SUPERIOR COURT OF THE STATE OF CALIFORNIA

FOR THE COUNTY OF LOS ANGELES - COMPLEX

NC, A MINOR,

PLAINTIFF,

VS.

CASE NO. 21STCV22822

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.

CERTIFIED TRANSCRIPT

REPORTER'S TRANSCRIPT OF PROCEEDINGS

JANUARY 31, 2022

(DAY 1)

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: KEVIN SHAPIRO, M.D., PH.D.

WITNESS: BEATE RITZ, M.D., PH.D.

E X H I B I T S

LOS ANGELES, CALIFORNIA;

MONDAY, JANUARY 31, 2022; 9:28 A.M.

BEFORE: HON. AMY D. HOGUE DEPARTMENT 7;

SUPERIOR COURT OF THE STATE OF CALIFORNIA

--OOO--

THE COURT: OKAY. I DID SPEND A LITTLE TIME OVER THE WEEKEND REVIEWING THE MOTION AND SOME OF THE OTHER PAPERS AND THE OPPOSITION AND REPLY AND I DID READ THROUGH THE EXPERT REPORTS, AND THIS MORNING I WAS JUST REVIEWING TO CLARIFY IN MY MIND SOME OF THE BASIC PRINCIPLES THAT WE HAVE AND I WAS USING THE RESTATEMENT FOR THAT PURPOSE, ALWAYS A HANDY SOURCE, AND OF COURSE WE HAVE IN CALIFORNIA, I THINK MOST EVERYWHERE ELSE NOW, A SUBSTANTIAL FACTOR TEST.

SO WHEN WE ARE ASKING THE QUESTION ARE METALS CAPABLE OF CAUSING A PARTICULAR CONDITION, I THINK WE ARE ASKING ARE THEY CAPABLE OF BEING A SUBSTANTIAL FACTOR CAUSING HARM.

AND THE RESTATEMENT GOES INTO A DISCUSSION THAT BASICALLY SAYS SOMETIMES WE CAN HAVE TWO INDEPENDENT CAUSES, NEITHER ONE OF WHICH WOULD HAVE CAUSED THE HARM AND SOMETIMES THERE IS A SYNERGY, AND IT SEEMED TO ME I SEE BOTH CONTINGENTS ON THE PLAINTIFF'S SIDE. AND THE RESTATEMENT GIVES AN EXAMPLE, A CASE WHERE THE PLAINTIFF CLAIMS THAT A VACCINATION CAUSED SEIZURES AND THE DEFENDANT CLAIMS THAT THE SEIZURES WERE NOT CAUSED BY

THE VACCINE, BUT BY A PREEXISTING TRAUMATIC INJURY THAT IS SOMEWHAT PARALLEL TO OUR CASE IF YOU ASSUME THAT THERE IS A GENETIC PREDISPOSITION TO ASD OR ADHD.

SO IT EXPLAINS THAT THE CAUSAL SET PRESENTS THESE AS ALTERNATIVE CAUSES. IF THERE'S ENOUGH EVIDENCE TO SUPPORT EACH OF THEM, THEN THE FACT-FINDER FIGURES OUT WHICH ONE IS BETTER SUPPORTED BY THE EVIDENCE, BUT IF THE EVIDENCE SHOWS THAT THE INJURY AND THE VACCINATION CAN INTERACT AND CAUSE SEIZURES, THEN EACH OF THEM MAY BE A SUBSTANTIAL CAUSE, AND SO ON.

SO THIS IS SORT OF A BASIC PRINCIPLE THAT'S GUIDING MY THINKING TODAY.

I JUST ALSO WANT TO SAY THAT WHAT I'M LISTENING FOR IS NOT WHETHER ANY OF THE EXPERTS ARE RIGHT OR WRONG, BUT WHETHER, UNDER SARGON, THERE'S ENOUGH BASIS IN SCIENCE FOR THE OPINIONS TO RENDER THEM SUFFICIENTLY RELIABLE TO GO TO THE JURY.

SO JUST THAT'S WHAT I'M LOOKING FOR, WHAT'S THE UNDERPINNING, WHAT DOES IT SAY AND WHAT HAVE WE GOT?

SO ANYWAY, WHO IS GOING TO TAKE THE LEAD TODAY?

YOU'RE GOING TO START, MR. WISNER, RIGHT?

MR. WISNER: THAT'S CORRECT, YOUR HONOR. I'M GOING TO KICK OFF WITH OUR OPENING STATEMENT TO BE FOLLOWED SHORTLY BY, I THINK, MR. PETROSINELLI, BUT I DON'T KNOW, SOMEONE ON THEIR SIDE GOING NEXT.

THE COURT: OKAY.

MR. WISNER: THEY SHOULD EACH ABOUT BE A HALF AN HOUR, AND THEN IMMEDIATELY WE'RE GOING TO CALL DR.

SHAPIRO FIRST TO THE STAND. OUR GOAL, YOU KNOW, ALL THINGS GOING RIGHT, IS TO HAVE HIM UP AND OFF BEFORE LUNCH. AND THEN IN THE AFTERNOON WE WILL HAVE DR. RITZ AND HOPEFULLY GET THROUGH MOST OF HER DIRECT -- ALL OF HER DIRECT AND MAYBE EVEN START CROSS, DEPENDING ON HOW THE TIMING GOES.

THE COURT: OKAY. AND I WILL NEED TO TAKE A BREAK AT 11:00 O'CLOCK, WHICH PROBABLY THE COURT REPORTER ALSO WILL NEED A BREAK AT 11:00 O'CLOCK, I HAVE A VERY QUICK HEARING, BUT OTHERWISE, I WOULD SUGGEST WE JUST GO STRAIGHT FROM NOW TILL 11:00.

MR. WISNER: SOUNDS GREAT, YOUR HONOR.

WITH THAT, I'M READY TO PROCEED, YOUR HONOR, IF YOU'RE READY AS WELL.

THE COURT: I'M READY.

MR. WISNER: OKAY. GREAT.

MAY IT PLEASE THE COURT, YOUR HONOR, I KNOW WE HAD A CONTENTIOUS HEARING ON FRIDAY ABOUT WHETHER OR NOT WE SHOULD EVEN GO FORWARD TODAY, AND I JUST WANT YOU TO KNOW THAT WE REALLY DO APPRECIATE YOU AND YOUR STAFF TAKING THE TIME TO HEAR US OUT AND TO LOOK AT THE SCIENCE. I THINK THIS IS A REALLY IMPORTANT CASE.

AND BEFORE I GET TO THE SARGON ISSUES, I THINK TAKING A MOMENT TO REFLECT SPECIFICALLY ON THE IMPORTANCE OF THIS CASE IS PIVOTAL.

WE KNOW IN FEBRUARY OF LAST YEAR WE HAD THIS CONGRESSIONAL REPORT WHICH INDICATED THAT THERE WERE REALLY, REALLY HIGH LEVELS OF LEAD, ARSENIC AND MERCURY

FOUND IN BABY FOODS. WE KNOW ARSENIC AND LEAD AND MERCURY ARE NEUROTOXINS. WE KNOW THAT THEY CAUSE BRAIN DAMAGE AND WE KNOW THAT WHEN YOU EXPOSE A BABY WHOSE BRAIN IS STILL DEVELOPING AT A YOUNG AGE TO THOSE NEUROTOXINS, IT CAN CAUSE PERMANENT LIFE-LONG DISABILITIES.

NOW, WE'RE GOING TO GO OVER A LOT OF THE SCIENCE THAT UNDERPINS THAT, BUT CONCEPTUALLY AND LOGICALLY, THE CONNECTION IS VERY CLEARLY THERE.

AND WHAT'S SO IMPORTANT ABOUT THIS CASE IS SINCE, YOU KNOW, FEBRUARY OF LAST YEAR, THESE PRODUCTS ARE STILL BEING SOLD, AND TODAY MILLIONS OF CHILDREN AND BABIES ARE EATING THESE FOODS, AND ALTHOUGH THE FDA IS TAKING ACTION TO GET THEM CLOSER TO ZERO IS THE PROGRAM, SO THERE'S NO MORE HEAVY METALS IN THEM, THEY ARE NOT GOING TO HAVE ANY REGULATORY ACTION UNTIL -- AT LEAST FOR LEAD UNTIL APRIL OF '24 AND AFTER THAT THEY MIGHT GET TO MERCURY AND ARSENIC SO WE HAVE A VERY LONG RUNWAY, AND DURING THAT TIME A LOT OF PEOPLE ARE GETTING HURT WHICH IS WHY WE BROUGHT THIS CASE AND THAT'S UNPRECEDENTED.

BUT THE OTHER REASON FOR IT, YOUR HONOR, AND I THINK THIS GOES FUNDAMENTALLY TO WHY WE'RE HERE IS BECAUSE WE HAVE A CLIENT WHO IS -- SORRY, THERE WE ARE -- WE HAVE A CLIENT NOAH WHO HAS AUTISM, AND YOU KNOW, HE FILED THIS CASE NINE MONTHS AGO, AND TO THIS DAY, WE'RE STILL WAITING TO SORT OF GET THIS CASE GOING.

YOU KNOW, HE'S AT A POINT IN HIS AGE IN HIS

LIFE WHERE HAVING RESOURCES AND MONEY MAKE A DIFFERENCE, AND SO WHILE WE THINK ABOUT THESE SARGON ISSUES, IT'S HARD -- WE CAN'T FORGET THAT THERE'S REAL PEOPLE BEHIND THIS AND PEOPLE'S WHOSE BRAINS HAVE BEEN DAMAGED BECAUSE OF THIS. I JUST WANT TO KEEP THAT IN CONTEXT.

NOW, AUTISM AWARENESS MONTH IS IN OCTOBER. AUTISM AWARENESS DAY IS APRIL. AND THE THEME VERY OFTEN FOR AUTISM IS ACTUALLY THE PUZZLE PIECES, AND SO TODAY WE HAVE PUT TOGETHER THE SARGON PUZZLE TO SORT OF OUTLINE HOW WE'RE GOING TO PROCEED FORWARD TODAY IN THIS OPENING STATEMENT.

THE FIRST THING WE'RE GOING TO TALK ABOUT, YOUR HONOR, IS THE LAW. I'M GOING TO SHOW YOU -- DISCUSS THREE IMPORTANT CASES THAT I THINK THE COURT SHOULD PAY VERY CLOSE ATTENTION TO; OBVIOUSLY ONE OF THEM IS SARGON.

THEN I WANT TO TALK ABOUT WHAT AUTISM IS, WHAT WE KNOW ABOUT AUTISM, WHEN IT DEVELOPS, HOW IT DEVELOPS, THE INFLUENCES OF GENETICS AND ENVIRONMENT AND WHAT IS KNOWN IN THE LITERATURE ABOUT IT.

THEN WE'RE GOING TO TALK ABOUT HEAVY METALS. WE'RE GOING TO TALK ABOUT WHAT WE KNOW ABOUT HEAVY METALS AND WHAT WE DON'T KNOW ABOUT HEAVY METALS, AND IMPORTANTLY, WHAT WE KNOW ABOUT HEAVY METALS AND AUTISM AND ADHD.

AND THEN FINALLY, YOUR HONOR, I WANT TO TALK BRIEFLY ABOUT OUR EXPERTS.

YOU'RE FIRST GOING TO HEAR THIS WEEK FROM DR.

SHAPIRO, THEN FROM DR. RITZ, THEN FROM DR. GARDENER AND THEN FINALLY DR. ASCHNER; ALL OF THESE EXPERTS HAVE VERY WELL REASONED AND THOROUGH REPORTS AND HAVE BEEN WORKING IN THESE AREAS MOST, IF NOT THEIR ENTIRE CAREERS. THEY ARE REALLY SEMINOLE EXPERTS IN THIS AREA.

SO WITH THAT SORT OF THE ROADMAP, YOUR HONOR, LET'S START OFF WITH THE FIRST PIECE. START OFF WITH CALIFORNIA LAW.

NOW, THE THREE CASES THAT I REALLY THINK THE COURT SHOULD PAY ATTENTION TO, TWO CALIFORNIA COURT OF APPEAL CASES, THE ROBERTI DECISION AND THE COOPER CASE AND OF COURSE SARGON.

NOW, ALL THREE OF THESE CASES ACTUALLY INVOLVE TRIAL COURT DECISIONS IN LOS ANGELES COUNTY SO THEY ARE PARTICULARLY ON POINT FOR US.

LET'S START WITH OFF WITH ROBERTI.

AND THIS CASE IS REALLY IMPORTANT, YOUR HONOR, BECAUSE IT SPECIFICALLY RELATES TO AUTISM.

IN THAT CASE A CHILD BROUGHT A CLAIM AGAINST A PESTICIDE SPRAYING COMPANY ALLEGING THAT THE PESTICIDE THAT THEY WERE EXPOSED TO SUBSTANTIALLY CONTRIBUTED TO HIS DEVELOPMENT OF AUTISM. THE DEFENDANTS FILED A MOTION IN LIMINE, THE TRIAL COURT GRANTED IT, AND ONE OF THE REASONS THAT WAS GIVEN IS AS IT SAYS RIGHT HERE: THAT THERE IS A CONSENSUS IN THE MEDICAL COMMUNITY THAT THERE IS NO KNOWN CAUSE OF AUTISM AND THAT THERE IS NO CONSENSUS AMONGST THE SCIENTIFIC COMMUNITY THAT PESTICIDES CAUSE AUTISM.

NOW, IN THAT CASE THERE ACTUALLY WASN'T ANY EPIDEMIOLOGY. THE EXPERTS THAT THE PLAINTIFFS HAD PROVIDED ONLY PROVIDED TESTIMONY BASED ON ANIMAL STUDIES. IT WENT UP TO THE COURT OF APPEAL AND THE COURT REVERSED THE TRIAL COURT.

AND BASICALLY THE COURT EXPLAINED THAT IF THE EXPERT IS RELYING UPON PEER-REVIEWED LITERATURE AND IF THE CONCLUSION THAT THEY ARE ARRIVING FROM THAT LITERATURE ARE NOT IRRATIONAL OR, YOU KNOW, CRAZY, THEN IT'S REALLY A QUESTION FOR THE JURY.

AND ULTIMATELY THE CASE CAME BACK ON APPEAL. THE CASE WENT TO TRIAL AND THE DEFENDANTS ACTUALLY WON. THEY WERE ABLE TO SHOW THE JURY THAT THERE WAS NO CAUSE BETWEEN THAT PESTICIDE EXPOSURE AND AUTISM.

WHY THIS IS SO IMPORTANT IS IT'S THE ONLY CALIFORNIA COURT OF APPEAL DECISION THAT SPECIFICALLY LOOKS AT THE CAUSE OF AUTISM. AND THEY MADE IT VERY CLEAR THAT YOU CAN PASS THAT THRESHOLD IF YOU RELY UPON RELIABLE DATA AND HAVE NON CONJECTURE, NON LEAPS OF LOGIC CONCLUSIONS. THAT WAS FORMALIZED, YOUR HONOR, ULTIMATELY IN THE SARGON DECISION.

RIGHT, HERE THE COURT LAID OUT SORT OF THE STANDARD OF THE DAY ON HOW THE COURT CONSIDERS EXPERT TESTIMONY. AND REALLY WHAT IT BOILS DOWN TO IS THAT WHETHER THE EXPERT'S OPINION IS FOUNDED ON SOUND LOGIC AND NOT A DECISION ON ITS PERSUASIVENESS, RIGHT, THE COURT MUST SIMPLY DETERMINE WHETHER THE MATTER RELIED ON CAN PROVIDE A REASONABLE FAITHFUL BASIS FOR THE OPINION

OR WHETHER THAT OPINION IS BASED ON A LEAP OF LOGIC OR CONJECTURE. THE COURT DOES NOT RESOLVE SCIENTIFIC CONTROVERSY.

AND WHAT SARGON IS SAYING AND THIS IS REALLY AT THE HEART AND SOUL OF IT, IS IF YOU'VE GOT REALLY QUALIFIED EXPERTS AND THEY ARE RELYING UPON PEER-REVIEWED LITERATURE, THE ONLY WAY THEY GET EXCLUDED FROM A JURY IS IF THEIR CONCLUSIONS RELY UPON LEAPS OF LOGIC OR CONJECTURE. THERE'S A REASONABLE BASIS, THERE'S PLAUSIBILITY IF IT -- A PERSON CAN MAKE SENSE OF IT, OUT OF THE EXPERT USING STANDARD PROCEDURES, THEN IT GETS TO A JURY AND THEY DECIDE THE CONTROVERSY. YOU DON'T NEED A CONSENSUS WITHIN THE COMMUNITY ABOUT A RESULT OR A BELIEF.

THAT SAID HERE, YOUR HONOR, WE KIND OF DO. WE ACTUALLY HAVE A HEAPING AMOUNT OF EVIDENCE AND WE ARE GOING TO GO THROUGH THAT IN A SECOND, BUT THE POINT IS WE DON'T EVEN NEED THAT TO GET OVER SARGON.

AND FINALLY, YOUR HONOR, THIS IS AN IMPORTANT CASE OUT OF, AGAIN, OUT THE COMPLEX COURT HERE IN LOS ANGELES, AND IN THIS CASE IT WAS A CANCER CASE. AND THE TRIAL JUDGE LET THE CASE GO TO THE JURY, RETURNED A VERDICT. AND THEN AFTER THE VERDICT WAS RETURNED, THE COURT STRUCK THE EXPERT SAYING THAT IT WAS NOT RELIABLE AND TOOK -- PUT -- SET THE VERDICT ASIDE AND IT WENT UP ON APPEAL.

IMPORTANTLY HERE, THERE, THE COURT DID EXACTLY WHAT THE DEFENDANTS ASKED HIM TO; SPECIFICALLY, HE

WEIGHED IT INTO THIS SPECIFIC EPIDEMIOLOGICAL STUDIES, HE WEIGHED THE FLAWS AND THE WEAKNESSES OF EACH STUDY, AND IN DOING SO, HE COMMITTED REVERSIBLE ERROR. AND THE COURT OF APPEAL SAID, LISTEN, YOU JUST CAN'T DO THAT, YOU CAN'T ENGAGE IN A PIECE-MEAL ANALYSIS OF THE EPIDEMIOLOGICAL DATA, YOU CAN'T DISAGREE WITH THE CONCLUSIONS IN THE PEER-REVIEWED LITERATURE, YOU HAVE TO LEAVE THAT TO THE JURY, AND THEY ULTIMATELY REINSTATED THE VERDICT AND, YOU KNOW, IT CAME DOWN.

AND THIS HAS REALLY BEEN THE LAW OF CALIFORNIA IN THE AREA OF SARGON, PARTICULARLY OF AN AREA OF, LIKE, AUTISM, JUST LIKE IN CANCER IN COOPER WHERE THERE'S MULTIPLE CAUSES, RIGHT, WHERE THERE IS NO SINGLE CAUSE OF CANCER, THERE IS NO SINGLE CAUSE OF AUTISM, THIS IS A MULTI-CAUSAL PHENOMENON.

SO WITH LEGAL BACKGROUND IN MIND, LET'S TALK ABOUT AUTISM.

NOW, AUTISM IS A SPECTRUM DISORDER, OKAY, AND THIS DIAGRAM HERE KIND OF ILLUSTRATES THAT. YOU HAVE VARIOUS BEHAVIORAL SYMPTOMATIC EXPRESSIONS IN A CHILD AND THOSE EXPRESSIONS MANIFEST IN DIFFERENT WAYS, IT HAS DIFFERENT AMOUNTS, RIGHT, SO YOU MIGHT HAVE A CHILD THAT HAS REALLY BAD REPETITIVE BEHAVIOR, BUT PRETTY GOOD MOTOR SKILLS. HIS EXECUTIVE FUNCTIONING IS VERY DEFECTIVE, BUT HE IS ABLE TO COMMUNICATE, RIGHT. THAT CHILD WOULD BE ON THE SPECTRUM, THE CHILD WOULD BE CONSIDERED AUTISTIC, BUT THEY HAVE DIFFERENT TYPES OF THINGS AND THAT'S WHY THE HISTORICAL LINEAR SORT OF

SPECTRUM DOESN'T REALLY APPLY ANYMORE, IT'S SORT OF CONSIDERED THIS SORT OF CIRCULAR AND GLOBAL MISMATCH OF SYMPTOMS, THERE IS NO BIOLOGICAL MARKER FOR AUTISM, THERE IS REALLY NOTHING BEYOND LOOKING AND OBSERVING THE CHILD.

AND WHAT WE KNOW IS THAT CAN HAPPEN AT DIFFERENT AGES, RIGHT, YOU CAN OBSERVE THIS PHENOMENA AT DIFFERENT TIMES.

