAUSE,

OBVIOUSLY, WHAT SHOULD BE CLEAR IS, YOU KNOW, WE ARE ALL OF US LIVING WITH METALS IN OUR BODY AND, FRANKLY, THEY ARE, YOU KNOW, YOU COULD SUE YOUR LOCAL WATER COMPANY. YOU COULD SUE YOUR BUILDER FOR THE SOIL YOUR HOUSE IS ON.

SO WE NEED TO BE VERY CAUTIOUS IN HOW WE PROCEED. WE APPRECIATE THE FACT THAT YOU'RE WILLING TO HEAR FROM OUR EXPERTS. WE WILL ABSOLUTELY -- YOU KNOW, WE WILL ABIDE BY YOUR REQUEST TO MEET WITH MR. WISNER, BUT WE APPRECIATE THE OPPORTUNITY TO FINISH OUT THIS PROCEEDING.

THE COURT: ABSOLUTELY. AND I THINK WHAT THE DEFENDANTS SHOULD START THINKING ABOUT IS, IDEALLY, WHAT WOULD YOU LIKE DISCOVERY TO LOOK LIKE? YOU KNOW, WHAT WOULD BE THE BEST FORM, FORMAT, AND TIMING FOR YOUR CLIENTS, AND YOU NEED TO TALK TO YOUR CLIENTS. YOU NEED TO GET A LAY OF THE LAND OF WHAT DOCUMENTS THERE ARE, HOW HARD THEY ARE TO RETRIEVE, AND ALL OF THESE THINGS, SO THAT YOU CAN TALK INTELLIGENTLY.

IN OTHER WORDS, UNDER THE CODE OF CIVIL PROCEDURE, THE PLAINTIFF SENDS OUT DISCOVERY. DEFENDANT LAWYERS READ IT, AND THEY OBJECT, OVERBROAD, ALL OF THOSE WONDERFUL OBJECTIONS, VAGUE AND AMBIGUOUS.

BUT THAT'S ALL, KIND OF, BESIDE THE FACT. THE QUESTION IS: ON A PRACTICAL LEVEL, WHAT'S RELEVANT TO THE CASE, HOW HARD IS IT TO DIG OUT? AND YOU CAN'T SPEAK INTELLIGENTLY ABOUT THAT UNLESS YOU REALLY UNDERSTAND HOW YOUR CLIENT DOES BUSINESS, AND THAT TAKES

A LOT OF TIME.

SO THAT WOULD BE MY ADVICE FOR THE DEFENDANT, TO START THINKING ABOUT THAT AND, OF COURSE, I HAVE NO IDEA HOW I WILL RULE IN THE CASE, BUT I AM, AS YOU CAN SEE, TAKING COPIOUS NOTES, WHICH MY PEN FINGER IS LINKED TO CERTAIN SYNAPSES, SO THAT'S NECESSARY FOR ME TO DO THAT JUST TO ABSORB THE INFORMATION. I THINK SOME OF THEM ARE DEGENERATING AS WE SPEAK.

SO ANYWAY, I ABSOLUTELY HAVE AN OPEN MIND BECAUSE I'M NOT A SCIENTIST.

MR. IMBROSCIO: YOUR HONOR, ON THAT POINT, JUST ON THE -- I THINK WE HAVE THE WHOLE DAY SET ASIDE FOR THE 4TH. WE THINK WE CAN DO THE EXPERT PORTION OF IT IN THE MORNING. SHOULD WE RESERVE THE AFTERNOON OR SOME PORTION OF IT FOR THE CLOSING THAT WE'VE TALKED ABOUT?

THE COURT: GOOD IDEA. YEAH, THAT'S A GOOD IDEA.

MS. FREIWALD: THAT MAKES SENSE. THANK YOU, YOUR HONOR.

THE COURT: OKAY. WELL, I APPRECIATE, AGAIN, THE HIGH LEVEL OF ADVOCACY. I'VE LEARNED A GREAT DEAL TODAY, AND I'LL BE CONTINUING TO THINK ABOUT THIS.