NOW, TO GIVE SOME SORT OF BASIC BACKGROUND, I'M GOING TO SHARE WITH THIS COURT THE CDC'S WEBSITE, OKAY. AND THIS, RIGHT, YOU CAN SEE THIS IS THE CDC'S WEBSITE, AND RIGHT HERE WE HAVE SOME DATA ON PREVALENCE, RIGHT, AND WE KNOW THAT ONE IN FOUR CHILDREN HAVE BEEN IDENTIFIED WITH AUTISM SPECTRUM DISORDER, WE KNOW THAT IT OCCURS IN ALL RACIAL, ETHNIC AND SOCIOECONOMIC GROUPS. ASD IS FOUR TIMES MORE COMMON AMONGST BOYS THAN AMONG GIRLS.

IT'S KIND OF INTERESTING BECAUSE IT GETS INTO OUR PLAUSIBILITY ARGUMENT, WHICH WE'LL EXPLAIN AS WE GO ON. WE ALSO KNOW THAT ONE IN SIX CHILDREN BETWEEN THREE AND SEVENTEEN WERE DIAGNOSED WITH A DEVELOPMENTAL DISABILITY WHICH INCLUDES STUFF LIKE ADHD.

AND THAT'S IMPORTANT. ADHD IS VERY OFTEN ASSOCIATED WITH AUTISM ITSELF; AGAIN, THAT LENDS A LOT MORE EVIDENCE TO OUR THEORY OF PLAUSIBILITY.

NOW, IF WE GO DOWN INTO THIS DOCUMENT, WE HAVE ON THE SECTION RIGHT HERE, "WHAT IS ASD?" THEY ACTUALLY HAVE A SECTION DOWN HERE CALLED, "CAUSES AND RISK

FACTORS." THIS IS WHAT THE CDC IS SAYING.

AND THEY SAY, "WE DO NOT KNOW ALL THE CAUSES OF ASD, HOWEVER, WE HAVE LEARNED THAT THERE ARE MANY CAUSES FOR MULTIPLE TYPES OF ASD, THERE MAY BE MANY DIFFERENT FACTORS THAT MAKE THE CHILD MORE LIKELY TO HAVE AN ASD, INCLUDING ENVIRONMENTAL, BIOLOGIC AND GENETIC FACTORS."

AND THAT'S REALLY IMPORTANT, YOUR HONOR, BECAUSE WHEN WE TALK ABOUT AUTISM, IF ANYBODY TELLS YOU IT'S ALL GENETIC, THEY'RE WRONG. IF ANYONE TELLS YOU IT'S ALL ENVIRONMENTAL, IT'S WRONG, RIGHT. NOT ONLY IS THERE A CONFLUENCE OF FACTORS FROM BOTH SIDES, BUT THERE'S SOMETHING CALLED EPI GENETICS WHERE THE GENES ARE ACTUALLY TURNING ON AND OFF IN RESPONSE TO ENVIRONMENTAL INFLUENCES, AND THAT EPI GENETICS IS AT CUTTING-EDGE SCIENCE RIGHT NOW. AND IN THAT CONTEXT, BOTH THE EXPOSURES AND THE GENETICS CAN PLAY A ROLE IN LEADING TO IT.

A GREAT EXAMPLE OF THAT, YOUR HONOR, IF A CHILD -- IF AUTISTIC CHILDREN HAVE A GENE THAT MAKES IT HARDER FOR THEM TO METABOLIZE METALS AND EXCRETE THEM, YOU COULD SEE A SITUATION WHERE YOU HAVE TWO CHILDREN WHO WERE EXPOSED TO THE SAME AMOUNT OF METAL, BUT THE ONES THAT AREN'T ABLE TO PROCESS IT SUFFER MORE BRAIN DAMAGE AND THEREFORE, DEVELOP ASD. THERE YOU HAVE A PURE SYNERGY BETWEEN THE GENETIC PREDISPOSITION AS WELL AS THE METALS THAT WOULD BE CAUSING IT.

INTERESTING ENOUGH HERE ON THIS WEBSITE WE HAVE

CHILDREN, YOU SEE IT'S BULLET POINT NUMBER TWO, IT SAYS:

"CHILDREN WHO HAVE A SIBLING WITH ASD ARE AT A HIGHER RISK OF ALSO HAVING ASD."

AND IF WE GO DOWN TO THE CITATIONS, YOU'LL SEE THAT THE FIRST CITATION THERE IS TO A STUDY BY HALLMAYER, NUMBER 6.

I'D LIKE TO SHOW THE COURT THAT STUDY.

SO THIS IS THE HALLMAYER STUDY, AND IT'S REALLY IMPORTANT BECAUSE WHAT THEY DID HERE, YOUR HONOR, IS THEY ACTUALLY LOOK AT TWINS AND WHO HAD CONCORDANCE AND DISCORDANCE; SPECIFICALLY WHAT WE REFER TO THERE IS THEY LOOKED AT CHILDREN WHO ONE OF THE TWINS HAS AUTISM AND THE OTHER ONE DOES NOT AND THEY LOOKED AT BOTH GENETICALLY IDENTICAL TWINS AND FRATERNAL TWINS.

AND, YOU KNOW, I CAN GET INTO THE NUANCES HERE, BUT THE RESULTS OF THE STUDY ARE PRETTY STRAIGHTFORWARD, RIGHT, ALTHOUGH THEY ARE KIND OF HARD TO FULLY UNDERSTAND.

IT SAYS RIGHT HERE, THE CONCORDANCE FOR MALE TWINS WAS .58 FOR MONOZYGOTIC TWINS.

SO WHAT THAT'S REFERRING TO, YOUR HONOR, IS GENETICALLY IDENTICAL TWINS IN THAT THEY WERE BOTH DIAGNOSED WITH AUTISM 58 PERCENT OF THE TIME, SO THAT MEANS 42 PERCENT OF THE TIME ONE OF THE GENETICALLY IDENTICAL TWINS HAD AUTISM AND THE OTHER DID NOT. WE HAVE SIMILAR RESULTS -- AND THAT'S FOR MALES. FOR FEMALES WE HAVE A SIMILAR RESULT. WE HAVE LOOKS LIKE CONCORDANCE OF ABOUT 60 PERCENT; SO AGAIN, A 40 PERCENT

DISCORDANCE, YOU CAN SEE RIGHT HERE.

AND THEN FOR PATERNAL TWINS WE HAVE AN INTERESTING THING, AND ALTHOUGH THEY DON'T HAVE IDENTICAL GENES, THEY HAVE VERY SIMILAR ONES, THEY COME FROM THE SAME WOMB, AND THERE WE HAVE DISCORDANCE -- WE HAVE CONCORDANCE OF .27, MEANING, WE HAVE DISCORDANCE OF OVER 70 PERCENT, 73 PERCENT, THAT'S AMONGST BOYS. AND AMONGST GIRLS OR WOMEN, THERE WAS A -- OH, SORRY -- THERE WAS 31 PERCENT. YOU CAN SEE IT DOWN HERE.

OKAY. THE POINT OF THIS, YOUR HONOR, IS THAT WHETHER IT'S A GENETICALLY IDENTICAL OR FRATERNAL TWINS, THERE IS CONSIDERABLE INSTANCES WHERE ONE OF THEM DEVELOPS AUTISM AND THE OTHER DOES NOT.

WHAT DOES THAT TELL YOU?

THAT TELLS US THAT GENES DON'T TELL THE WHOLE STORY. WHEN TWO TWINS WHO HAVE THE SAME GENES, ONE OF THEM DEVELOPS AUTISM, THE OTHER DOESN'T, GENES OBVIOUSLY CAN'T TELL THE WHOLE STORY. SOMETHING ELSE IS HAPPENING.

AND THIS IS WIDELY ACCEPTED WITHIN THE AUTISM COMMUNITY.

THE GENERAL IDEA, YOUR HONOR, IS THAT THERE IS A CONNECTION BETWEEN THE GENES AND THE ENVIRONMENT AND ONE OF THOSE ENVIRONMENTAL EXPOSURES IS METAL.

NOW, INTERESTING ENOUGH, I'M GOING TO GO BACK TO THE CDC WEBSITE FOR JUST ONE SECOND.

AND AS WE SEE HERE UNDER THE GENETIC RISK FACTORS, AND THIS IS IMPORTANT BECAUSE IT SAYS RIGHT

HERE, "THERE IS SOME EVIDENCE THAT THE CRITICAL PERIOD FOR DEVELOPING ASD OCCURS BEFORE, DURING AND IMMEDIATELY AFTER BIRTH."

AND WHAT'S INTERESTING ABOUT THAT IS THEY ARE SAYING THAT THE CRITICAL WINDOW OF VULNERABILITY ISN'T JUST PRENATAL, RIGHT, IT'S ALSO AFTER BIRTH BECAUSE THE BRAIN IS DEVELOPING AND THERE'S PLASTICITY THAT IS OCCURRING IN THAT -- THOSE YOUNGER YEARS AND THAT CAN LEAD TO WHAT WE KNOW AS AUTISM.

AND SO YOU KNOW, NOW LOOKING AT SOME OF THE CDC, YOUR HONOR, IF YOU LOOK AT EXHIBIT 17 OR CITATION 17, THE AUTHOR ON HERE IS ACTUALLY DR. GARDENER. IT'S OUR EXPERT IN THIS CASE. AND THAT'S JUST A REFLECTION THAT, YOU KNOW, A LOT OF WHAT OUR EXPERTS ARE DOING IN THIS CASE, AND YOU'LL SEE THIS THROUGHOUT THE WEEK, THEY ALL HAVE OPINIONS THAT THEY DID NOT ARRIVE AT FOR THE FIRST TIME IN LITIGATION, THEY ARE PUBLISHED IN THIS AREA, THEY ARE WIDELY ACCEPTED WITHIN THE SCIENTIFIC COMMUNITY AND I THINK WITHIN THE AUTISM COMMUNITY AS WELL.

SO GOING BACK TO THE CONNECTION HERE.

THE NEXT STEP, THEN, IS LOOKS LIKE YOU HAVE METALS.

NOW, WHAT DO WE KNOW ABOUT METALS, YOUR HONOR? WELL, WE KNOW THEY ARE NEUROTOXIC, THAT'S JUST ESTABLISHED. AND WE KNOW THAT THEY HAVE A DELETERIOUS EFFECT ON THE BRAIN. AND YOU'RE GOING TO HEAR AT LENGTH FROM DR. ASCHNER ABOUT THIS WHO HAS BEEN STUDYING HEAVY

METALS AND THEIR EFFECTS ON THE BRAIN SINCE THE BEGINNING OF TIME. HE'S PROBABLY THE MOST RENOWNED EXPERT IN THE WORLD ON THIS AREA. THERE'S MUSEUMS BASED ON HIS WORK. I MEAN, HE REALLY IS INCREDIBLY WELL CREDENTIALED AND HE'S GOING TO TALK ABOUT WHAT THEY DO.

BUT I WANT TO TAKE JUST A QUICK MOMENT TO SHOW YOU AN INTERESTING STUDY, AND I'M JUST GOING TO DO THIS QUICKLY BECAUSE I DON'T WANT TO SPEND TOO MUCH TIME ON IT. BUT THIS IS A STUDY THAT WAS DONE OUT THE CLEVE -- I'M SORRY -- THE CINCINNATI LEAD CITE, AND IN THIS STUDY WHAT THEY DID IS THEY LOOKED AT CHILDREN PRE-BIRTH SO WHEN THEY -- WHEN THOSE MOTHERS WERE PREGNANT, AND THEY FOLLOWED THEM FOR 25 YEARS TAKING LEAD MEASUREMENTS OF THEIR BLOOD AT VARIOUS POINTS THROUGHOUT THEIR LIVES WHEN THEY WERE YOUNG, A COUPLE YEARS OLD, ET CETERA.

AND WHAT THEY FOUND -- WHAT THEY DID THEN AFTER 25 YEARS IS THEY TOOK THESE NOW GROWN ADULTS AND THEY LOOKED AT THEIR BRAIN. THEY LOOKED TO SEE WHAT WAS -- WHAT HAD HAPPENED IN THEIR ACTUAL BRAINS. THEY TOOK MRI'S. AND WHAT THEY FOUND WAS PRETTY AMAZING. THEY FOUND THAT IN CHILDHOOD EXPOSURES TO LEAD LED TO THESE SPECIFIC AREAS OF THE BRAIN BEING UNDERDEVELOPED OR DAMAGED. THERE WAS LESS BRAIN VOLUME THERE, RIGHT.

AND WHY THIS IS SO KEY IS IF WE LOOK AT -- SORRY -- LET ME GO DOWN TO THE BOTTOM PAGE, SORRY, IT'S THE CONCLUSIONS.

WHAT THEY FOUND HERE IS THAT IN SUMMARY, WE FOUND THAT EARLY CHILDHOOD LEAD EXPOSURE IS ASSOCIATED

WITH STRUCTURAL VOLUME LOSS IN THE BRAIN. THE INJURY AFFECTS BRAIN REGIONS CLASSICALLY CONSIDERED RESPONSIBLE FOR EXECUTIVE FUNCTION, BEHAVIOR REGULATION AND FINE MOTOR CONTROL.

THOSE ARE THE VERY PARTS OF THE BRAIN THAT WE SEE DEFECTS IN THAT WE THEN CHARACTERIZE AS AUTISM. AND SO YOU HAVE THIS REALLY ROBUST KNOWLEDGE BASE ABOUT THE EFFECTS OF CHILDHOOD EXPOSURE AND HEAVY METALS. HERE WE HAVE A VERY GOOD ONE ON LEAD AND HOW IT LEADS TO LITERALLY BRAIN DAMAGE IN THE AREA OF THE BRAIN THAT YOU WOULD EXPECT TO HAVE BRAIN DAMAGE FOR ASD.

I MEAN, THE CONNECTIONS HERE ARE TRULY UNBELIEVABLE.

AND THE THING, YOUR HONOR, IS WHEN YOU ACTUALLY CALL -- LOOK AT THE DATA, RIGHT, AND SO WE'RE GOING TO LOOK AT THIS OBVIOUSLY TODAY WITH DR. RITZ, BUT THIS IS THE BODY, THE CORPUS OF STUDIES ON LEAD.

AND AS YOU SEE HERE, EVERYTHING ON THE LEFT THAT'S POSITIVE AND STATISTICALLY SIGNIFICANT. WE HAVE THIS AREA HERE, THESE ARE POSITIVE, BUT NOT SIGNIFICANT, THEN WE HAVE THE NULL STUDIES RIGHT HERE. WE HAVE NEGATIVE AND NOT SIGNIFICANT. WE HAVE NEGATIVE AND STATISTICALLY SIGNIFICANT.

AND WHEN YOU, FOR EXAMPLE, JUST TAKE OUT THE NON SIGNIFICANT RESULTS AND YOU COMPARE THE POSITIVE VERSUS THE NEGATIVE, I MEAN, IT'S NOT EVEN CLOSE, RIGHT. AND THIS IS SUPPORTED BY A WHOLE HOST OF LITERATURE THAT WE'RE GOING TO GET INTO OBVIOUSLY WITH THE COURT

THROUGHOUT THIS WEEK, OKAY, RIGHT.

ONE OF THOSE STUDIES I THINK IS GOING TO BE REALLY POWERFUL AND HELPFUL FOR THE COURT AND THAT IS SPECIFICALLY A STUDY THAT WAS DONE AT THE NIH. AND THIS WAS A STUDY THAT WAS PRETTY COOL.

SO LET ME KIND OF WALK YOU THROUGH WHAT THEY DID.

SO THEY TOOK SETS OF TWINS THAT HAD DISCORDANCE, MEANING, ONE OF THE TWINS HAD AUTISM AND ONE OF THEM DIDN'T, AND THEY COMPARED THEM TO TWINS THAT HAD CONCORDANCE AND THEY BOTH WERE IN THE SENSE THAT THEY DIDN'T HAVE AUTISM. THEN THEY TOOK THEIR BABY TEETH AND THEY ACTUALLY DRILLED INTO THEM TO FIND OUT EXACTLY WHAT THEIR LEAD EXPOSURES WERE AT PRENATALLY AND POSTNATALLY DOWN TO THE DAY, PRETTY UNBELIEVABLY EXACT EXPOSURES, AND WHAT THEY FOUND WAS PRETTY REMARKABLE.

THEY SAID -- THEY FOUND, "WHEN COMPARING ASD DISCORDANT TWINS WITH NON ASD CONTROLLED TWIN PAIRS, WE FOUND THAT LEAD LEVELS WERE CONSISTENTLY HIGHER IN ASD CASES THAN THEIR NON ASD CO-TWINS FROM 20 WEEKS BEFORE BIRTH TO 30 WEEKS AFTER BIRTH," RIGHT.

AND THEN LATER ON THEY GO ON TO TALK ABOUT HOW THE ASSOCIATION -- AND THIS IS REFERRING TO SEVERITY OF AUTISM -- THAT THE ASSOCIATION WAS STATISTICALLY SIGNIFICANT FROM 10 WEEKS BEFORE BIRTH TO 30 WEEKS AFTER BIRTH. THE STRONGEST ASSOCIATION TO BE 5 WEEKS PRENATALLY.

AND WHAT THIS IS SAYING, YOUR HONOR, IS WHEN YOU ACTUALLY LOOK AT THE ACTUAL MEDICAL CONTENT THAT THEY WERE EXPOSED TO AT THAT TIME, CHILDREN WHO DEVELOPED ASD HAD POST-NATAL INCREASED LEVELS OF LEAD, AND THAT, YOUR HONOR, IS 100 PERCENT CONSISTENT, RIGHT, WITH THIS CORPUS OF LITERATURE WHICH SHOWS US THAT THE CHILDREN WHO ARE HAVING ASD, WHETHER IT BE IN THE URINE, WHICH IS THE YELLOW STUDIES OR THE BLOOD, WHICH IS THE RED BIOMARKERS OR WHETHER THEIR HAIR OR WHETHER THEIR TEETH AND TOENAILS OR WHETHER JUST ECOLOGICALLY THE AIR POLLUTION THEY ARE BREATHING HAS MORE LEAD IN IT, WHEN YOU LOOK AT ALL OF THIS, IT'S CONSISTENTLY SHOWING THAT CHILDREN WHO HAVE AUTISM HAVE HIGHER EXPOSURES TO LEAD.

AND WHEN YOU ADD THAT TO OUR UNDERSTANDING OF THE BIOLOGICAL PLAUSIBILITY AND WHAT HE KNOW LEAD AT A CHILDHOOD AGE DOES TO THE BRAIN, REACHING THE CONCLUSION THAT EARLY LIFE EXPOSURE TO LEAD IS A CAUSAL FACTOR IN DEVELOPING ADHD -- ASD DOES NOT REQUIRE A LEAP OF LOGIC, IT DOES NOT REQUIRE CONJECTURE, IT JUST REQUIRES COMMON SENSE.

AND THE THING IS, YOUR HONOR, AND YOU'LL SEE THIS AS WELL FOR -- AND I'LL QUICKLY GO THROUGH BECAUSE I DON'T WANT TO SPEND TOO MUCH TIME GOING INTO THE STUDY -- THIS IS THE LITERATURE ON ADHD AND LEAD, RIGHT.

AGAIN, THERE ISN'T A SINGLE NEGATIVE STUDY THAT'S STATISTICALLY SIGNIFICANT. THERE'S TWO THAT ARE NULL THAT ARE NOT STATISTICALLY SIGNIFICANT, AND THERE IS JUST OVERWHELMING NUMBER OF STUDIES SHOWING THAT IN

FACT IT DOES -- IT'S ASSOCIATED.

AND A LOT OF THESE STUDIES ARE PROSPECTIVE, YOUR HONOR. THIS IS WHERE THEY ARE MEASURING A CHILD AT A YOUNG AGE AND THEN FOLLOWING THEM FOR YEARS AND MEASURING THEIR LEVELS IN THEIR BLOOD, AND AS LOW AND BEHOLD, THOSE WHO HAVE GREATER EXPOSURES TO LEAD HAVE GREATER INCIDENCE OF ADHD.

THE SCIENCE, YOUR HONOR, IS VERY SIMILAR FOR MERCURY, AGAIN, HERE IS THE CORPUS OF DATA. HERE THERE'S DEFINITELY MORE NULL RESULTS AND NOT IN THE SIGNIFICANT RESULTS, BUT THERE'S STILL AN OVERWHELMING AMOUNT OF POSITIVE AND STATISTICALLY SIGNIFICANT DATA, VARIOUS BIOMARKERS AND DIFFERENT POPULATIONS ACROSS THE WORLD.

AND FINALLY, WE HAVE VERY STRONG EVIDENCE AS WELL WITH ARSENIC, ALTHOUGH THERE IS AGAIN A LARGER NUMBER OF NOT SIGNIFICANT RESULTS. WHEN YOU TAKE OUT THOSE NON SIGNIFICANT RESULTS, WHICH ARE HARD TO INTERPRET ONE WAY OR THE OTHER, AGAIN, THE LITERATURE IS CLEAR, IT'S CLEARLY SAYING ONE THING.

AT THE BEGINNING OF THIS CASE, YOUR HONOR, SIX MONTHS AGO WHEN YOU FIRST SAID, HEY, LET'S DO AN EARLY SARGON, YOU SAID, I TOLD YOU THAT, YOU KNOW, WE REALLY WEREN'T JUST TALKING, YOU KNOW, WE WEREN'T BS'ING YOU, RIGHT, THAT THIS WAS A LEGIT SCIENCE BACKING IT UP.

AND I WANT TO SHOW YOU ONE LAST THING THAT I THINK IS PRETTY TELLING, AND I DISCOVERED THIS RECENTLY MOSTLY BECAUSE IT TURNS OUT THAT ONE OF OUR AUTHORS --

ONE OF OUR EXPERTS IS AN AUTHOR ON IT.

NOW, THIS IS A DOCUMENT BY PROJECT TENDR, "TARGETING ENVIRONMENTAL NEURODEVELOPMENTAL RISKS," AND TENDR CONSENSUS STATEMENT, AND THIS WAS PUBLISHED IN 2016 LONG BEFORE ANY LITIGATION, LONG BEFORE ANYONE WAS INVOLVED.

AND IF WE GO DOWN TO THE SIGNATORIES HERE, YOU'LL SEE THAT IT'S SIGNED BY A WHOLE HOST OF SCIENTISTS. YOU HAVE PEOPLE FROM UNIVERSITY, UC DAVIS, FROM HARVARD, YOU HAVE THE DIRECTOR OF THE NATIONAL TOXICOLOGY PROGRAM ON HERE, YOU SEE DOWN HERE, AND OBVIOUSLY, YOU KNOW, YOU HAVE DR. RITZ ON HERE AS WELL. GOING DOWN HERE WE HAVE A WHOLE HOST OF PROFESSIONALS. MANY OF THESE AUTHORS ON MANY OF THE EPIDEMIOLOGICAL STUDIES WE'RE TALKING ABOUT.

WE HAVE DOWN HERE CHILDREN HEALTH AND DISABILITY ADVOCATES. WE HAVE ALL THESE ADVOCACY GROUPS THAT SUPPORT THIS STATEMENT.

AND THEN DOWN HERE WE HAVE ORGANIZATIONS THAT SUPPORT OR ENDORSE THE TENDR CONSENSUS STATEMENT, INCLUDING THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS, WHICH SUPPORTS THIS VALUE WHICH SUPPORTS THIS DOCUMENT AS AN EDUCATIONAL TOOL, CHILD NEUROLOGY SOCIETY, THE ENDOCRINE SOCIETY, THE NATIONAL MEDICAL ASSOCIATION. I MEAN, THESE ARE THE WOLF AND WHARF OF THE AUTISM COMMUNITY.

AND HERE'S WHAT THEY SAY BACK IN 2016.

IT SAYS, "THE FOLLOWING LIST PROVIDES A PRIME

EXAMPLES -- PROVIDES PRIME EXAMPLES OF TOXIC CHEMICALS THAT CAN CONTRIBUTE TO LEARNING, BEHAVIORAL OR INTELLECTUAL IMPAIRMENT AS WELL AS SPECIFIC NEURODEVELOPMENTAL DISORDERS SUCH AS ADHD OR AUTISM SPECTRUM DISORDER."

AND THEN IF YOU GO DOWN THIS LIST, IT SAYS RIGHT HERE "LEAD AND MERCURY."

SO WE HAVE THIS CONSENSUS STATEMENT FROM FIVE YEARS AGO SAYING WE AGREE THAT THIS IS AN ISSUE THAT THIS IS A PRIME EXAMPLE OF SOMETHING THAT CONTRIBUTES TO THE DEVELOPMENT OF ADHD OR AUTISM RIGHT HERE.

AND SO EARLIER IN THIS CASE WHEN YOU WERE TOLD THE AUTISM COMMUNITY DOESN'T SEE THAT, IT'S JUST NOT TRUE.

I'D ALSO POINT OUT THAT HERE IN THIS CONSENSUS STATEMENT, AND I'M GOING TO GO OVER THIS WITH DR. RITZ A LITTLE BIT LATER TODAY, IT SAYS, "RESEARCH IN NEUROSCIENCE HAS IDENTIFIED CRITICAL WINDOWS OF VULNERABILITY AND DURING EMBRYONIC AND FETAL DEVELOPMENT, INFANCY, EARLY CHILDHOOD AND ADOLESCENCE, AND DURING THESE WINDOWS OF DEVELOPMENT, TOXIC CHEMICAL EXPOSURES MAY CAUSE LASTING HARM TO THE BRAIN THAT INTERFERES WITH A CHILD'S ABILITY TO REACH HIS OR HER FULL POTENTIAL."

AGAIN, THIS IS CONSENSUS LEVEL SCIENTIFIC OPINIONS FROM DOZENS OF THE MOST REPUTABLE EPIDEMIOLOGISTS AND SCIENTISTS IN THE WORLD, THE

DIRECTOR OF THE NATIONAL TOXICOLOGY PROGRAM. AT SOME POINT WE ASK OURSELVES IS THE ISSUE OF HEAVY METALS, IS IT EVEN A CONTROVERSY AT ALL? IT SEEMS TO BE GENERALLY ACCEPTED WITHIN THE COMMUNITY.

SO THAT'S WHAT WE KNOW ABOUT LEAD AND AUTISM.

FINALLY, LET'S BRIEFLY TALK ABOUT OUR EXPERTS.

I'M GOING TO LET THEM SPEAK FOR THEMSELVES, YOUR HONOR. YOU'RE GOING TO GET A CHANCE TO ASK THEM QUESTIONS OR GET WHATEVER YOU WANT FROM THEM AND DIG DEEP INTO THEIR METHODOLOGIES AND APPROACHES.

AND IMPORTANTLY -- AND THIS IS A BIG PART IN THE BRIEFING -- WAS DISCUSSIONS ABOUT THE BRADFORD HILL FACTORS.

I WAS THERE WHEN DR. RITZ WAS QUESTIONED ABOUT THEM AT LENGTH BY MR. PETROSINELLI, AND THERE IS -- YOU KNOW, WE'RE GOING TO GO THROUGH THEM WITH DR. RITZ AND WHAT SHE DID AND DIDN'T DO.

BUT SOMETHING THAT I THINK IS REALLY IMPORTANT, AND IT'S THE LAST THING I WANT TO LEAVE THE COURT WITH, IS THIS QUOTE FROM SIR BRADFORD HILL HIMSELF. THIS IS IN THE VERY ARTICLE WHERE HE LISTS OUT THE NINE FACTORS.

HE SAYS, "WHAT I DO NOT BELIEVE, AND THIS HAS BEEN SUGGESTED, IS THAT WE CAN LOOSELY LAY DOWN SOME HARD AND FAST RULES OF EVIDENCE THAT MUST BE OBSERVED BEFORE WE ACCEPT CAUSE AND EFFECT. NONE OF MY NINE VIEWPOINTS CAN BRING INDISPUTABLE EVIDENCE FOR OR AGAINST THE CAUSE AND EFFECT HYPOTHESIS AND NONE CAN BE REQUIRED

AS A SINE QUA NON.

"WHAT THEY CAN DO WITH GREATER OR LESS STRENGTH IS TO HELP US MAKE UP OUR MINDS ON THE FUNDAMENTAL QUESTION, IS THERE ANY OTHER WAY OF EXPLAINING THE SET OF FACTS BEFORE US? IS THERE ANY OTHER ANSWER EQUALLY OR MORE LIKELY THAN CAUSE AND EFFECT?"

AT THE END OF DAY, YOUR HONOR, I THINK THAT'S WHAT IT COMES DOWN TO IS OUR EXPERTS HAVE SPENT A LOT OF TIME, THEY HAVE READ HUNDREDS OF STUDIES, THEY HAVE ENGAGED IN A RIGOROUS ANALYTICAL REVIEW OF THE DATA AND THEY HAVE DONE IT CONSISTENT WITH THE WAY THEY ALWAYS DO IT, THEY'VE APPLIED THE BRADFORD HILL FACTORS TO THE EXTENT THEY ARE EPIDEMIOLOGISTS. DR. ASCHNER USES THE PRINCIPLES OF TOXICOLOGY TO GET TO HIS RESULT, BUT ULTIMATELY THE CONCLUSIONS THEY REACH AND THE DATA THEY RELY UPON ARE RELIABLE AND WE HOPE TO SHOW THAT THROUGHOUT THE REST OF THIS PRESENTATION, YOUR HONOR, AND I THANK YOU FOR YOUR TIME.

THE COURT: OKAY. THANK YOU VERY MUCH.

WHO IS GOING TO SPEAK FOR THE DEFENDANTS?

MR. PETROSINELLI: YOUR HONOR, GOOD AFTERNOON. THIS IS -- OR GOOD MORNING FOR YOU -- THIS IS JOE PETROSINELLI FOR GERBER, BUT I'M GOING TO SPEAK ON BEHALF OF THE DEFENDANTS, SO THANK YOU FOR HEARING ME TODAY.

YOUR HONOR, I THINK THE QUESTION IN THIS CASE IS -- OR WITH THIS MOTION -- IS HAVE THE PLAINTIFFS PUT

FORWARD RELIABLE EVIDENCE THAT PASSES MUSTER UNDER SARGON ON GENERAL CAUSATION? AND GENERAL CAUSATION AT THIS STAGE OF THE CASE MEANS WHETHER LEAD, ARSENIC AND MERCURY CAN CAUSE ASD OR ADHD OR WHETHER LEAD CAN CAUSE ADHD.

AND WHEN I USE THE WORD "CAUSE" THERE, YOUR HONOR, TO YOUR POINT AT THE OUTSET, I MEAN IT BOTH WAYS; WHETHER INDIVIDUALLY OR SYNERGISTICALLY. THAT'S THE QUESTION. DO THEY HAVE ENOUGH EVIDENCE UNDER SARGON TO MEET THAT TEST?

AS MR. WISNER JUST ALLUDED TO, YOU'RE GOING TO HEAR FROM FOUR EXPERTS THIS WEEK FROM THE PLAINTIFFS. I OUGHT TO SAY THAT, AS YOUR HONOR KNOWS, THAT IS THE FIRST PART OF THIS MOTION HEARING, WE HAVE A DAY SET ASIDE IN MARCH FOR A COUPLE OF THE DEFENSE EXPERTS, AND I'LL TALK ABOUT THAT IN A SECOND AND WHY THAT'S IMPORTANT.

BUT THIS WEEK IT'S THE PLAINTIFF'S TURN.

THEY HAVE DR. SHAPIRO, WHO IS THE ONLY EXPERT IN THEIR GROUP WHO ACTUALLY TREATS PATIENTS WITH AUTISM. HE DOES NOT OFFER A CAUSATION OPINION. HE DOESN'T COME IN HERE TO SAY THAT AUTISM IS CAUSED BY OR CAN BE CAUSED BY EXPOSURE TO HEAVY METALS. HE HAS A BIOLOGICAL PLAUSIBILITY OPINION; THAT IS, THERE ARE BIOLOGICAL MECHANISMS BY WHICH IT COULD, BUT HE EXPRESSLY DISCLAIMS A CAUSATION OPINION.

AND THEN YOU HAVE THE TWO EPIDEMIOLOGISTS, DR. RITZ AND DR. GARDENER, WHO I THINK WILL BE THE FOCUS

OF THIS WEEK'S TESTIMONY, BUT THEN YOU HAVE DR. ASCHNER, WHO IS A TOXICOLOGIST WHO ALSO OFFERS A BIOLOGICAL PLAUSIBILITY OPINION AND HE SORT OF TACKS ON A CAUSATION OPINION AT THE END. AND WE WILL GO INTO IT, YOUR HONOR, BUT SORT OF HE DISCLAIMS ANY EXPERTISE IN EPIDEMIOLOGY AND DEFERS TO THE EPIDEMIOLOGISTS ON THAT PARTICULAR QUESTION.

SO WE HAVE SARGON.

AND FROM OUR PERSPECTIVE, YOUR HONOR, FROM THE DEFENSE'S PERSPECTIVE THERE ARE THREE PRINCIPLES UNDER SARGON THAT ARE THE MOST IMPORTANT HERE, AND MR. WISNER ONLY TALKED ABOUT ONE OF THEM. THE MOST KEY ONE HE DIDN'T TALK ABOUT, WHICH IS THAT -- THIS QUOTE FROM SARGON: "THE COURT CAN INQUIRE INTO NOT ONLY THE TYPE OF MATERIAL THEY RELY ON, BUT WHETHER THAT MATERIAL ACTUALLY SUPPORTS THE EXPERT'S REASONING."

AND THE COURT -- AND THIS IS SORT OF THE CALIFORNIA SUPREME COURT QUOTING THE U.S. SUPREME COURT: "IF THERE'S TOO GREAT AN ANALYTICAL GAP BETWEEN THE DATA THEY SAY SUPPORTS THEIR OPINION AND THEIR OPINIONS, THAT IS INADMISSIBLE UNDER SARGON."

AND THAT IS PRINCIPALLY WHAT THIS MOTION IS ABOUT AS I'LL TALK ABOUT MORE IN A SECOND.

THE ANALYTICAL GAPS HERE ARE MASSIVE, UNEXPLAINED AND UNACCOUNTED FOR.

THE SECOND PRINCIPLE IS ONE THAT MR. WISNER

FLAGGED, WHICH IS IF THERE'S TOO GREAT A LEAP OF LOGIC OR CONJECTURE, AGAIN, BASED ON THE EVIDENCE THAT IS BEING PRESENTED AS SUPPORTING THE OPINION AND WHAT THE OPINION ACTUALLY IS, THAT'S NOT ADMISSIBLE.

AND THEN FINALLY, REALLY IMPORTANT HERE BECAUSE OF WHAT I'M ABOUT TO TALK ABOUT IN A SECOND IS THAT THE EXPERT HAS TO EMPLOY THE SAME LEVEL OF INTELLECTUAL RIGOR INSIDE THE COURT AS EXPERTS DO OUTSIDE THE COURT WHEN EVALUATING WHATEVER THE BODY OF EVIDENCE IS.

SO THAT'S -- THOSE ARE THE THREE PRINCIPLES UNDER SARGON THAT ARE MOST IMPORTANT TO OUR MOTION.

NOW, WHERE WOULD ONE START TO FIGURE OUT WHETHER THE PLAINTIFFS MEET THESE STANDARDS?

WELL, THE FIRST PLACE WE SHOULD START IS WITH AN UNDISPUTED FACT.

THERE ARE NO STUDIES, ZERO, STUDYING WHETHER THE CONSUMPTION OF BABY FOOD OR THE INGREDIENTS IN BABY FOOD, FRUITS, VEGETABLES, GRAINS CAN CAUSE AUTISM OR ADHD. ZERO. NOTHING.

SO WHY IS THAT IMPORTANT HERE?

WE KNOW -- IT'S NOT IMPORTANT BECAUSE OF THE LEVELS IN BABY FOOD. WE'VE TALKED ABOUT THERE HAVE BEEN NO DISCOVERY YET, AND SO WE'RE NOT AT THE POINT IN THIS STAGE OF THE CASE WHERE WE'RE TALKING ABOUT THE LOW LEVELS ACTUALLY THAT ARE IN BABY FOOD. IF WE GET PAST THIS STAGE, WE'D TALK ABOUT THAT, BUT IT'S IMPORTANT BECAUSE IT'S RELEVANT TO THE TIMING OF EXPOSURE. THIS TEMPORALITY QUESTION.

CHILDREN EAT BABY FOOD FROM AGES SIX MONTHS TO ABOUT TWO, MAYBE SOMETIMES A LITTLE BIT LATER, BUT IN THAT WINDOW. AND SO TO PASS THE GENERAL CAUSATION STAGE AS ITS FRAMED RIGHT NOW, THE PLAINTIFF'S EXPERTS HAVE TO HAVE RELIABLE SCIENTIFIC EVIDENCE THAT EXPOSURE TO LEAD, ARSENIC AND MERCURY IN THAT WINDOW CAN CAUSE AUTISM OR ADHD. THEY HAVE NO SUCH EVIDENCE.

NOW, HOW DO I KNOW THAT? HOW DO WE KNOW THAT?

LET'S START WITH THE FACT THAT, AS MR. WISNER ACKNOWLEDGES, THIS SUBJECT OF WHAT CAUSES AUTISM IN GENERAL AND WHETHER ENVIRONMENTAL FACTORS LIKE EXPOSURES TO METALS CAUSE AUTISM HAS BEEN STUDIED ESPECIALLY IN THE PAST COUPLE OF YEARS.

THE RESEARCH ON WHAT CAUSES AUTISM IN GENERAL HAS BEEN GOING ON FOR 40 YEARS, AND AS YOU SEE AND AS I'LL SHOW IN A SECOND, MOST PEOPLE, I THINK BASICALLY EVERYONE SAYS, NO ONE KNOWS WHAT THE ACTUAL CAUSES OF AUTISM ARE. I THINK MR. WISNER SHOWED SOME QUOTES TO THAT EFFECT. THE PLAINTIFF'S EXPERTS HAVE TESTIFIED AS SUCH.

BUT ESPECIALLY AS TO ENVIRONMENTAL FACTORS, THAT HAS BEEN STUDIED OVER THE PAST COUPLE OF YEARS, AND THE SCIENTIFIC COMMUNITY HAS REVIEWED AND SCRUTINIZED THAT DATA AND WHAT HAS THE COMMUNITY SAID? NO ONE -- NO ONE -- NO GOVERNMENT AGENCY, NO AUTISM RESEARCH INSTITUTION, NO MEDICAL ORGANIZATION HAS CONCLUDED THAT THESE METALS CAN CAUSE AUTISM.

I'M GOING TO SHOW YOU, YOUR HONOR, NOW I'VE

PICKED OUT THREE FROM AMONG THE MANY EXAMPLES WE CITE IN OUR BRIEF OF POSITION STATEMENTS. THIS IS NOT FOR -- THIS IS NOT ABOUT AGENCIES WHO HAVEN'T SAID THINGS, ONE THING -- ONE WAY OR THE ANOTHER. IT IS AGENCIES, ORGANIZATIONS, RESEARCH INSTITUTIONS WHO HAVE SPOKEN ON THE TOPIC.

THIS IS WHAT THE NATIONAL INSTITUTES OF HEALTH SAYS. THEY ARE PROBABLY THE PREEMINENT FEDERAL AGENCY IN CONNECTION WITH HEALTH-BASED RESEARCH IN THE UNITED STATES. THEY TALK ABOUT AUTISM. THEY HAVE A FACT SHEET ABOUT AUTISM. IT'S NOT DATED, DATED IN THE SENSE OF IT'S NOT OUTDATED. THEY EDIT THIS ALL THE TIME. IT WAS EDITED LAST IN JANUARY OF 2022, A COUPLE OF WEEKS AGO, AND THIS IS WHAT THEY SAY:

OF COURSE THEY RECOGNIZE THE PREEMINENT ROLE OF GENETICS IN THE CAUSE OF AUTISM, AND THEN THEY SAY:

"ENVIRONMENTAL FACTORS MAY ALSO PLAY A ROLE IN GENE FUNCTION DEVELOPMENT, BUT NO SPECIFIC ENVIRONMENTAL CAUSES HAVE YET BEEN IDENTIFIED."

THAT'S WHAT THE NATIONAL INSTITUTES OF HEALTH SAYS.

MEDICAL ORGANIZATIONS: THE AMERICAN ACADEMY OF PEDIATRICS, THE LARGEST ORGANIZATION I THINK IN THE WORLD DEDICATED TO THE PROTECTION OF CHILDREN'S HEALTH, THIS IS THEIR STATEMENT FROM JANUARY OF 2020, AGAIN, FOCUSED ON THE HIGHLY HERITABLE -- THAT'S THE GENETIC PIECE OF AUTISM, BUT THEN, "POTENTIAL ENVIRONMENTAL FACTORS THAT MAY BE RELATED TO AN INCREASED

REPORTED PREVALENCE IS AN AREA OF ACTIVE STUDY THAT AS YET IS WITHOUT FIRM CONCLUSIONS."

AND THEN FINALLY, THIS IS AN INSTITUTION THAT MR. WISNER MENTIONED JUST NOW IN HIS OPENING, THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS, ACOG, OBVIOUSLY THE LARGEST ORGANIZATION IN THE UNITED STATES OF SUCH DOCTORS WHO LOOK AFTER THE HEALTH OF MOTHERS AND THEIR CHILDREN, THEIR NEWBORNS, THIS IS -- WAS REAFFIRMED THIS MONTH, JANUARY OF 2022, THIS IS WHAT ACOG SAYS ABOUT THE STATE OF THE LITERATURE ON ENVIRONMENTAL CAUSES, WHICH INCLUDES HEAVY METALS AND AUTISM.

"ALTHOUGH THE CAUSE OF AUTISM IS UNCLEAR, STRONG GENETIC PREDISPOSITION..."

LOOK AT THAT LAST SENTENCE:

"WIDE VARIETY OF EXPOSURES HAVE BEEN LINKED TO AUTISM, BUT THE SUGGESTED ASSOCIATIONS ARE WEAK INCONSISTENT, OR BOTH, AMONG STUDIES AND CANNOT BE EQUATED WITH A CAUSE AND EFFECT RELATIONSHIP."