I THINK OUR NEXT GET-TOGETHER WILL BE ON MARCH 4TH, BUT I'LL REMIND YOU THAT YOU CAN USE THE BULLETIN BOARD TO MAKE A JOINT POSTING IF SOMETHING COMES UP WHERE YOU THINK I COULD BE HELPFUL IN BETWEEN.

IF YOU DO THE MEET AND CONFER PROCESS, AND YOU THINK, GEE, YOU KNOW, MAYBE IT WOULD BE HELPFUL TO HAVE

THE JUDGE SIT IN, LET ME KNOW ON THE BULLETIN BOARD. I CAN PROBABLY FIND TIME. SO I JUST GIVE YOU THAT.

I WILL BE GONE FOR A WEEK, THE WEEK OF THE 14TH OF FEBRUARY, BUT ANYWAY, YOU KNOW HOW TO FIND ME.

MS. FREIWALD: THANK YOU SO MUCH FOR ALL YOUR TIME AND ATTENTION, YOUR HONOR. WE REALLY APPRECIATE IT.

MR. WISNER: THANK YOU, YOUR HONOR. I APPRECIATE IT. I HOPE YOU APPRECIATE THAT I GENERALLY CARE ABOUT MY CLIENTS, AND I GET FRUSTRATED WHEN I HEAR THE EQUIVOCATION OF WATER COMPANIES AND FOOD MANUFACTURERS THAT HAVE HIGHLY, HIGHLY TOXIC LEVELS OF HERE THESE NEUROPOISONS IN BABY FOOD. IT'S NOT IN THE EVEN IN THE SAME UNIVERSE TO ME.

SO BUT I -- THAT'S WHY I WAS GAWKING WHEN WE DID THAT. I APOLOGIZE. I SHOULD BE MORE PROFESSIONAL. THANK YOU.

THE COURT: WE'RE NOT ARGUING THE MERITS OF THE CASE TODAY, AS I'M SURE YOU KNOW.

BUT ANYWAY, THANK YOU SO MUCH. THANKS FOR -- IT'S VERY LATE YOUR TIME, BUT IT'S ENDING EARLY ENOUGH MY TIME, AND I APPRECIATE EVERYBODY BEING TIMELY. ALL RIGHT.

MS. FREIWALD: THANK YOU.

MR. PETROSINELLI: THANK YOU, YOUR HONOR. GOOD NIGHT.

MS. FREIWALD: HAVE A WEEKEND, YOUR HONOR, THANK YOU.

THE COURT: OKAY. THANKS.

{TIME NOTED: 4:23 P.M.}

STENOGRAPHIC REPORTER'S CERTIFICATION

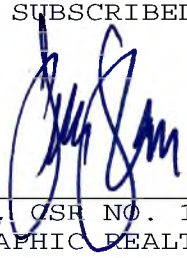
I, JEANESE JOHNSON, CERTIFIED SHORTHAND REPORTER, OFFICIAL REPORTER PRO TEMPORE, IN AND FOR THE STATE OF CALIFORNIA, DO HEREBY CERTIFY:

THAT THE FOREGOING PROCEEDINGS WERE REPORTED STENOGRAPHICALLY BY ME;

THAT THE FOREGOING IS A TRUE RECORD OF THE PROCEEDINGS TAKEN AT THAT TIME.

I FURTHER CERTIFY THAT I AM NOT ATTORNEY OR COUNSEL OF ANY OF THE PARTIES, NOR AM I A RELATIVE OR EMPLOYEE OF ANY ATTORNEY OR COUNSEL OF ANY PARTY CONNECTED WITH THE ACTION, NOR AM I FINANCIALLY INTERESTED IN THE ACTION.

IN WITNESS WHEREOF, I HAVE SUBSCRIBED MY NAME THIS 6TH DAY OF FEBRUARY, 2022.



JEANESE JOHNSON, CSR NO. 11635, CLR
CERTIFIED STENOGRAPHIC REALTIME REPORTER
OFFICIAL REPORTER PRO TEMPORE

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