THAT IS WHAT THE ORGANIZATION THAT IS DEDICATED TO THE PROTECTION OF PUBLIC HEALTH AND CHILDREN'S HEALTH SAY RIGHT NOW TODAY ABOUT THE BODY OF LITERATURE THAT THE PLAINTIFF'S EXPERTS RELY ON WITH RESPECT TO HEAVY METALS.

IT'S NOT JUST THAT.

THE OTHER THING THAT'S REMARKABLE ABOUT THIS CASE IS THAT THE VERY INSTITUTIONS WHERE THE PLAINTIFF'S

EXPERTS WORK ALBERT EINSTEIN, UCLA, UNIVERSITY OF MIAMI, THEY ALL HAVE PUBLISHED FACT SHEETS, ANALYSES OF AUTISM AND ITS CAUSES, NONE OF THEM -- ZERO -- IDENTIFY HEAVY METALS AS A -- EVEN A POTENTIAL CAUSE AND CERTAINLY NOT THAT IT CAN CAUSE AUTISM.

I FOCUSED -- I FOCUS ON UCLA FOR A SECOND BECAUSE WE ARE IN LOS ANGELES IN THIS CASE.

UCLA HAPPENS TO HAVE ONE OF THE PREEMINENT AUTISM RESEARCH CENTERS IN THE ENTIRE WORLD.

DR. RITZ, WHO IS AT UCLA, IS NOT IN THAT RESEARCH CENTER. SHE'S IN A DIFFERENT PART OF THE UNIVERSITY.

THE AUTISM RESEARCH CENTER AT UCLA, WHICH HAS BEEN STUDYING THE CAUSES OF AUTISM FOR 30 YEARS, NEVER HAS SAID, HAS NOT SAID THAT LOOKING AT THE BODY OF LITERATURE THAT AUTISM CAN BE CAUSED BY EXPOSURE TO HEAVY METALS.

THE THING THAT'S REALLY REMARKABLE -- AND BY THE WAY, BEFORE I LEAVE THIS SLIDE, MR. WISNER TALKED ABOUT THE CDC. I DON'T KNOW IF YOU SAW. IT WAS SORT OF FLASHED QUICKLY. THE CDC HAS A FACT SHEET ON AUTISM WHERE THEY SAY, OF COURSE THAT GENETICS AND MAYBE SOME ENVIRONMENTAL FACTORS, WHICH WE'RE STUDYING, COULD BE RELATED TO THE CAUSES OF AUTISM, AND THEN THEY LIST THE FACTORS THAT THEY THINK FALL INTO THAT CATEGORY AND THEY LIST ONE ENVIRONMENTAL FACTOR.

"WHEN TAKEN DURING PREGNANCY, THE PRESCRIPTION DRUGS VALPROIC ACID AND THALIDOMIDE HAVE BEEN

LINKED WITH A HIGHER RISK OF AUTISM."

NOWHERE DOES THE CDC SAY THAT HEAVY METALS CAN CAUSE AUTISM.

FINALLY ON THIS POINT, YOUR HONOR, THIS IS WHAT'S TRULY REMARKABLE ABOUT THIS CASE.

THE STUDY AUTHORS, THE AUTHORS OF THE VERY STUDIES ON WHICH THE PLAINTIFF'S EXPERTS RELIED, DO NOT SAY -- NOT ONLY DO THEY NOT SAY CAUSATION, THEY SAY THE OPPOSITE OF CAUSATION. I'VE PICKED THREE HERE. THERE ARE A DOZEN. THESE ARE, AGAIN, THE STUDIES ON WHICH THE PLAINTIFF'S EXPERT PRINCIPALLY RELY.

YOU SEE ARORA HERE. MR. WISNER JUST TALKED ABOUT THE ARORA STUDY. THAT'S THE ONE WITH THE TEETH AND THE TWINS. THAT'S THE ONE AT THE BOTTOM. BUT LOOK AT THESE STUDIES AND LOOK AT WHAT THE AUTHORS SAY.

SKOGHEIM, WHICH IS A 2021 STUDY, LIMITED KNOWLEDGE ON WHETHER EXPOSURE TO METALS IS LINKED TO ASD AND ADHD DIAGNOSES IN CHILDHOOD.

A META ANALYSIS, THE ONE IN THE MIDDLE, WANG IS A META ANALYSIS WHOSE SOLE -- WHO VERY PURPOSE IS TO SURVEY THE LITERATURE, THE SAME LITERATURE THAT THE PLAINTIFF'S EXPERTS ARE RELYING ON TO SEE IF THERE'S ANY CAUSAL LINK.

YOU CAN SEE THIS META ANALYSIS SAYS "NOT BEEN ESTABLISHED."

AND THEN ARORA. THE TOOTH STUDY.

"CAUTION SHOULD BE EXERCISED. ADDITIONAL STUDIES ARE NEEDED. WE CAN'T SAY CAUSATION."

EVERY SINGLE ONE OF THE STUDIES ON WHICH THE PLAINTIFF'S EXPERTS RELIED IN THAT DIAGRAM MR. WISNER SHOWED YOU WITH THE VARIOUS STUDIES IN DIFFERENT BUCKETS, THEY ALL SAY, "NO CAUSATION/NEED MORE STUDIES/HASN'T BEEN ESTABLISHED."

FINALLY, YOUR HONOR, THESE ARE TWO OF OUR EXPERTS WHO YOU'LL HEAR FROM IN MARCH AND WHY I THINK WE TALKED TO THE COURT ABOUT THIS, WHY WE WANTED, YOUR HONOR, TO HEAR FROM THEM IS THESE ARE TWO EXPERTS, TWO DOCTORS, DR. GESCHWIND AND DR. FOMBONNE, WHO ARE TRULY WORLD RENOWNED EXPERTS IN AUTISM AND ITS CAUSES. THEY RUN TWO OF THE MOST RENOWNED AUTISM RESEARCH FACILITIES IN THE WORLD, DR. GESCHWIND BEING THE ONE AT UCLA THAT I JUST MENTIONED, AND THEY WILL COME HERE AND EXPLAIN TO YOU WHY -- WHAT THE MASSIVE ANALYTICAL GAP IS BETWEEN THE BODY OF LITERATURE THAT THE PLAINTIFF'S EXPERTS ARE RELYING ON AND THE CONCLUSIONS THAT THEY ARE DRAWING, AND THEY WILL ALSO EXPLAIN TO YOU WHAT EXPERTS IN THE FIELD, THE INTELLECTUAL RIGOR THOSE EXPERTS IN AUTISM, GO THROUGH BEFORE THEY DECIDE THAT ANYTHING CAUSES AUTISM, WHICH HAS SERIOUS IMPLICATIONS FOR PUBLIC HEALTH AND CHILDREN'S HEALTH WHEN SOMEONE DECIDES THAT SOMETHING IS A CAUSE OF AUTISM. THAT'S WHAT THEY WILL BE HERE TO TALK TO YOU ABOUT.

NOW, LET ME SAY THREE THINGS ABOUT WHAT THIS HEARING AND THIS MOTION IS NOT ABOUT BECAUSE IT DIRECTLY RELATES FROM WHAT YOU JUST HEARD FROM MR. WISNER.

THE FIRST THING IS THIS HEARING, THIS MOTION IS

NOT ABOUT WHETHER GENETIC OR ENVIRONMENTAL FACTORS CAN CAUSE ASD OR ADHD, LIKE WHAT IS THE RELATIVE CONTRIBUTION OF EACH AND ARE THEY SYNERGISTIC OR NOT SYNERGISTIC.

THE HEARING IS ABOUT THREE SPECIFIC -- VERY SPECIFIC ENVIRONMENTAL FACTORS; THAT IS LEAD, ARSENIC AND MERCURY.

THERE'S BEEN RESEARCH ON DOZENS OF ENVIRONMENTAL FACTORS, THINGS IN THE ENVIRONMENT THAT PEOPLE MIGHT BE EXPOSED TO, PESTICIDES, FOR EXAMPLE, PLASTIC COMPOUNDS, AIR POLLUTION. THERE'S ALL SORTS OF RESEARCH.

THE QUESTION IN THIS CASE IS NOT HOW MUCH OF IT IS GENETIC VERSUS HOW MUCH IS ENVIRONMENTAL. IT'S ARE THESE THREE SPECIFIC ENVIRONMENTAL FACTORS, HAVE THEY BEEN SHOWN TO CAUSE OR CAN CAUSE AUTISM?

THEN THE SECOND AND RELATED POINT IS YOU HEARD MR. WISNER SAY, OH, THERE'S NO DOUBT THAT LEAD, ARSENIC AND MERCURY HAVE NEUROLOGIC EFFECTS. HE SAID THEY ARE NEUROTOXINS.

THIS HEARING, THIS MOTION, THIS CASE IS NOT ABOUT WHETHER LEAD, ARSENIC OR MERCURY CAN CAUSE NEUROLOGICAL EFFECTS OTHER THAN ASD AND ADHD.

ADHD AND ASD ARE SPECIFIC DISORDERS. THAT'S WHY THEY ARE ALL AUTISM SPECTRUM DISORDER/ATTENTION DEFICIT HYPERACTIVITY DISORDERS, THEY ARE DSM 5 DISORDERS WITH SPECIFIC DIAGNOSTIC CRITERIA.

AND THE QUESTION IS WHETHER EXPOSURE TO LEAD,

ARSENIC AND MERCURY CAUSES THOSE DISORDERS, NOT SOME OTHER NEUROLOGICAL EFFECT.

AND IN THAT REGARD, YOUR HONOR, JUST TO GIVE YOU AN EXAMPLE, MR. WISNER I THINK SAID LEAD EXPOSURE HAS BEEN ASSOCIATED WITH DECREASED IQ, FOR EXAMPLE.

IQ, INTELLECTUAL, RIGHT, CAPA- -- IS NOT A DIAGNOSTIC CHARACTERISTIC OF AUTISM, AND IN FACT, MOST AUTISTIC KIDS HAVE NORMAL TO HIGH IQ, AND THAT SHOWS YOU, YOU CAN'T JUST SAY, OH, I THINK MR. WISNER SAID, IT MAKES SO MUCH SENSE, LEAD IS A NEUROTOXIN SO IT'S NOT A GREAT LEAP OF LOGIC TO SAY THAT IT WOULD CAUSE AUTISM.

COMPLETELY UNTRUE AND UNSOUND SCIENCE.

THERE ARE NEUROLOGICAL DEFICITS THAT HAVE NOTHING TO DO WITH AUTISM OR ADHD, THEY ARE NOT RELATED TO THEM AT ALL.

AND THE FINAL THING IS -- THIS WAS REALLY COVERED IN THE PAPERS -- IS WHETHER EXPERTS SHOULD BE EXERCISING THEIR JUDGMENT AS THEY ARE ASSESSING CAUSATION. AND THERE WERE QUOTES IN THE PLAINTIFF'S OPPOSITION BRIEF THAT YOU MAY HAVE SEEN THAT SAID, WELL, OUR EXPERTS EXERCISE THEIR JUDGMENT, SO WHAT'S THE PROBLEM, BASICALLY?

THAT IS NOT WHAT THIS HEARING -- OF COURSE EXPERTS HAVE TO EXERCISE JUDGMENT WHEN REVIEWING STUDIES AND APPLYING THE BRADFORD HILL CRITERIA.

THE QUESTION IS HOW DID THEY EXERCISE THE JUDGMENT? HOW CAN IT BE REPLICATED? DID THEY EXERCISE IT IN A WAY THAT THERE AREN'T ANALYTICAL GAPS AND LEAPS

OF LOGIC?

THAT'S WHAT THIS MOTION AND THIS HEARING IS ABOUT.

AND THERE'S A REASON FOR THAT.

WE CITED TO, YOUR HONOR, IN THE BRIEFS MANY, MANY COURTS HAVE EXCLUDED BRADFORD HILL ANALYZES. THIS COMES UP QUITE FREQUENTLY IN COMPLEX MEDICAL CAUSATION LITIGATION WHERE EPIDEMIOLOGISTS COME IN PURPORTING TO APPLY A BRADFORD HILL METHOD, AND THE COURTS -- MANY COURTS HAVE SAID, THESE ARE TWO EXAMPLES, YOU REALLY HAVE TO SCRUTINIZE THAT, BECAUSE AS YOU SAW FROM THE BRIEFS AND MR. WISNER'S PRESENTATION, THERE ARE THESE NINE FACTORS, AND IT'S NOT A CHECKLIST. WE AGREE WITH THAT, THAT THE METHOD DOESN'T TELL YOU, WELL, IF THE SIX ARE PRESENT AND THREE AREN'T, THEN THERE'S CAUSATION. OR VICE VERSA. THAT'S NOT WHAT IT'S ABOUT.

BUT BECAUSE IT'S NOT ABOUT THAT, COURTS HAVE BEEN VERY RIGOROUS IN MAKING SURE THAT THE EXPERTS AREN'T REDEFINING THE FACTORS. THEY AREN'T -- OR THEY EXPLAINED HOW THEY WEIGHTED THE FACTORS. THEY EXPLAIN HOW THEY REACHED THE CONCLUSION ABOUT ANY FACTOR BECAUSE, OTHERWISE, YOU HAVE A CONCLUSION-ORIENTED SELECTION PROCESS AS THIS ONE COURT SAID.

SO LET ME START WITH, I WANT TO TALK ABOUT REALLY JUST IN THE OPENING, TWO OF WHAT WE THINK ARE THE MOST IMPORTANT BRADFORD HILL FACTORS AS IT RELATES TO THIS BODY OF LITERATURE, AND THE FIRST ONE IS TEMPORALITY.

TEMPORALITY IS THE ONE FACTOR, THE ONLY BRADFORD HILL FACTOR YOU ABSOLUTELY MUST HAVE IN ORDER TO CONCLUDE CAUSATION. IT MUST BE PRESENT, AND OF COURSE THAT'S COMMON SENSE.

THIS IS FROM THE REFERENCE MANUAL DISCUSSION OF THE TEMPORALITY FACTOR.

"IF AN EXPOSURE IS GOING TO CAUSE AN OUTCOME, IT HAS TO PRECEDE THE OUTCOME."

YOU HAVE TO HAVE STUDIES THAT SHOW AND THAT ARE CAPABLE OF SHOWING THAT IN THIS CASE EXPOSURE TO THESE HEAVY METALS OCCURRED BEFORE THE DEVELOPMENT OF AUTISM OR BEFORE THE DEVELOPMENT OF ADHD, AND THAT'S AN ABSOLUTELY REQUIRED THRESHOLD SHOWING.

AND THAT IS THE MAIN PROBLEM HERE. THAT IS THE MAIN PROBLEM WITH THE BODY OF STUDIES THAT MR. WISNER REFERRED TO. HE SAID THERE'S HUNDREDS OF STUDIES. I DON'T KNOW IF THERE'S HUNDREDS. THERE'S QUITE A FEW STUDIES, AND THEY GO IN ALL DIFFERENT DIRECTIONS, WHICH IS ANOTHER ISSUE, BUT THE BIGGEST PROBLEM IS WHAT ARE THE TYPE OF STUDIES?

IN THE REFERENCE MANUAL, THIS COMES FROM IT AS WELL, THERE'S A HIERARCHY OF HUMAN CLINICAL EVIDENCE, AN ESTABLISHED HIERARCHY THAT EVERYONE, PLAINTIFF'S EXPERTS INCLUDED, AGREES WITH. YOU HAVE AT THE TOP OF THE HIERARCHY THE THING THAT TELLS YOU THE MOST, THE MOST RELIABLE, CLINICAL TRIALS LIKE IN, RIGHT, LIKE IN A PHARMACEUTICAL CONTEXT. IF YOU GIVE ONE GROUP THE DRUG AND THE OTHER A PLACEBO AND YOU SEE WHAT HAPPENS GOING

FORWARD. WE DON'T HAVE THAT HERE. YOU COULD HAVE THAT, RIGHT, THERE COULD BE -- THERE ARE NO RANDOMIZED CLINICAL TRIALS. YOU COULD HAVE -- LOOK AT SOME KIDS WHO EAT COMMERCIALLY MANUFACTURED BABY FOOD AND SOME WHO DON'T AND FOLLOW THEM, RIGHT, THAT WOULD BE A RANDOMIZED CLINICAL TRIAL. WE DON'T HAVE THAT HERE.

WHAT THE PLAINTIFF'S EXPERTS ARE RELYING ON IS THAT MIDDLE LEVEL OF EVIDENCE, OBSERVATIONAL STUDIES, ALSO KNOWN AS EPIDEMIOLOGICAL STUDIES, BUT IMPORTANTLY, THERE ARE THREE KINDS, AND THESE ARE THE THREE KINDS; COHORT STUDIES, CASE CONTROL STUDIES, CROSS-SECTIONAL STUDIES.

THERE ARE VERY, VERY FEW COHORT STUDIES IN THIS -- THAT THE PLAINTIFF'S EXPERTS RELY ON, AND THAT'S IMPORTANT BECAUSE THE COHORT STUDIES ARE THE ONES THAT GIVE YOU TEMPORALITY.

A COHORT STUDY BRIEFLY IS SIMPLE. IT'S YOU LOOK AT A GROUP OF PEOPLE, YOU MEASURE THEIR LEVEL OF EXPOSURE IN THIS CASE, LET'S SAY LEAD, YOU MEASURE THE LEVEL OF LEAD, AND THEN YOU FOLLOW THAT GROUP, THE COHORT, GOING FORWARD AND USUALLY FOR YEARS AND YOU SEE DO THEY DEVELOP, IN THIS CASE, LET'S SAY, AUTISM. AND THEN YOU LOOK, AND IF THERE'S DIFFERENCES BETWEEN THE KIDS WHO DEVELOPED AUTISM AND THE KIDS WHO DIDN'T IN THE LEAD LEVELS THAT WERE MEASURED BEFORE THE AUTISM DEVELOPED, THEN YOU MIGHT HAVE SOMETHING THAT YOU CAN LOOK AT.

WE DON'T HAVE THAT, LARGELY SPEAKING, HERE.

THERE ARE A FEW SUCH STUDIES THAT I'LL TALK ABOUT. I WOULD SAY 95 PERCENT OF THE STUDIES THAT THE PLAINTIFF'S EXPERTS RELY ON ARE CASE CONTROL AND CROSS-SECTIONAL STUDIES.

AND WHAT IS THE PROBLEM WITH THOSE? THE PROBLEM IS THAT, WITH SOME RARE EXCEPTIONS, YOU CANNOT ESTABLISH TEMPORALITY. AND I'M GOING TO SHOW YOU WHY THAT IS WITH THIS SIMPLE HYPOTHETICAL -- NOT HYPOTHETICAL -- AN ACTUAL EXAMPLE.

WE PICKED ONE STUDY THAT THE PLAINTIFF'S EXPERTS RELY ON. IT'S A CASE CONTROLLED STUDY CALLED AL-AYADHI WHERE THEY MEASURED LEAD LEVELS IN CHILDREN WHO HAD ASD VERSUS KIDS WHO DIDN'T. AND HERE'S THE PROBLEM. DOWN AT THE AXIS, THIS IS THE AGE OF THE CHILD. WE KNOW THAT THE DISEASE OCCURS BEFORE AGE THREE. EVERYONE AGREES THAT AUTISM OCCURS -- WE THINK IT OCCURS A LOT EARLIER, THE PLAINTIFF'S EXPERTS SAY IT CAN OCCUR AT AGES TWO OR THREE. IT OCCURS IN THE EARLY CHILDHOOD YEARS.

AND SO WHAT THIS STUDY DID IS THEY LOOKED AT KIDS WHO WERE DIAGNOSED WITH AUTISM AND KIDS WHO WEREN'T AND THEY CREATED A CASE AND A CONTROL, RIGHT. THE CASE IS THE KIDS WITH AUTISM. THE CONTROL IS THE KIDS WITHOUT.

AND THEN THEY MEASURED THE EXPOSURE, AND AGAIN, THIS IS ONE EXAMPLE, THIS IS TRUE IN ALMOST ALL CASE CONTROL STUDIES, YEARS AFTER THE DEVELOPMENT OF AUTISM, YEARS AFTER THE DEVELOPMENT, THEY MEASURED -- IN THIS

CASE THEY MEASURED HAIR, BUT IT COULD BE ANY BIOMARKER. THE AVERAGE AGE AT MEASUREMENT WAS NINE -- ALMOST NINE YEARS OLD, AND THEY FOUND THAT KIDS WITH AUTISM HAD HIGHER -- IN THIS STUDY -- HAD HIGHER LEVELS OF LEAD IN THEIR HAIR THAN KIDS WHO DIDN'T.

YOU SEE THE PROBLEM, HOW YOU CANNOT ESTABLISH THE TEMPORALITY, LET ALONE CAUSATION THERE? YOU'VE GOT THIS GAP OF FIVE AND A HALF YEARS, OR WHATEVER IT IS BETWEEN, WHEN THE KIDS ACTUALLY GOT AUTISM AND WHEN THEIR LEVELS OF LEAD WERE MEASURED AND THAT RAISES THE POSSIBILITY OF WHAT EPIDEMIOLOGISTS CALL REVERSE CAUSATION.

AND REVERSE CAUSATION MEANS IT'S NOT THE EXPOSURE THAT CAUSED THE DISEASE, IT'S THE DISEASE THAT CAUSED THE EXPOSURE. AND THAT IS A FATAL PROBLEM WITH RELYING ON THESE CASE CONTROL AND CROSS-SECTIONAL STUDIES IN THIS CASE.

AND THE PLAINTIFF'S EXPERTS ACKNOWLEDGE IT'S A PROBLEM, THIS REVERSE CAUSATION. AND IT'S NOT THEORETICAL. I SAY THAT BECAUSE THE POPULATION, CHILDREN WITH AUTISM, ARE DIFFERENT. THEY HAVE CERTAIN CHARACTERISTICS ABOUT THEM THAT INCREASE THE LEVELS OF METALS IN THEIR BIOMARKERS, A MASSIVE NUMBER OF CHILDREN HAVE PICA WHO HAVE AUTISM. PICA MEANS YOU EAT THINGS THAT AREN'T FOOD, LIKE DIRT OR PAINT CHIPS OR TOYS THAT HAVE LEAD IN THEM.

AND SO IF YOU FIND THAT AGE 8.8 YEARS THAT SOME OF THE ASD KIDS HAVE HIGHER LEVELS OF LEAD THAN THE KIDS

WHO DON'T, THEY COULD -- WHAT IF THEY HAD PICA? A DECREASED ABILITY TO METABOLIZE METALS. THERE'S SOMETHING THE RESEARCH SUGGEST GENETICALLY DIFFERENT ABOUT KIDS WITH AUTISM THAT THEY HAVE THE SAME LEVEL OF EXPOSURE AS KIDS WITHOUT BUT THEY CAN'T METABOLIZE THE METALS AS QUICKLY, AND SO WHEN YOU MEASURE THE METALS, THERE'S HIGHER -- THERE MIGHT BE HIGHER THAN IN KIDS WITHOUT AUTISM.

AND NUTRITIONAL DEFICITS. KIDS WITH AUTISM HAVE IDIOSYNCRATIC EATING HABITS WHERE THEY OFTEN DON'T GET ZINC, CALCIUM, IRON, THE VITAMINS AND MINERALS THAT DO MANY THINGS, BUT AMONG THE THINGS THEY DO IS HELP EXCRETE METALS FROM THE BODY.

AND THIS AUTHOR OF THIS VERY STUDY THAT THE PLAINTIFFS RELY ON RAISED THIS PROPERLY. HERE'S THE QUOTE FROM THE ARTICLE:

"THE POSSIBLE EXPLANATION FOR THESE RESULTS IS THAT AUTISTIC CHILDREN MIGHT LACK THE ABILITY TO DETOXIFY TOXINS."

THAT IS THE PROBLEM THAT IS SEEN IN ALL THESE CASE CONTROL STUDIES AND WHY TEMPORALITY CAN'T BE SHOWN.

THERE ARE, AS I SAID, YOUR HONOR, SOME STUDIES WHERE TEMPORALITY CAN BE SHOWN, AND AS WE'LL SHOW THROUGH THIS HEARING, ALMOST ALL OF THE STUDIES WHERE TEMPORALITY CAN BE SHOWN, THERE'S NO ASSOCIATION BETWEEN EXPOSURE TO THE METALS AND AUTISM.

THE COURT: LET ME INTERRUPT YOU FOR ONE SECOND.

MR. PETROSINELLI: YES.

THE COURT: MY ASSISTANT TELLS ME THAT A GENTLEMAN NAMED CHRISTIAN JOHNSON IS SIGNED INTO L.A. COURT CONNECT AND ASKING FOR THE ZOOM LINK. DOES ANYBODY KNOW WHO THIS PERSON IS?

MR. PETROSINELLI: I DO NOT KNOW, NO.

MR. WISNER: OUR SIDE EITHER, YOUR HONOR, THAT I'M AWARE OF.

THE COURT: HE SAID HE'S A MEMBER OF THE GENERAL PUBLIC.

MR. WISNER: OKAY.

THE COURT: WELL, I THINK WHAT YOU CAN TELL HIM IS THAT IF HE WISHES TO ATTEND, HE CAN --

MR. WISNER: IF HE SENDS AN E-MAIL TO ME, YOUR HONOR, I CAN HAVE A LINK SENT TO HIM THAT HE CAN LISTEN IN ON.

THE COURT: I DON'T WANT TO SEND A LINK TO SOMEBODY I DON'T KNOW AND WHO HASN'T SIGNED A ORDER BECAUSE I COULD DO THAT. THAT'S NOT THE PROBLEM.

MR. WISNER: FAIR ENOUGH.

THE COURT: WE CAN SWOOP HIM INTO ZOOM. THE QUESTION IS WHO IS HE? IS HE GOING TO RECORD? IT DOESN'T MEAN ANYTHING TO ANY OF THE LAWYERS, I GATHER, THIS NAME CHRISTIAN JOHNSON, A MEMBER OF THE PUBLIC?

MR. WISNER: NO, YOUR HONOR.

MR. PETROSINELLI: NOT TO US, YOUR HONOR.

THE COURT: OKAY. I CANNOT BE SIMULTANEOUSLY ON ZOOM AND L.A. COURT CONNECT BECAUSE OF THE CAMERA

HOOKUP. WHAT I CAN DO IS LET THIS PERSON -- LET ME JUST THINK THIS THROUGH. THE SOLUTION TO THIS PROBLEM HAS BEEN TO WELCOME PEOPLE TO COME INTO OUR COURTROOM AND SIT AND LISTEN, SO I COULD WELCOME HIM TO COME INTO MY COURTROOM AND SIT AND LISTEN VIA TELEPHONE IF HE WISHES. HE'S NOT LOCAL.

MR. WISNER: YOUR HONOR, WE DO HAVE A LINK THAT IS AVAILABLE. THEY CAN'T -- THEY DON'T HAVE TO SPEAK OR INTERRUPT THE PROCEEDINGS, BUT THEY CAN LISTEN TO WHAT'S HAPPENING, AND PROVIDED HE AGREES TO NOT RECORD, THAT COULD PROBABLY SOLVE THE PROBLEM.

THE COURT: OKAY.

SO, TERESA, TELL HIM THAT WE WILL BRING HIM INTO THE ZOOM AS AN OBSERVER, BUT HE HAS TO SIGN OFF ON THE ORDER THAT I SIGNED THIS MORNING AND THEN E-MAIL IT TO YOU OR SOMETHING OR TO ALFREDO. SO ALFREDO WILL KNOW THE ORDER, I SIGNED IT, LIKE, YOU KNOW, 8:30 THIS MORNING OR SOMETHING. AND SO IF HE WILL CONSENT TO FOLLOWING THE RULE OF NO RECORDING, NO VIDEOTAPING, ET CETERA, THEN ONCE I HAVE A COPY OF THAT SIGNED, I WILL ASK PLAINTIFF'S COUNSEL TO SHARE THE LINK WITH HIM THAT IS OBSERVATION ONLY, OKAY.

MR. WISNER: PERFECT.

THE COURT: ALL RIGHT.

MR. PETROSINELLI: SHALL I PROCEED, YOUR HONOR?

THE COURT: YES, PLEASE. SORRY ABOUT THAT.

MR. PETROSINELLI: I'M JUST ABOUT DONE. I'M JUST GOING TO WRAP UP SOON.

I WANTED TO TALK ABOUT ONE OTHER BRADFORD HILL FACTOR, I TOLD YOU THERE WERE TWO THAT WE THOUGHT WERE PARTICULARLY IMPORTANT HERE. THE OTHER ONE IS CONSISTENCY, AND THIS IS THE DEFINITION IN THE REFERENCE MANUAL, AND IT'S A DEFINITION THAT IS A COMMON SENSE DEFINITION; THAT YOU JUST LOOK AT ALL OF THE STUDIES THAT ARE OUT THERE ON A PARTICULAR TOPIC, EXPOSURE AND THEN OUTCOME, AND YOU SEE ARE THE RESULTS THE SAME OR SIMILAR, CONSISTENT IN DIFFERENT POPULATIONS, DIFFERENT INVESTIGATORS, DIFFERENT STUDY DESIGNS WITH EACH OTHER? IN THIS CASE WOULD THEY SHOW A CONSISTENTLY POSITIVE ASSOCIATION?

AND WE KNOW WHAT THE ANSWER HERE IS BECAUSE, AGAIN, HERE ARE THE STUDY AUTHORS, THE AUTHORS OF THE VERY STUDIES ON WHICH PLAINTIFF'S EXPERTS RELY, THIS IS WHAT THEY SAY ABOUT CONSISTENCY TIME AND AGAIN, THEY LOOK BACK WHEN THEY ARE LOOKING BACK AT THE LITERATURE, THEY SAY, INCONSISTENT, INCONCLUSIVE, MIXED RESULTS, CONTRADICTORY EVIDENCE, THESE ARE THE STUDIES THAT THE PLAINTIFF'S EXPERTS RELY ON, AND THEY SAY THE LITERATURE IS ALL OVER THE MAP ON THIS.

BY THE WAY, THAT'S WHY, LIKE I SHOWED YOU AT THE BEGINNING, NO GOVERNMENT AGENCY OR REGULATORY ORGANIZATION OR MEDICAL ORGANIZATION HAS CONCLUDED CAUSATION BECAUSE THE RESULTS ARE NOT CONSISTENT.

AND SO YOU MIGHT SAY, WELL, HOW COULD THE PLAINTIFF'S EXPERTS HAVE CONCLUDED THIS BRADFORD HILL FACTOR IS SATISFIED?

AND THE REASON IS PRETTY SIMPLE. THEY REDEFINED THE FACTOR. I DEPOSED DR. RITZ. I ASKED HER, TELL ME HOW YOU DEFINE CONSISTENCY. THIS IS WHAT SHE SAID.

"IT'S CONSISTENT WITH THE EXPECTATION WITH RESPECT TO WHAT I THINK THE ANSWER SHOULD BE IF THIS OR THAT, WHAT I KNOW, WHAT I DON'T KNOW."

THEN I ASKED HER AGAIN LATER IN THE DEPOSITION TO GIVE HER ANOTHER CHANCE JUST TO BE SURE, AND SHE SAID:

"IT'S NOT CONSISTENCY OF STUDY RESULTS, IT'S NOT CONSISTENCY OF STUDY RESULTS."

WHICH OF COURSE IT IS. THAT IS THE BRADFORD HILL FACTOR. IT'S CONSISTENCY OF WHAT YOU WOULD EXPECT.

AND YOU CAN SEE, YOUR HONOR, THAT IF THAT IS THE DEFINITION OF CONSISTENCY THAT ONE IS APPLYING, IT WILL ALWAYS BE SATISFIED BECAUSE YOU'LL ALWAYS SAY, I EXPECT A CERTAIN THING, AND IF I SEE A STUDY THAT SHOWS ANOTHER RESULT, WELL, THEN I CAN DISMISS THAT STUDY AS PART OF MY CONSISTENCY ANALYSIS.

THAT IS NOT -- THAT IS THE OPPOSITE OF SOUND SCIENCE. IT'S NOT WHAT EXPERTS IN THE FIELD DO. IT'S NOT WHAT ANYONE DOES WHEN APPLYING THE BRADFORD HILL FACTORS.

AND SO, YOUR HONOR, THIS IS WHAT I WANT TO LEAVE WITH, THIS QUOTE, WHICH WE CITED IN OUR BRIEF, WHICH HAS BEEN REPEATED DOZENS AND DOZENS OF TIMES, I THINK IT ORIGINATED WITH THIS 7TH CIRCUIT CASE, WHICH IS

THAT "LAW MUST LAG SCIENCE, NOT THE OTHER WAY AROUND."

AND THAT IS ESPECIALLY -- IT'S IMPORTANT IN EVERY CASE, BUT HERE THE AUTISM COMMUNITY HAS BEEN DOWN THIS ROAD BEFORE.

WE CITED THE CASES, YOUR HONOR, IN THE BRIEF WHERE SEVERAL YEARS AGO SOME RESEARCHERS SAID MERCURY THAT WAS IN VACCINES CAUSED AUTISM AND THAT WAS WIDELY DISSEMINATED IN THE PUBLIC AND THE INTERNET AND IT WAS ALL OVER THE PLACE.

AND THEN PLAINTIFFS' LAWYERS STARTED FILING LAWSUITS ON BEHALF OF THAT SCIENCE CLAIMING THAT CHILDREN HAD AUTISM BECAUSE MERCURY WAS IN VACCINES. AND HAPPILY, AS YOU SEE FROM THE CASES WE'VE CITED, THE COURTS FOUND THAT TESTIMONY TO BE SCIENTIFICALLY UNRELIABLE, DID NOT PASS MUSTER UNDER DAUBERT, IF THEY WERE FEDERAL COURT CASES, AND THERE ARE SEVERAL STATE COURT CASES. AND THAT'S GOOD. BUT UNFORTUNATELY, THAT TOOK A WHILE AND THAT HURT PUBLIC HEALTH.

THERE ARE PARENTS IN THIS COUNTRY WHO READ ABOUT THIS AND STOPPED VACCINATING THEIR CHILDREN. THAT IS WHY IT'S SO IMPORTANT HERE, PARTICULARLY IN THE CONTEXT OF AUTISM WHEN THE COMMUNITY IS SO DESPERATE TO FIND OUT WHAT THE CAUSES ARE BUT NEEDS TO BE CAREFUL ABOUT WHAT THE CAUSES ARE.

"LAW MUST LAG SCIENCE."

AND HERE THE PLAINTIFF'S EXPERTS BY WHAT THEY HAVE DONE, THE ANALYTICAL GAPS AND THE DATA AND THE CONCLUSIONS THEY DRAW FROM IT, THE LEAPS OF LOGIC THEY

ARE ASKING LAW TO LEAD SCIENCE, AND THAT IS NOT WHAT SHOULD HAPPEN, AND THAT IS WHY THEIR OPINIONS SHOULD BE EXCLUDED UNDER SARGON.

THANK YOU, YOUR HONOR.

THE COURT: THANKS VERY MUCH.

OKAY. MR. WISNER, THE BALL'S BACK IN YOUR COURT.

MR. WISNER: THANK YOU, YOUR HONOR. I'M GOING TO HAVE MR. ESFANDIARY TAKE THE LEAD WITH DR. SHAPIRO AND THEN I'M GOING TO GO MAKE SURE DR. SHAPIRO'S ROOM IS WORKING. I'LL BE RIGHT BACK.

THE COURT: OKAY.

GOOD MORNING. I'M JUDGE HOGUE. IT'S NICE TO MEET YOU.

THE WITNESS: NICE TO MEET YOU AS WELL.

MR. ESFANDIARY: DR. SHAPIRO, ARE YOU READY?

THE WITNESS: YES, MR. ESFANDIARY, I AM READY.

MR. ESFANDIARY: YOUR HONOR, WITH YOUR PERMISSION, I CAN PROCEED?

THE COURT: PLEASE.

MR. ESFANDIARY: ALL RIGHT.

DIRECT EXAMINATION

MR. ESFANDIARY:

Q GOOD MORNING, DOCTOR.

A GOOD MORNING.

Q HOW ARE YOU THIS MORNING?

A VERY WELL. THANK YOU.

Q GOOD. GOOD.

AND, DOCTOR, CAN YOU PLEASE INTRODUCE YOURSELF BRIEFLY TO THE COURT AND WHAT IT IS THAT YOU CURRENTLY DO.

A YEAH. MY NAME IS KEVIN SHAPIRO. I'M A CHILD NEUROLOGIST. MY --

THE COURT: JUST A MOMENT. JUST ONE MOMENT, PLEASE. MY CLERK IS REMINDING US WE NEED TO SWEAR THE WITNESS.

SO YOU'LL HEAR MY CLERK IN A MOMENT TO SWEAR YOU IN, DOCTOR. THANK YOU.

THE WITNESS: OF COURSE.

THE COURT: WE HAVE SO MUCH TROUBLE COMMUNICATING AND HE'S WEARING A MASK. I CAN'T HEAR HIM. THE LUXURY OF ZOOM IS THERE'S NO MASKS.

I DON'T THINK HE CAN HEAR YOU, ALFREDO. DID YOU WANT TO COME IN HERE?

THE CLERK: YES.

THE COURT: HE'LL HEAR YOU. JUST STAND OVER THERE. NO PROBLEM.

THE CLERK: MR. SHAPIRO, 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: I DO.

THE CLERK: PLEASE SPELL YOUR FIRST AND LAST

NAME FOR THE RECORD.

THE WITNESS: K-E-V-I-N IS MY FIRST NAME. LAST NAME IS S-H-A-P-I-R-O.

THE CLERK: THANK YOU.

THE COURT: ALL RIGHT. GO AHEAD, COUNSEL.

MR. ESFANDIARY: THANK YOU, YOUR HONOR.

Q SO LET'S START AGAIN, DOCTOR.

CAN YOU PLEASE BRIEFLY INTRODUCE YOURSELF TO THE COURT AND WHAT IT IS THAT YOU CURRENTLY DO.

A SURE.

AS I SAID, MY NAME IS KEVIN SHAPIRO. I AM CURRENTLY -- I CURRENTLY WORK AT A ORGANIZATION CALLED CORTICA, WHICH IS A HEALTHCARE PROVIDER FOR CHILDREN WITH AUTISM AND OTHER NEURODEVELOPMENTAL DISABILITIES, AND I'M MEDICAL DIRECTOR FOR OUR LOS ANGELES AREA SITES, OF WHICH THERE ARE CURRENTLY THREE, AND ALSO HEAD OF RESEARCH FOR THE ORGANIZATION AS A WHOLE.

Q THANK YOU, DOCTOR.

AND TO HELP ORIENT US IN OUR DISCUSSION TODAY, I'D JUST LIKE TO PRESENT THIS ROADMAP IF IT WILL POP UP. THERE IT IS.

SO, DOCTOR, WE'RE GOING TO START OFF BY DISCUSSING YOUR QUALIFICATIONS AND BACKGROUND, AND WE'RE GOING TO PROCEED TO DISCUSSING WITH WHAT IS ASD THAT WE'RE HERE TO TALK ABOUT, AND THEN WE'RE GOING TO FINISH OFF WITH THE BIOLOGICAL PLAUSIBILITY OPINION; OKAY?

A OKAY.

Q THANK YOU.

NOW --

THE COURT: LET ME INTERRUPT YOU, COUNSEL, FOR ONE SECOND.

MR. ESFANDIARY: YES, YOUR HONOR.

THE COURT: IS THERE ANY DISPUTE AS TO THE QUALIFICATIONS OF ANY OF THE PLAINTIFF'S EXPERTS? I'M WONDERING IF WE CAN GET THROUGH HIS BACKGROUND.

THAT QUESTION IS FOR THE DEFENDANTS.

MR. ESFANDIARY: IT WILL BE VERY BRIEF, YOUR HONOR. I WOULDN'T EXPECT IT TO TAKE MORE THAN TWO TO THREE MINUTES.

THE COURT: OKAY. THAT'S FINE.

MR. IMBROSCIO: THAT'S FINE BY US. WE'RE NOT MAKING AN EXPRESS QUALIFICATION CHALLENGE, ALTHOUGH I DO THINK SOME OF DR. SHAPIRO'S QUALIFICATIONS WILL BE RELEVANT AS THE COURT CONSIDERS THE BROADER ISSUES AND WE'LL BE VERY BRIEF AS WELL.

THE COURT: NO PROBLEM. I MEAN, I HAVE READ THE EXPERT REPORTS SO I'VE SEEN THEIR QUALIFICATIONS. THANK YOU.

GO AHEAD. GO AHEAD, COUNSEL.

MR. ESFANDIARY: THANK YOU, YOUR HONOR.

Q DOCTOR, VERY BRIEFLY.

YOU ARE IN FACT A DOCTOR; CORRECT?

A CORRECT.

Q AND YOU'RE A CHILD NEUROLOGIST; IS THAT RIGHT?

A THAT'S RIGHT, YES.

Q OKAY.

AND PART OF YOUR WORK CURRENTLY AS A DOCTOR, DO YOU TREAT CHILDREN WITH AUTISM?

A I WOULD SAY THAT'S THE BULK OF MY CURRENT CLINICAL WORK.

Q YOU ALSO DIAGNOSE CHILDREN WITH AUTISM?

A THAT'S RIGHT.

Q OKAY.

SO WHERE DID YOU RECEIVE YOUR MEDICAL DEGREE, DOCTOR?

A I RECEIVED MY MEDICAL DEGREE FROM HARVARD MEDICAL SCHOOL.

Q AND YOUR PH.D.?

A ALSO FROM HARVARD UNIVERSITY.

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

A MY PH.D. WAS FOCUSED ON BRAIN MECHANISMS IMPORTANT FOR LANGUAGE PLASTICITY.

Q AND DO YOU HAVE ANY EXPERIENCE CONDUCTING RESEARCH IN THE FIELD, EITHER EPIDEMIOLOGICAL RESEARCH OR CLINICAL RESEARCH, AS IT PERTAINS TO ASD AND OTHER NEUROLOGICAL DEFICITS IN CHILDREN?

A I HAVE NOT -- WELL, I HAVE A LIMITED EXPERIENCE WITH THE EPIDEMIOLOGY RESEARCH. I'VE BEEN INVOLVED IN THE INTERNATIONAL PEDIATRIC STROKE STUDY, WHICH IS A LARGE STUDY LOOKING AT THE DEMOGRAPHIC AND EPIDEMIOLOGIC RISK FACTORS FOR STROKE IN CHILDREN.

I HAVE BEEN INVOLVED IN CLINICAL RESEARCH IN THE ORIGIN OF NEUROCOGNITIVE ISSUES AND I'M CURRENTLY

ENGAGED IN TWO CLINICAL TRIALS THAT ARE LOOKING AT NOVEL TREATMENT FOR SYMPTOMS OF AUTISM.

Q AND, DOCTOR, WHERE DID YOU DO YOUR RESIDENCY?

A I DID A RESIDENCY IN PEDIATRICS AT BOSTON'S CHILDRENS HOSPITAL AND RESIDENCY IN NEUROLOGY AND CHILD NEUROLOGY AT MASSACHUSETTS GENERAL HOSPITAL AND BRIGHAM YOUNG'S HOSPITAL.

Q AND I UNDERSTAND AT SOMETIME YOU WERE OVER AT UCSF; IS THAT CORRECT?

A THAT'S CORRECT. AFTER COMPLETING RESIDENCY, I COMPLETED A FELLOWSHIP IN VASCULAR NEUROLOGY AT UCSF AND WAS ON THE FACULTY THERE FOR A COUPLE OF YEARS AFTERWARDS.

Q VERY GOOD.

NOW, DOCTOR, I WANT TO GET INTO YOUR PRIMARY OPINIONS IN THIS MATTER, SPECIFICALLY AS IT PERTAINS TO ASD.

AND TO HELP US DO THAT, I'D LIKE TO SHOW YOU A DOCUMENT. AND THIS IS EXHIBIT 137.

AND AS THE COURT CAN SEE THIS IS A DOCUMENT TITLED "AUTISM SPECTRUM DISORDER AND THE ENVIRONMENT."

CAN YOU SEE THAT, DOCTOR?

A YES, I CAN.

Q AND IT'S A PUBLICATION I OBTAINED FROM THE NATIONAL INSTITUTES OF ENVIRONMENTAL HEALTH SCIENCES.

CAN YOU SEE THAT?

A YES.

Q DOCTOR, HAVE YOU HAD A CHANCE TO REVIEW THIS

DOCUMENT?

A I HAVE LOOKED AT THAT DOCUMENT.

Q AND DO YOU CONSIDER THE NIH A TRUSTED INSTITUTION?

A I THINK THAT'S FAIR TO SAY, YES.

Q AND WHY IS THAT, DOCTOR? WHY IS THE NIH A TRUSTED INSTITUTION, CONSIDERED A TRUSTED INSTITUTION?

A WELL, I -- I THINK THAT NIH SORT OF REPRESENTS THE SCIENTIFIC CONSENSUS ACROSS VARIOUS FIELDS OF STUDY.

NOW, HAVING SAID THAT, THERE ARE VARIOUS -- NIH IS NATIONAL INSTITUTES OF HEALTH, WHICH MEANS THAT IT COMPRISES SEVERAL INSTITUTES THAT ARE, YOU KNOW, FUNCTIONALLY SOMEWHAT INDEPENDENT OF EACH OTHER, BUT EACH OF THOSE INSTITUTES IS SORT OF CHARGED WITH THE DEVELOPMENT OF SCIENCE WITHIN A PARTICULAR FIELD.

SO IN THIS CASE, IT'S THE INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, AND THEY ARE PARTICULARLY FOCUSED ON LOOKING AT ENVIRONMENTAL CONTRIBUTIONS TO HEALTH.

Q AND, DOCTOR, I JUST WANT TO ORIENT US HERE.

I WANT TO CALL OUT VERY BRIEFLY THAT THIS WAS A PUBLICATION FROM APRIL OF 2019.

CAN YOU SEE THAT?

A I SEE THAT.

Q OKAY. NOW, LET'S DELVE INTO -- OH, SORRY -- LET'S DELVE INTO SOME OF THE THINGS THAT THE NIH SAYS IN THIS DOCUMENT.

LET'S HAVE --

MR. IMBROSCIO: YOUR HONOR.

THE COURT: YES.

MR. IMBROSCIO: I'M SORRY TO INTERRUPT. I GUESS I'M NOT SURE WHAT THE PURPOSE OF THIS IS. I THINK WE'RE HERE TO GET DR. SHAPIRO'S OPINIONS, NOT TO HAVE HIM READ A DOCUMENT FROM THE NIH. I'M JUST TRYING TO UNDERSTAND WHAT THE -- WHAT'S GOING ON HERE.

THE COURT: IT'S ALSO HEARSAY, SO I HAVE A CONCERN ABOUT IT AS WELL.

MR. ESFANDIARY: BUT, YOUR HONOR, I'M SIMPLY USING THIS DOCUMENT TO GUIDE US, AND DR. SHAPIRO IS GOING TO PROVIDE HIS OPINION KIND OF USING THIS DOCUMENT AS A SPRINGBOARD AND IT IS SOMETHING THAT HE RELIED UPON IN HIS REFERENCE LIST, AND AS YOU WELL KNOW, EXPERTS ARE PERMITTED TO RELY UPON HEARSAY DOCUMENTS.

MR. IMBROSCIO: WELL, THAT'S --

THE COURT: THEY ARE -- THEY ARE -- I'M SORRY, COUNSEL. THEY ARE PERMITTED TO RELY, BUT IF IT'S PRESENTED IN DIRECT TESTIMONY, IT'S HEARSAY; CERTAINLY THE OTHER SIDE CAN BRING OUT PARTICULAR DOCUMENTS OR STUDIES, AND THE WORDS IN THOSE DOCUMENTS OR STUDIES, IT'S NOT HEARSAY ON CROSS EXAMINATION, BUT IT IS HEARSAY ON DIRECT EXAMINATION.

MR. ESFANDIARY: I THINK I CAN --

MR. IMBROSCIO: AND THERE'S ANOTHER PROBLEM HERE, YOUR HONOR, IS THIS IS A DOCUMENT THAT WE CONFIRMED IN THE DEPOSITION HE DID NOT REVIEW PRIOR TO DOING HIS REPORT AND OFFERING HIS OPINIONS, IT'S A

DOCUMENT THAT MR. ESFANDIARY SHOWED HIM A FEW DAYS BEFORE HIS DEPOSITION, SO IT'S ALL THE MORE REASON WE THINK THAT LET'S JUST GET TO HIS OPINIONS AND MOVE FORWARD.

MR. ESFANDIARY: THAT IS JUST FACTUALLY UNTRUE, AND DR. SHAPIRO SUBMITTED A PREFERENCE LIST, THIS DOCUMENT WAS ON HIS REFERENCE LIST PRIOR -- BEFORE HE WAS DEPOSED SO THIS IS COMPRISED AS PART OF HIS OPINIONS. BUT, YOUR HONOR, IF IT WILL PLEASE THE COURT, IF I CAN DO THIS WITHOUT DIRECT REFERENCE TO THE DOCUMENT, I HAVE NO PROBLEM WITH THAT.

THE COURT: THANK YOU.

MR. ESFANDIARY: YES.

Q DR. SHAPIRO, IS IT FAIR TO CHARACTERIZE AUTISM SPECTRUM DISORDER AS A DEVELOPMENTAL DISORDER THAT APPEARS IN THE EARLY LIFE PERIOD?

A I WOULD SAY THAT'S FAIR, YES.

Q NOW, WHAT COMPRISES THE EARLY LIFE PERIOD?

A WELL, THE EARLY DEVELOPMENTAL PERIOD IS NOT STRICTLY DEFINED, BUT IT'S THE PERIOD OF SORT OF BRAIN MATURATION THAT SORT OF ENCOMPASSES LATE POST-NATAL -- SORRY -- LATE PRENATAL/EARLY POST-NATAL DEVELOPMENT UP UNTIL ABOUT TWO OR THREE YEARS OF AGE USUALLY.

SO WHAT IT ENCOMPASSES ARE THE TIMES DURING DEVELOPMENT WHERE THE BRAIN IS SORT OF ACTIVELY MATURING AND THERE CONTINUE TO BE STRUCTURAL AND ANATOMICAL CHANGES IN BRAIN NETWORKS.

SO THERE ARE, YOU KNOW, VARIOUS SUCH PROCESSES

THAT UNFOLD OVER TIME, SO LARGELY IN THE PRENATAL PERIOD, YOU HAVE THE PROCESSES OF NEUROGENESIS OR THE FORMATION OF NEURONS, NEURONAL MIGRATION, SO THE BASIC FORMATION OF THE ARCHITECTURE OF BRAIN TISSUE.

BUT IN THE POST-NATAL PERIOD UP UNTIL AROUND ROUGHLY TWO YEARS OF LIFE IS WHEN I SEE SYNAPTIC CONNECTIVITY SYNAPTOGENESIS AND MAINTENANCE OF SYNAPSIS OCCURS.

SO SYNAPSIS ARE THE CONNECTIONS BETWEEN BRAIN CELLS AND THOSE CONNECTIONS REALLY MOSTLY GET FORMED POST-NATALLY OR AT LEAST THOSE NETWORKS REALLY DEVELOP AFTER BIRTH WITH ENVIRONMENTAL INPUT.

Q I THINK IT'S VERY IMPORTANT, DOCTOR, WHAT YOU JUST SAID. I'D LIKE TO FOCUS IN ON THAT A LITTLE BIT.

THE DEFENDANTS IN THIS LITIGATION HAVE SAID THAT EVERYTHING THAT NEEDS TO HAPPEN FOR ASD TO HAPPEN OCCURS PRENATALLY OR IN UTERO.

IS THAT TRUE?

A I DON'T THINK IT'S TRUE THAT EVERYTHING THAT NEEDS TO HAPPEN OCCURS IN UTERO. THERE ARE CERTAIN -- AS I SAID, THERE'S AN UNFOLDING SET OF PROCESSES THAT CONTRIBUTE TO THE DEVELOPMENT OF THE MATURE BRAIN, SOME OF THOSE OF COURSE START IN UTERO, THE FORMATION OF NEURONS, THE, YOU KNOW, BASIC FORMATION OF BRAIN ARCHITECTURE, BUT THERE ARE PROCESSES THAT CONTINUE AFTER BIRTH AND THOSE PROCESSES ARE VERY RELEVANT TO THE DEVELOPMENT OF PATHOLOGY IN OUR EARLY CHILDHOOD.

MR. IMBROSCIO: AND, YOUR HONOR, I DON'T PLAN

TO MAKE OBJECTIONS ABOUT CHARACTERIZATIONS OF OUR POSITIONS, IDEALLY. MR. ESFANDIARY CAN ASK JUST HIM WHAT HIS OPINIONS ARE WITHOUT TYING HIM TO SOME CHARACTERIZATION OF WHAT WE SAID.

THE COURT: OVERRULED. LET'S TRY TO MINIMIZE OBJECTIONS.

MR. ESFANDIARY: THANK YOU, YOUR HONOR.

Q NOW, DOCTOR, AT WHAT AGE IS ASD TYPICALLY DIAGNOSED?

A TYPICALLY ASD IS DIAGNOSED AROUND THREE YEARS OR THREE TO FOUR YEARS OF AGE. BUT, AGAIN, YOU KNOW, TO SOME EXTENT, IT DEPENDS ON THE SEVERITY OF SYMPTOMS AND THE TYPE OF SYMPTOMS THAT ARE PRESENTED.

SO THERE ARE CASES WHERE CLINICAL SIGNS AND SYMPTOMS OF AUTISM ARE CLEARLY EVIDENCED, YOU KNOW, PRIOR TO THREE YEARS OF AGE AT 18 MONTHS OR SOMETIMES EVEN EARLIER, AND THERE ARE CASES WHERE SYMPTOMS MAY BE MILD OR UNRECOGNIZED AND THE DIAGNOSIS IS NOT MADE UNTIL LATER IN CHILDHOOD OR ADOLESCENCE OR SOMETIMES EVEN ADULTHOOD.

THERE IS A GENERAL CONSENSUS THAT SYMPTOMS SHOULD HAVE BEEN PRESENT IN THE EARLY DEVELOPMENTAL PERIOD, SO THAT MEANS -- BY GENERAL CONSENSUS, I MEAN, THAT'S PART OF THE DSM 5 DEFINITION OF AUTISM.

THE EARLY DEVELOPMENTAL PERIOD IS NOT -- YOU KNOW, THERE'S NOT A TIME LIMIT THAT'S SPECIFIED IN THAT DEFINITION, BUT GENERALLY IT'S FELT TO BE BEFORE THE AGE OF THREE YEARS.

Q DOCTOR, CAN ASD BE DIAGNOSED AT LATER AGES PAST THE AGE OF FOUR -- LET ME ASK IT IN THIS WAY.

A YEAH.

Q CAN THE SYMPTOMS OF ASD OR SYMPTOMS THAT ARE RECOGNIZED AS ASD BE IDENTIFIED PAST THE AGE OF FOUR?

A YEAH, CERTAINLY. THERE'S NO CUTOFF AS TO WHEN YOU CAN IDENTIFY THE SYMPTOMS OF ASD.

Q AND, DOCTOR, IS THERE A BIOLOGICAL MARKER TO ASD?

A THERE IS NO BIOLOGICAL TEST THAT CAN DEFINE ASD. IT'S PURELY A SET OF BEHAVIORAL CRITERIA.

Q FAIR TO SAY THAT ASD IS RECOGNIZED BY A CONSTELLATION OF SYMPTOMS?

A THAT'S RIGHT. SO THE DEFINITION IS BASED ON A CONSTELLATION OF SYMPTOMS.

Q OKAY. AND CAN THOSE SYMPTOMS OF ASD BE ALSO IDENTIFIED IN OTHER DISEASES THAT WOULDN'T BE CHARACTERIZED AS ASD?

A SOME OF THOSE SYMPTOMS CAN BE IDENTIFIED IN OTHER CONDITIONS. ASD IS SORT OF THE UNIQUE CONFLUENCE OF ALL OF THOSE CRITERIA WITH, AGAIN, WITH ONSET OF AT LEAST SOME SYMPTOMS IN THE EARLY DEVELOPMENTAL PERIOD, SO IF YOU HAVE ALL OF SYMPTOMS OF ASD, YOU HAVE ASD.

Q OKAY. WHY CAN A CHILD BE DIAGNOSED AFTER THREE YEARS OLD? IN WHAT CIRCUMSTANCES WOULD THAT HAPPEN?

A SO, FOR EXAMPLE, IF YOU HAVE A CHILD WITH -- WELL, THERE ARE VARIOUS CIRCUMSTANCES. ONE IS THAT THEY MIGHT NOT COME TO MEDICAL ATTENTION UNTIL AFTER THE AGE

OF THREE, SO, YOU KNOW, YOU MIGHT NOT -- YOU MIGHT SIMPLY NOT HAVE HAD A DIAGNOSTIC EVALUATION, BUT YOU MAY HAVE A DIAGNOSTIC EVALUATION AT THE AGE OF THREE AND FOUR AND PERHAPS, YOU KNOW, IT'S UNCLEAR AT THE TIME WHETHER OR NOT THEY MEET CRITERIA FOR AUTISM, BUT ON LATER EVALUATION IT BECOMES CLEAR THAT IN FACT THEY DO MEET THE CRITERIA.

Q DOCTOR, IS ASD A CURABLE DISORDER?

A I WOULD NOT SAY THAT IT IS A CURABLE DISORDER, AND IN FACT I SORT OF DISPUTE THE ASSERTION THAT IT'S A DISORDER. I THINK IT'S A DIFFERENCE IN BRAIN DEVELOPMENT THAT LEADS TO CERTAIN FUNCTIONAL CHALLENGES, BUT IT IS A SORT OF A PERMANENT DIFFERENCE IN THE WAY THAT THE BRAIN MATURES AND DEVELOPS.

Q ARE YOU FAMILIAR WITH THE CONSEPT OF REGRESSION IN THE CONTEXT OF ASD?

A YEAH, REGRESSION REFERS TO THE LOSS OF SKILLS THAT WERE PREVIOUSLY ACQUIRED. THIS TYPICALLY OCCURS AROUND THE AGE OF 18 MONTHS TO TWO YEARS AND IS SEEN, DEPENDING ON WHAT STUDY YOU LOOK AT, IN ABOUT A THIRD, 30 PERCENT TO A THIRD OR SO OF CHILDREN WITH AUTISM.

SO IN THESE CASES CHILDREN ARE TYPICALLY DEVELOPING THROUGHOUT THE FIRST YEAR OF LIFE USUALLY AROUND -- UNTIL AROUND 18 MONTHS OR SO, THEY MAY ACQUIRE SOME LANGUAGE AND SOCIAL SKILLS THAT TYPICALLY THEY WILL HAVE SOME WORDS AND WILL SEEM TO ENGAGE IN TYPICAL SOCIAL INTERACTIONS, AND THEN STARTING, AS I SAID, USUALLY AROUND THE AGE OF 18 MONTHS OR SO, THEY START TO

LOSE LANGUAGE AND SOCIAL SKILLS.

Q WHAT DOES THE CONCEPT OF THE REGRESSION TELL US ABOUT WHAT THE RELEVANT ETIOLOGICAL TIME FRAME FOR ASD IS?

A WELL, IT TELLS US THAT SOMETHING IS HAPPENING IN THE BRAIN AT AROUND THAT AGE THAT CONTRIBUTES TO THE EMERGENCE OF SYMPTOMS, SO, YOU KNOW, THERE'S SOMETHING THAT'S HAPPENING IN BRAIN DEVELOPMENT THAT DOESN'T LEAD TO SYMPTOMS OR AT LEAST NOT TO OVERT SYMPTOMS UNTIL AROUND THAT AGE, NOW IT CAN BE ARGUED THAT, YOU KNOW, THERE ARE STUDIES, IN FACT, THAT SHOW THAT SOME CHILDREN WITH AUTISM HAVE MORE SUBTLE SYMPTOMS EVEN PRIOR TO THE AGE OF 18 MONTHS OF, YOU KNOW, IN SOME CASES THERE ARE MARKERS OF POTENTIAL ABNORMALITIES THAT EXIST PRIOR TO THAT AND OF COURSE NOT ALL CHILDREN WITH AUTISM EXHIBIT REGRESSION, SOME EXHIBIT SYMPTOMS FROM A VERY, VERY EARLY AGE.

BUT THE OCCURRENCE OF REGRESSION IN A SUBSTANTIAL PORTION OF CASES IS TELLING YOU THAT THERE'S SOMETHING THAT'S HAPPENING IN THE BRAIN AROUND THAT TIME THAT LEADS TO A BREAKDOWN IN BEHAVIOR AND IN THE ACQUISITION OF DEVELOPMENTAL SKILLS AND FROM THE BIOLOGICAL PERSPECTIVE THAT SORT OF COINCIDES WITH PROCESSES OF SYNAPTIC FORMATION AND MAINTENANCE AND ALSO MYELINATION OF WHITE MATTER TRACTS.

Q NOW, WHAT DOES THAT MEAN WHAT YOU JUST EXPLAINED, THE PROCESS OF SYNAPTIC FORMATION IN WHITE MATTER TRACTS?

A SO SYNAPSES ARE THE CONNECTIONS BETWEEN NEURONS, SO IN ORDER, YOU KNOW, FOR ANY COGNITIVE PROCESS TO HAPPEN IN THE BRAIN, YOU NEED BRAIN CELLS TO COMMUNICATE WITH EACH OTHER TO, YOU KNOW, TRANSFER INFORMATION, PROCESS SENSORY INFORMATION THAT IS COMING IN FROM THE WORLD, INTEGRATE INFORMATION FROM DIFFERENT SOURCES, INTERPRET IT, AND, YOU KNOW, COME UP WITH A PLAN OR PRODUCE ACTION TO THOSE SPEAKING, MOVING, BEHAVING, AND SO FORTH.

SO ALL OF THOSE LINKS ARE MEDIATED BY BRAIN NETWORKS THAT RELY ON CONNECTIONS BETWEEN BRAIN CELLS IN DIFFERENT AREAS TO COMMUNICATE INFORMATION.

THE PROCESS OF FORMING THOSE CONNECTIONS IS SYNAPTOGENESIS SO THAT THE ACTUAL THE FORMATION OF THE SYNAPSIS ARE THE LINKS THAT ALLOW COMMUNICATION BETWEEN NERVE CELLS, SO THAT'S WHAT WE MEAN BY SYNAPTOGENESIS. AND THAT IS I THINK UNIVERSALLY REGARDED TO BE AN EXPERIENCE-DEPENDENT PROCESS. CERTAINLY THERE ARE GENETIC FACTORS THAT ARE IMPLICATED IN SYNAPTIC DEVELOPMENT AND THERE ARE GENES THAT CAN -- THE DISRUPTION OF WHICH CAN CAUSE YOU NOT TO BE ABLE TO FORM NORMAL SYNAPSIS, BUT THE ACTUAL SORT OF ENCODING OF INFORMATION IS DEPENDENT ON ASSIMILATING ENVIRONMENTAL INPUTS, BOTH SENSORY, BUT ASSUMING THAT'S WHAT KIND OF GUIDES THE NATURE OF OUR EXPERIENCES, AND THEN OTHER KIND OF EXOGENOUS BIOLOGICAL FACTORS CAN EFFECT THE DEGREE TO WHICH SYNAPSIS ARE STRONGER OR WEAKER OR WHETHER THEY FORM OR DON'T FORM UNDER APPROPRIATE

CIRCUMSTANCES.

Q DOCTOR, I THINK YOU HIT THE NAIL ON THE HEAD THERE.

AS A NEUROLOGIST WHO IS INVOLVED IN TREATING CHILDREN, IS IT YOUR OPINION THAT THERE IS AN ENVIRONMENTAL COMPONENT TO ASD ETIOLOGY?

A I THINK THAT THERE IS CERTAINLY AN ENVIRONMENTAL COMPONENT TO ASD ETIOLOGY. I THINK THAT THE -- CERTAINLY THE EXPRESSION OF SYMPTOMS IN ASD HAS A LOT TO DO WITH ENVIRONMENTAL INPUT IN THE EARLY DEVELOPMENTAL PERIOD.

Q TO HELP US PUT SOME FLESH ON THAT TESTIMONY, DOCTOR, I'D JUST LIKE TO PULL UP AN EXHIBIT.

THIS IS EXHIBIT NUMBER 71.

AND IT'S A STUDY TITLED "THE GENETIC INHERITABILITY AND SHARED ENVIRONMENTAL FACTORS AMONG TWIN PAIRS WITH AUTISM," AND AS WE CAN SEE HERE, IT WAS PUBLISHED IN THE ARCHIVES OF GENERAL PSYCHIATRY.

CAN YOU SEE THAT, DOCTOR?

A YES, I CAN.

Q IN 2011.

A YES.

Q IS THAT CONSIDERED A RESPECTED JOURNAL?

A YES, I WOULD SAY SO.

Q OKAY. AND IF WE JUST LOOK AT THE AUTHORS OF THIS DOCUMENT, WE HAVE LOT OF AUTHORS HERE, DOCTOR, AND FROM VARIOUS INSTITUTIONS. WE HAVE INDIVIDUALS HERE FROM STANFORD UNIVERSITY SCHOOL OF MEDICINE.

CAN YOU SEE THAT, DOCTOR?

A YES.

Q ALL RIGHT. WE HAVE PEOPLE HERE FROM THE CALIFORNIA DEPARTMENT OF THE PUBLIC HEALTH; CORRECT?

A I SEE THAT.

Q AND WE ALSO HAVE UC DAVIS?

A YES, SIR.

Q AND WE HAVE THE INSTITUTION YOU REPRESENTED WITH UCSF AS WELL?

A YES, I SEE THAT THERE.

Q DO YOU CONSIDER THESE INSTITUTIONS WELL RESPECTED INSTITUTIONS WHEN IT COMES TO UNDERSTANDING ASD AND THE ETIOLOGIES OF ASD AND THE RESEARCH THAT THEY HAVE DONE?

A YES, I THINK SO.

Q OKAY. NOW, DOCTOR, I'D LIKE TO JUST TAKE A LOOK AT WHAT THEY DID IN THIS STUDY EXACTLY AND AUTHORS THEY PROVIDE, THIS VERY HELPFUL -- WHOOPS -- THEY PROVIDE THIS VERY HELPFUL SUMMARY RIGHT HERE.

IT SAYS THAT, "THIS REPORT DESCRIBES THE RESULTS OF A TWIN STUDY OF AUTISM, THE CALIFORNIA AUTISM TWIN STUDY."

DOCTOR, WHAT IS A CALIFORNIA AUTISM TWIN STUDY?

A WELL, IT WAS ESSENTIALLY A STUDY THAT WAS DESIGNED TO LOOK AT THE GENETIC VERSUS ENVIRONMENTAL CONTRIBUTIONS TO THE PATHOGENESIS OF AUTISM.

MR. IMBROSCIO: YOUR HONOR, YOUR HONOR, I'M SORRY TO INTERRUPT AND MINDFUL OF YOUR COMMENT, BUT I

BELIEVE THIS IS A STUDY THAT IS NOT EVEN MENTIONED IN HIS REPORT, WAS NOT ON HIS RELIANCE LIST UNTIL I THINK A FEW DAYS AGO, AND SO I'M JUST NOT SURE HE'S THE RIGHT WITNESS IF THEY WANT TO SPONSOR THIS STUDY, WE DON'T REALLY HAVE NOTICE THAT THIS IS SOMETHING HE WAS GOING TO BE TALKING ABOUT AND IT'S NOT IN HIS REPORT, I HAVEN'T DEPOSED HIM ON IT, I HAD NO BASIS TO DEPOSE HIM ON IT. YOU KNOW, GIVEN WHAT HIS LIMITED ROLE IS HERE, I JUST THINK THAT IS NOT AN APPROPRIATE AVENUE.

AND IF MR. ESFANDIARY CAN TELL ME THIS WAS IN HIS REPORT OR ON HIS EARLY FIRST RELIANCE LIST, HE CAN CORRECT ME, BUT I DON'T THINK IT WAS.

MR. ESFANDIARY: IT'S ON DR. SHAPIRO'S RELIANCE LIST, YOUR HONOR. THE DEFENDANTS HAD A CHANCE TO DEPOSE HIM ABOUT THIS STUDY. MR. IMBROSCIO'S OBJECTIONS I THINK AT THIS POINT IS OBSTRUCTIONIST AND WASTING TIME SERIOUSLY. I WOULD LIKE TO PROCEED WITH EXAMINATION OF THIS WITNESS, WHO IS A NEUROLOGIST TALKING ABOUT A NEUROLOGICAL PAPER DEALING WITH HIS VERY OWN EXPERTISE.

MR. IMBROSCIO: BUT I'M SORRY, SIR. IT WAS NOT ON HIS RELIANCE LIST UNTIL A FEW DAYS AGO, I'VE CONFIRMED THAT.

THE COURT: GENTLEMAN, GENTLEMAN.

MR. IMBROSCIO: AND IT WAS NOT IN HIS REPORT.

THE COURT: GENTLEMEN, YOU NEED TO TALK TO ME, NOT TO EACH OTHER, PLEASE.

MR. IMBROSCIO: YES.

THE COURT: THANK YOU.

MR. IMBROSCIO: SORRY ABOUT THAT, YOUR HONOR.

THE COURT: THANK YOU. SOMEHOW THE DECORUM FALLS AWAY, I FIND, WHEN WE'RE ON ZOOM, BUT NOT IN THE COURTROOM. SO THANK YOU.

WELL, LET'S JUST THINK THIS THROUGH TOGETHER.

AS I SAID EARLIER, IT'S HEARSAY TO PULL UP -- YOU COULD NOT SHOW THIS ARTICLE TO A JURY AND, IN FACT, IT'S MAKING ME WONDER WHETHER WE HAVE THE ORDER OF PROOF REVERSED FOR THESE PROCEEDINGS AND WHETHER OR NOT IT WOULD BE THE DEFENDANT THAT GOES FIRST WITH THE ADVERSE CROSS EXAMINATION.

BUT I THINK THAT WE CAN ANTICIPATE THAT AS TO ANY ARTICLES IDENTIFIED IN THE REPORT AS MATERIALS ON WHICH THE DOCTOR RELIED, THERE IS GOING TO BE VIGOROUS CROSS EXAMINATION. I THINK IT IS A LITTLE UNFAIR TO ASK HIM ABOUT AN ARTICLE ON DIRECT THAT IS HEARSAY, ESPECIALLY IF IT WAS NOT IDENTIFIED PREVIOUSLY, SO I THINK IF IT'S NOT ON THE LIST, THAT'S A PROBLEM.

MR. WISNER: BUT, YOUR HONOR, A COUPLE OF THINGS, AND I THINK THIS IS JUST REALLY IMPORTANT, YOU KNOW, THIS IS NOT A JURY TRIAL, THIS IS A SARGON HEARING AND THE DEFENDANTS HAVE LITERALLY PUT THE ISSUE OF THE UNDERLYING STUDIES AT ISSUE AS CLEARLY DEMONSTRATED IN THE LENGTHY DEPOSITIONS ABOUT THESE STUDIES AND EVIDENCE THAT THE DEFENSE WOULD LIKE THE COURT TO EXAMINE, SO I THINK IT WOULD BE A LITTLE BIT DIFFICULT FOR US TO PARTICIPATE IN A MEANINGFUL SARGON HEARING WHICH IS MEANT TO THE GET THE BASIS OF THEIR OPINIONS AND WHAT

THEY RELIED UPON WITHOUT SHOWING THE COURT WHAT THEY RELIED UPON.

THE COURT: I DON'T DISAGREE WITH THAT, BUT IF IT WASN'T ON LIST, I'M NOT SURE IT'S FAIR.

MR. WISNER: WELL, ABOUT THAT, YOUR HONOR, MY UNDERSTANDING IS IT WAS ON HIS RELIANCE LIST, I DON'T KNOW IF IT WAS ON HIS RELIANCE LIST PRIOR TO HIS DEPOSITION, BUT IT HAS BEEN ON HIS RELIANCE LIST AND THEY ARE FREE TO CROSS EXAMINE HIM ABOUT IT TO THE EXTENT THAT THEY WISH. I MEAN, THAT'S WHAT WE'RE HERE TO DO. WE'RE HERE TO GET TO THE TRUTH, NOT RESTRICT OPINIONS NEEDLESSLY.

I KNOW YOUR HONOR HAD AN 11:00 A.M. MEETING SO THAT JUST OCCURRED TO ME.

THE COURT: I JUST GOT A NOTE ON THAT SO WE NEED TO TAKE ABOUT A FIVE-MINUTE BREAK. THANK YOU.

MR. WISNER: YES, YOUR HONOR.

MR. IMBROSCIO: THANK YOU, YOUR HONOR.

THE COURT: I'M GOING TO LEAVE ALTOGETHER, BUT I'LL COME BACK.

(RECESS)

THE COURT: OKAY. I AM BACK.

I WAS JUST ABOUT TO SAY THAT WE HAVE TWO ISSUES HERE; ONE IS WHETHER ON CROSS -- AND I AGREE WITH YOU MR. WISNER THAT SINCE THE WHOLE POINT OF THIS EXERCISE IS TO LOOK AT THE DATA UNDERLYING THE EXPERT'S REPORTS, IT'S OKAY, AND I WILL NOT BE CONCERNED ABOUT THE HEARSAY OBJECTION FOR THAT PURPOSE, BUT THERE'S A FAIRNESS ISSUE

HERE ABOUT IT NOT BEING ON THE LIST.

CAN YOU VERIFY WHETHER IT WAS OR IT WASN'T?

MR. ESFANDIARY: YES, YOUR HONOR. SO IT WASN'T ON HIS LIST PRIOR TO HIS DEPOSITION. IT WAS PUT ON HIS LIST AFTER WE RECEIVED THE DEFENDANTS' SARGON MOTION BECAUSE THEY MAKE ACCUSATIONS IN THAT MOTION REGARDING THE EXTENT OF GENES AND THE ENVIRONMENT SPECIFICALLY REGARDING DR. SHAPIRO'S OPINION, AND HE HAS A RIGHT TO RESPOND TO THAT. AND WE TOOK A LOOK AT THE MOTION AND WE PUT THIS STUDY ON HIS REFERENCE LIST.

DEFENDANTS HAVE HAD WEEKS AND WEEKS --

THE COURT: I WILL ALLOW IT. PLEASE CONTINUE.

MR. ESFANDIARY: THANK YOU.

Q ALL RIGHT. DOCTOR, CAN YOU HEAR ME?

A YES, I CAN.

Q ALL RIGHT. GREAT. I'D JUST LIKE TO TURN OUR ATTENTION BACK TO THIS DOCUMENT.

SO WE WERE TALKING ABOUT THE HALLMAYER STUDY FROM 2011 AND YOU WERE TESTIFYING ABOUT THE CALIFORNIA AUTISM TWIN STUDY.

WHAT IS THAT, DOCTOR?

A YES. SO THAT WAS SORT OF A BROAD STUDY THAT AIMED TO EXAMINE THE RELATIVE CONTRIBUTIONS OF GENETIC AND ENVIRONMENTAL INFLUENCES TO THE PATHOGENESIS OR TO THE DIAGNOSIS OF AUTISM IN A SORT OF A VERY BROAD COHORT, SO IT WAS A POPULATION-BASED STUDY WITHIN THE STATE OF CALIFORNIA, I THINK THEY SCREENED -- I DON'T HAVE THE STUDY IN FRONT OF ME, BUT I THINK THEY SCREENED

SOMETHING LIKE 1,100 TWIN COHORTS AND ENDED UP ENROLLING 404 TWINS OR ENDED UP ANALYZING, I THINK WITH GENETIC DATA, SOMETHING LIKE 202 TWIN PAIRS.

Q VERY GOOD.

AND, DOCTOR, IT'S SAYING THAT THE CHIEF AIMS WERE, NUMBER ONE, COLLECT A SAMPLE OF TWINS WITH VALIDATED DIAGNOSIS OF AUTISM FROM A POPULATION-BASED SAMPLE.

WHAT IS A VALIDATED DIAGNOSIS OF AUTISM?

A SO A VALIDATED DIAGNOSIS OF AUTISM AS THEY ARE USING IT HERE MEANS A DIAGNOSIS THAT IS MADE CLINICALLY AND CONFIRMED BY TWO STANDARDIZED INSTRUMENTS, THE AUTISM DIAGNOSTIC OBSERVATION SCHEDULE FOR THE ADOS AND THE AUTISM DIAGNOSTIC INTERVIEW REVISED OR THE ADIR, SO THOSE ARE TWO KIND OF STANDARDIZED INSTRUMENTS THAT ARE RECOGNIZED AS AMONG THE GOLD STANDARD FOR MAKING AN AUTISM DIAGNOSIS.

Q SO THEY ARE USING THE GOLD STANDARD HERE TO DETERMINE DIAGNOSIS, THEN, IS THAT FAIR TO SAY?

A ESSENTIALLY, YES. SO THOSE ARE THE INSTRUMENTS THAT ARE MOST WIDELY USED TO MAKE THAT DIAGNOSIS IN THE UNITED STATES.

Q OKAY.

AND NUMBER TWO, IT SAYS EXAMINE SET-SPECIFIC CONCORDANCE RATES FOR NARROW AND BROAD DEFINITIONS OF AUTISM.

DOCTOR, WHAT ARE THEY GETTING AT HERE? WHAT DOES SET-SPECIFIC CONCORDANCE RATE?

A CONCORDANCE RATE MEANS, YOU KNOW, IF ONE TWIN IS DIAGNOSED WITH AUTISM, HOW LIKELY IS IT OR IN WHAT PERCENTAGE OF CASES THE OTHER TWIN DIAGNOSED WITH AUTISM, AND THEY LOOKED AT THAT SEPARATELY FOR MALE/MALE TWINS, MALE/FEMALE TWINS, AND SEX DISCORDANT TWINS, AND THE RELEVANCE OF THAT IS THAT THE RATE OF AUTISM IS KNOWN TO DIFFER BETWEEN MALES AND FEMALES FOR REASONS THAT ARE NOT ENTIRELY UNDERSTOOD.

AND WHEN THEY DISTINGUISHED NARROW AND BROAD DEFINITIONS OF AUTISM, WHAT THEY ARE TALKING ABOUT THERE IS THAT SORT OF THE STRICT DEFINITION OF AUTISM, "SO MEETS ALL CRITERIA ON THE ADOS AND ALL CRITERIA ON THE ADIR" FROM SORT OF A WIDER SET OF SYMPTOMS WHERE YOU MAY -- YOU MEET CRITERIA ON THE ADOS BUT YOU MAY NOT COMPLETELY FULFILL ALL THE CRITERIA ON THE OTHER TEST.

SO IN OTHER WORDS, THE BROADER DEFINITION ENCOMPASSES PEOPLE WHO WOULD CLINICALLY BE DIAGNOSED WITH AN AUTISM SPECTRUM DISORDER, BUT THEY DON'T STRICTLY MEET CRITERIA ON BOTH OF THOSE INSTRUMENTS.

Q DOCTOR, THE PREFACE OF THE STUDY WAS TO DETERMINE THE EXTENT TO WHICH GENETIC SHARED ENVIRONMENTAL FACTORS UNDERLIE SUSCEPTIBILITY.

DO YOU SEE THAT, DOCTOR?

A YES.

Q I THINK IT'S IMPORTANT HERE.

THEY ARE ASSUMING THERE ARE ENVIRONMENTAL FACTORS TO SUSCEPTIBILITY, THEY ARE JUST TRYING TO FIND OUT TO WHAT EXTENT THOSE ENVIRONMENTAL FACTORS PLAY A

ROLE; CORRECT?

A I THINK THAT'S FAIR TO SAY.

Q NOW, LET'S TAKE A LOOK AT THE RESULTS HERE, DOCTOR. I THINK THEY PRESENT THEM PAGE 1. I'M JUST GOING TO CALL THIS OUT.

UNDER "RESULTS" THEY SAY, "FOR STRICT AUTISM, PROGRAMWIDE CONCORDANCE FOR MALE TWINS WAS .58 FOR 40 MONOZYGOTIC PAIRS."

DO YOU SEE THAT, DOCTOR?

A YES.

Q AND CONCORDANCE REFERS TO WHAT IN THIS CONTEXT?

A SO IN THIS CONTEXT IT MEANS THAT 58 PERCENT OF THE TIME BOTH TWINS SHARED A DIAGNOSIS OF AUTISM.

Q AND THESE ARE IDENTICAL TWINS, CORRECT, MONOZYGOTIC?

A CORRECT. MONOZYGOTIC TWINS ARE IDENTICAL TWINS WHO SHARE A HUNDRED PERCENT OF THEIR GENETIC MATERIAL.

Q SO IF 58 PERCENT SHARED A DIAGNOSIS OF AUTISM, DOES THAT MEAN THAT 42 PERCENT DID NOT SHARE A DIAGNOSIS OF AUTISM?

A THAT IS THE DIRECT IMPLICATION.

Q OKAY.

AND FOR FEMALE TWINS, THE CONCORDANCE WAS -- IS THAT 60 PERCENT, DOCTOR, FOR IDENTICAL PAIRS?

A YES.

Q AND DOES THAT MEAN THAT 40 PERCENT DID NOT SHARE THE DIAGNOSIS OF AUTISM? 40 PERCENT OF TWINS DID NOT SHARE THE DIAGNOSIS OF AUTISM; IS THAT CORRECT?

A YES.

Q OKAY.

AND FOR ASD AND THE SPECTRUM DISORDERS, IT SAYS THE PROGRAMWISE FOR CONCORDANCE FOR MALE TWINS WAS 77 PERCENT; CORRECT?

A THAT'S CORRECT. SO YOU KNOW WHAT THAT IS SAYING IS THAT IF YOU LOOSEN THE CRITERIA A LITTLE BIT, THE CONCORDANCE ACTUALLY GOES UP, AND WHAT THAT IS SUGGESTING IS THAT ONE TWIN HAD MORE SEVERE SYMPTOMS THAN THE OTHER TWIN OR MET MORE CRITERIA FOR THE DIAGNOSIS THAN THE OTHER TWIN; SO EVEN THOUGH THEY BOTH HAVE THE DIAGNOSIS OR MEET THE CUTOFF CRITERIA FOR ASD, ONE TWIN IS MORE SEVERELY AFFECTED THAN THE OTHER.

Q IT SAYS HERE THAT THEY CONCLUDE FROM THE BASIS OF THIS DATA THAT A LARGE PROPORTION OF THE VARIANCE IN LIABILITY CAN BE SHARED BY ENVIRONMENTAL FACTORS IN ADDITION TO MODERATE GENETIC HERITABILITY.

DO YOU SEE THAT, DOCTOR?

A YES.

Q OKAY. CAN YOU UNPACK THAT FOR US? WHAT IS YOUR UNDERSTANDING OF WHAT THAT'S REFERRING TO, THAT CONCLUSION?

A SO HERITABILITY IS THE DIFFERENCE BETWEEN THE CONCORDANCE RATE IN MONOZYGOTIC AND DIZYGOTIC TWINS, SO THE EXTENT TO WHICH THE VARIATION IN A TRAIT IS ATTRIBUTABLE TO GENETIC FACTORS; SO IF YOU TAKE MONOZYGOTIC TWINS WHO SHARE A HUNDRED PERCENT OF THEIR DNA AND DIZYGOTIC TWINS WHO SHARE 50 PERCENT OF THEIR

DNA, THE AMOUNT OF VARIATION IN A PARTICULAR DIAGNOSIS OR SUSCEPTIBILITY TO A DIAGNOSIS THAT CAN BE EXPLAINED BY GENETIC FACTORS CAN BE CALCULATED DIRECTLY FROM THAT DIFFERENCE.

SO WHAT THEY ARE SAYING HERE IS THAT, FIRST OF ALL, THAT THE HERITABILITY IN THIS STUDY WAS -- IS LOWER THAN IN THIS OTHER PUBLISHED STUDIES NOT NESS -- PARTLY BECAUSE THE CONCORDANCE RATE IN MONOZYGOTIC TWINS MAY BE LOWER, BUT ALSO BECAUSE THE CONCORDANCE RATE IN DIZYGOTIC TWINS IS HIGHER THAN WHAT HAS BEEN OBSERVED IN OTHER STUDIES.

SO THE HERITABILITY IS STILL, YOU KNOW, FOR NEUROBEHAVIORAL DISORDER, IT'S STILL A SUBSTANTIAL HERITABILITY, BUT LESS THAN WHAT HAS BEEN DEMONSTRATED IN OTHER STUDIES. AND TO THE EXTENT THAT THE VARIATION IN DIAGNOSIS OR SUSCEPTIBILITY TO THE DIAGNOSIS CAN'T BE EXPLAINED BY GENETIC FACTORS MUST BE EXPLAINED BY ENVIRONMENTAL FACTORS.

AND THOSE -- IN THIS CASE THEY ARE SHARED ENVIRONMENTAL FACTORS BECAUSE THEY ARE TWINS. I BELIEVE IN THIS CASE THEY ARE ALL TWINS WHO WERE RAISED TOGETHER SO THEY SHARED AN ENVIRONMENT. YOU CAN ALSO LOOK AT NON SHARED ENVIRONMENT, BUT IT'S VERY HARD TO DO THAT IN THIS TYPE OF STUDY BECAUSE OF COURSE, YOU KNOW, IN TWINS WHO ARE RAISED TOGETHER THEY ARE SHARING MOST OF THEIR EARLY ENVIRONMENTAL EXPOSURES.

Q DOCTOR, TO JUST FOCUS IN ON THAT LAST POINT, I WANT TO JUST LOOK AT THIS PARAGRAPH TOWARDS THE END OF

THE PAPER WHERE THEY SAY, "TO OUR KNOWLEDGE THIS STUDY IS THE LARGEST POPULATION BASED TWIN STUDY OF AUTISM THAT USED CONTEMPORARY STANDARDS FOR THE DIAGNOSIS OF AUTISM."

DO YOU SEE THAT, DOCTOR?

A YES.

Q AND THEY SAY HERE THAT THE RESULTS SUGGEST THAT THE ENVIRONMENTAL FACTORS COMMON TO TWINS EXPLAIN ABOUT 55 PERCENT OF THE LIABILITY TO AUTISM.

DO YOU SEE THAT, DOCTOR?

A CORRECT. I SEE THAT.

Q AND WHAT DO THEY MEAN WHEN THEY SAY THAT 55 PERCENT OF THE ENVIRONMENTAL FACTORS EXPLAIN THE LIABILITY TO AUTISM? WHAT ARE THEY GETTING AT?

A SO LIABILITY, AGAIN, THE SUSCEPTIBILITY TO DEVELOP THE DIAGNOSIS OF AUTISM.

SO LIABILITY IS WHAT'S CALLED AN UNSEEN TRAIT, SO IT'S THE TRAIT THAT KIND OF DETERMINES YOUR LIKELIHOOD TO HAVE A DIAGNOSIS, AND ABOUT 55 PERCENT OF THE VARIABILITY IN THAT TRAIT IS ATTRIBUTABLE TO ENVIRONMENTAL FACTORS.

NOW, AS I SAID THEY USE THE TERM SHARED ENVIRONMENTAL FACTORS. THEY ACTUALLY CAN'T REALLY DISTINGUISH BETWEEN SHARED AND NON SHARED IN THIS CASE. I THINK THE ASSUMPTION IS THAT THEY ARE SHARED ENVIRONMENTAL FACTORS.

Q AND WHAT IS IT -- FOR YOU WHAT IS THE PRIMARY TAKEAWAY FROM THE HALLMAYER STUDY?

A SO I WOULD SAY THAT THE TAKEAWAY HERE IS THAT THERE IS CERTAINLY AN IMPORTANT GENETIC INFLUENCE ON SUSCEPTIBILITY OR LIABILITY TO AUTISM, AND, YOU KNOW, IT'S CLEARLY THE CASE THAT IF -- THAT GENETICS PLAYS A ROLE IN LIABILITY.

BUT IT CAN'T BE THE ONLY FACTOR IN DETERMINING WHETHER OR NOT YOU RECEIVE A DIAGNOSIS BECAUSE, YOU KNOW, A SUBSTANTIAL PROPORTION OF THE TIME TWO CHILDREN, TWO TWINS WITH EXACTLY THE SAME GENETICS MAY NOT HAVE THE SAME DIAGNOSIS, AND EVEN IF THEY HAVE THE SAME CATEGORICAL DIAGNOSIS, THEY MAY NOT HAVE THE SAME SYMPTOMS OR LEVEL OF SEVERITY SO SOMETHING ABOUT THAT DIFFERENCE HAS TO BE EXPLAINED BY ENVIRONMENTAL FACTORS.

THE COURT: AND IF I COULD INTERJECT A QUESTION.

ENVIRONMENTAL FACTORS IN THIS STUDY MEANS ANYTHING OTHER THAN GENETICS?

THE WITNESS: CORRECT. YES. THAT'S WHAT THEY MEAN IN THIS STUDY.

THE COURT: ALL RIGHT.

MR. ESFANDIARY:

Q DOCTOR, DO HEAVY METALS QUALIFY AS ENVIRONMENTAL FACTORS?

A THEY DO.

Q I'M SORRY?

A THEY COULD IF THEY ARE PRESENT IN THE PERIOD THAT IS RELEVANT FOR THE DEVELOPMENT OF SYMPTOMS OF AUTISM, SO THEY OF COURSE DO NOT MENTION HEAVY METALS AS

A SPECIFIC ENVIRONMENTAL FACTOR, NOR DO THEY MENTION INGESTION OF BABY FOOD OR EXPOSURE TO OTHER CHEMICALS OR LIVING NEAR A HIGHWAY OR ANY OF THE OTHER, YOU KNOW, EPIDEMIOLOGIC FACTORS THAT HAVE BEEN CITED AS CONTRIBUTING TO AUTISM, SO NONE OF THOSE ARE CALLED OUT SPECIFICALLY, BUT THEY COULD ALL BE INCLUDED.

Q NOW, DOCTOR, IS THIS APPROPRIATE TO THINK ABOUT ASD RISK IN ANY GIVEN CASE IN TERMS OF STRICT PERCENTAGES? 60 PERCENT ENVIRONMENTAL/40 GENETIC AND VICE VERSA? IS IT APPROPRIATE TO THINK ABOUT ASD RISK IN INDIVIDUAL CASES THAT WAY?

A SO HERITABILITY -- SO IT -- THE WAY IN WHICH WE THINK ABOUT THAT FOR INDIVIDUAL CASES AS OPPOSED TO IN THE POPULATION IS A LITTLE BIT DIFFERENT, SO HERITABILITY IS A POPULATION ESTIMATE, AND IN PART THAT, YOU KNOW, GETS THE QUESTION OF WHY THERE ARE DIFFERENCES IN MEASURED HERITABILITY ACROSS DIFFERENT STUDIES.

SO IN THIS HALLMAYER STUDY, FOR EXAMPLE, THEY POINTED OUT THAT A LOT OF OTHER STUDIES LOOKING AT HERITABILITY OF AUTISM WERE DONE IN RELATIVELY HOMOGENOUS POPULATIONS IN NORTHERN EUROPE AND SCANDINAVIA, FOR EXAMPLE; WHEREAS, THIS STUDY WAS DONE IN CALIFORNIA AND INCLUDED SORT OF A BROADER ARRAY OF INDIVIDUALS IN THE POPULATION, SO WIDER VARIATION IN SOCIOECONOMIC STATUS, ETHNICITY, AND SO FORTH.

AND THE RELEVANCE OF THAT IS THAT HERITABILITY -- ACTUALLY, THE WAY IN WHICH YOU MEASURE HERITABILITY ALSO DEPENDS A LOT ON ENVIRONMENTAL FACTORS.

SO AN ANALOGY THAT YOU COULD USE IS THAT IMAGINE THAT YOU HAVE, LIKE, A GARDEN OR A PLOT OF LAND AND YOU SEED IT WITH GRASS SEED, ASSUMING, YOU KNOW, THE GRASS SEED IS NOT ALL GENETICALLY IDENTICAL AND, YOU KNOW, THE GRASS WILL GROW. AND IF THE ENTIRE PLOT, THE LAND HAS ACCESS TO THE SAME ENVIRONMENTAL RESOURCES, SUNLIGHT, WATER NUTRIENTS, YOU KNOW, THE SAME QUALITY SOIL, THEN THE VARIATION IN THE HEIGHT OF THE GRASS IS GOING TO BE PRIMARILY BASED ON GENETIC FACTORS.

SO ALL OF THOSE, YOU KNOW, GRASS PLANTS HAVE ACCESS TO THE SAME ENVIRONMENT, AND SO THE EXTENT TO WHICH ONE IS TALLER THAN THE OTHER IS GOING TO BE EXPLAINED BY GENETIC FACTORS.

ON THE OTHER HAND, YOU KNOW, IF YOU COVER PART OF THE PATCH WITH AN UMBRELLA SO THAT SOME OF IT IS IN THE SHADE OR IF YOU TAKE LEAD PELLETS AND SPRINKLE IT ON ANOTHER PART OF THE GRASS, YOU KNOW, THAT THAT'S GOING TO BE AN ADVERSE IMPACT ON GROWTH OF THE PLANTS, THERE'S GOING TO BE A LOT MORE VARIABILITY BECAUSE, YOU KNOW, THESE ENVIRONMENTAL DIFFERENCES THAT YOU'VE INTRODUCED IN THE HERITABILITY, SO THE PROPORTION OF THAT HERITABILITY THIS A DUE STRICTLY TO GENETIC FACTORS IS GOING TO BE LESS.

Q DOCTOR, THAT SEGUES PERFECT INTO THE NEXT PART OF OUR DISCUSSION HERE.

I WOULD JUST LIKE TO BRING UP THIS WITH THE COURT'S PERMISSION, CAN WE GO BACK TO THE NIH DOCUMENT, YOUR HONOR, SINCE THE HEARSAY ISSUE HAS BEEN RESOLVED?

THE COURT: YES.

MR. ESFANDIARY: THANK YOU.

Q NOW, DOCTOR, THEY SAY HERE THAT, "RESEARCH SHOWS THAT BOTH ENVIRONMENTAL AND GENETIC FACTORS LIKELY PLAY A ROLE IN AUTISM SPECTRUM DISORDER."

DO YOU SEE THAT, DOCTOR?

A YES.

Q AND THAT'S WHAT WE WERE JUST TALKING ABOUT; CORRECT?

A CORRECT.

Q ALL RIGHT.

AND HERE THEY SAY THAT, "NIH IS FINDING NEW WAYS TO RESEARCH FUND RESEARCH TO UNDERSTAND HOW ENVIRONMENTAL FACTORS INTERACT WITH GENES IN WAYS THAT MAY LEAD TO ASD."

DO YOU SEE THAT, DOCTOR?

A YES.

Q DOCTOR, CAN YOU JUST EXPLAIN TO US IN WHAT WAYS CAN ENVIRONMENT INTERACT WITH GENES TO CAUSE ASD?

A WELL, SO FOR EXAMPLE, YOUR GENETIC PROFILE MAY LEAD YOU TO HAVE DIFFERENTIAL SUSCEPTIBILITY TO ENVIRONMENTAL INFLUENCES, AND SO, YOU KNOW, ONE OF THE STUDIES THAT LOOKED AT ENVIRONMENTAL CONTRIBUTORS TO AUTISM DIAGNOSIS WAS THE CHARGE STUDY WHICH LOOKED AT AIR POLLUTANTS, AND AMONG THE FINDINGS OF THAT STUDY WAS THAT CHILDREN WITH A PARTICULAR VARIANCE IN THE NAD RECEPTOR KINASE GENE WERE MORE SUSCEPTIBLE TO DEVELOP AUTISM WHEN EXPOSED TO POLLUTANTS.

SO IN OTHER WORDS, YOU HAVE THE SAME -- WITH ANY SORT OF THE GIVEN LEVEL OF EXPOSURE TO A POLLUTANT THAT MAY CAUSE -- THAT MAY CAUSE AUTISM, SOME CHILDREN DEVELOP IT AND OTHERS DON'T AND PART OF THE DIFFERENCE THERE HAS TO DO WITH THEIR GENETIC SUSCEPTIBILITY.

SAME THING WITH, YOU KNOW, A LOT OF THE GENES THAT PLAY A ROLE IN BRAIN DEVELOPMENT. WE TALKED A LITTLE BIT EARLIER ABOUT THE VARIOUS KIND OF STAGES OF THE BRAIN DEVELOPMENT. IF YOU HAVE A GENETIC RISK FACTOR THAT, YOU KNOW, THAT IMPAIRS THE FORMATION OF CONNECTIONS OF THE GROWTH OF SYNAPSIS, YOU MIGHT BE MORE VULNERABLE TO ANY ADDITIONAL INPUTS THAT ARE GOING TO FURTHER DISRUPT THAT PROCESS.

I THINK ONE OF THE THINGS THAT HAS COME UP, FOR EXAMPLE, IN THIS CONTEXT AS WELL IS THE DIFFERENTIAL SORT OF SUSCEPTIBILITY OF -- OR THE DIFFERENT ABILITY OF KIDS WITH AUTISM TO HANDLE AND METABOLIZE METALS, AND THAT IS, YOU KNOW, THE BASIS FOR THAT ARE NOT ENTIRELY UNDERSTOOD. IT COULD MEAN THAT, YOU KNOW, FOR GENETIC REASONS THESE CHILDREN HAVE THE DECREASED ABILITY TO HANDLE AND EXCRETE METALS FROM THEIR SYSTEM, BUT THAT, YOU KNOW, THAT MIGHT ALSO MAKE THEM MORE SUSCEPTIBLE TO DAMAGE CAUSED BY METAL EXPOSURE, THE METALS ARE HANGING AROUND LONGER IN THEIR SYSTEM, AND THEREFORE HAVE MORE OF AN OPPORTUNITY TO INTERFERE WITH THE DEVELOPMENT OF BRAIN CONNECTIVITY AND PROMOTE OXIDATIVE STRESS, AND SO FORTH.

Q DOCTOR, IS THERE ONE CAUSE -- WELL, LET ME

PHRASE IT THIS WAY: SO EVEN IN CASES WHERE THERE'S A WELL-DEFINED UNDERSTOOD GENETIC COMPONENT, CAN ENVIRONMENTAL TRIGGERS STILL PLAY A ROLE IN CAUSING AUTISM?

A I THINK THAT'S CERTAINLY THE CASE.

AND, YOU KNOW, EVEN IF YOU HAVE A GENETIC RISK FACTOR THAT IS HIGHLY ASSOCIATED WITH AUTISM, THE DEGREE AND THE SEVERITY OF YOUR SYMPTOMS IS GOING TO BE QUITE DEPENDENT ON ENVIRONMENTAL INPUTS.

AND SO, FIRST OF ALL, YOU KNOW, THERE IS THIS QUESTION OF WHETHER YOU MEET CRITERIA FOR A BINARY DIAGNOSIS, AND TO MY KNOWLEDGE I'M NOT AWARE OF ANY GENES THAT CONFER A HUNDRED PERCENT RISK OF AUTISM, EVEN IN THE CONDITIONS THAT ARE MOST CLOSELY GENETICALLY ASSOCIATED WITH AUTISM, YOU KNOW, THE RISKS ARE NOT ABSOLUTE.

BUT IN CHILDREN WHO HAVE AUTISM AND HAVE GENETIC SUSCEPTIBILITY EVEN WHEN GENETICS IS RECOGNIZED TO PLAY AN EXTREMELY IMPORTANT ROLE IN BRAIN DEVELOPMENT AND THERE MAY BE, YOU KNOW, OBVIOUS EVEN STRUCTURAL ABNORMALITIES IN THE BRAIN, STILL YOU KNOW, THE ENVIRONMENT TO WHICH THAT CHILD IS EXPOSED HAS A BIG ROLE IN THE EXPRESSION OF SYMPTOMS, AND THAT'S WHY, YOU KNOW, AS CLINICIANS WE ALL THINK IT'S CRITICAL THAT CHILDREN HAVE, YOU KNOW, CERTAIN KINDS OF SUPPORTS THAT, FIRST OF ALL, TO IDENTIFY CONCERNS FOR AUTISM AS EARLY AS POSSIBLE AND NOT TO WAIT.

I THINK, SORRY IF THIS IS A DIGRESSION, BUT IN

THE CLINICAL WORLD, YOU KNOW, WE DON'T WAIT UNTIL THREE OR FOUR YEARS TO BE CONCERNED THAT A CHILD MIGHT DEVELOP AUTISM. IF YOU -- YOU WANT TO MAKE SURE THAT YOU'RE ADDRESSING ANY CONCERNS BEFOREHAND AND PART OF THAT IS BY OPTIMIZING THE ENVIRONMENT.

IF WE DIDN'T THINK THAT CHANGING THE ENVIRONMENT COULD MODULATE THE EXPRESSION OF SYMPTOMS, WE WOULDN'T BOTHER WITH THAT, BUT I THINK EVERYONE AGREES THAT ENVIRONMENTAL INFLUENCES HAVE A BIG ROLE ON YOUR ULTIMATE PROGNOSIS.

Q DOCTOR, I WANT TO TALK ABOUT YOUR BIOLOGICAL PLAUSIBILITY OPINION.

NOW, OTHER EXPERTS ARE GOING TO COME AND TALK ABOUT CAUSATION. I THINK DR. ASCHNER IS GOING TO TALK ABOUT BIOLOGICAL PLAUSIBILITY IN A LOT MORE DEPTH, BUT I DO WANT TO FOCUS BRIEFLY ON YOUR BIOLOGICAL PLAUSIBILITY OPINION, OKAY?

A SURE.

Q AND IF WE JUST TAKE A LOOK AT THE NIH DOCUMENT. AND HERE THEY HAVE A SECTION WHERE THEY SAY, "ENVIRONMENTAL FACTORS PLAY A ROLE," AND SPECIFICALLY THEY SAY "PRENATAL AND EARLY CHILDHOOD EXPOSURE TO HEAVY METALS, ALTERED LEVELS OF METALS IN THE BODY, PESTICIDES, AND OTHER CONTAMINANTS MAY BE LINKED TO AUTISM SPECTRUM DISORDER."

DO YOU SEE THAT, DOCTOR?

A I SEE IT.

Q DOES THAT STATEMENT THAT EARLY CHILDHOOD EXPOSURE TO HEAVY METAL MAY BE LINKED TO AUTISM SPECTRUM DISORDER, DOES THAT MAKE BIOLOGICAL SENSE, DOCTOR?

A I THINK IT DOES, YEAH. I THINK THAT EXPOSURE TO ANYTHING, AGAIN, THAT ALTERS THE PROCESSES OF BRAIN DEVELOPMENT THAT ARE STILL ONGOING PRIOR TO THE DIAGNOSIS DEFINITELY COULD PLAY A ROLE IN THE SYMPTOMATOLOGY.

Q AND LET'S TALK ABOUT IN IT A BIT MORE DEPTH.

CAN YOU IDENTIFY SOME OF THE BIOLOGICAL PROCESSES THAT HAVE BEEN RECOGNIZED IN ASD ETIOLOGY?

LET START THERE.

A SURE.

YEAH, THERE ARE A NUMBER, BUT I THINK THAT AMONG THE MOST IMPORTANT ARE DIFFERENCES IN SYNAPTIC CONNECTIVITY AND BRAIN NETWORK FORMATION, INFLAMMATION AND OXIDATIVE STRESS.

Q AND WHAT ARE SOME OF THE KNOWN BIOLOGICAL PROCESSES THAT METALS LIKE LEAD, MERCURY AND ARSENIC ARE CAPABLE OF AFFECTING IN THE BRAIN?

A SO LEAD AND ARSENIC, FOR EXAMPLE, ARE KNOWN TO DISRUPT THE FUNCTION OF THE N-METHYL-D ASPARTATE RECEPTORS, SO THAT IS A GLUTAMATE RECEPTOR IN THE BRAIN THAT IS REALLY CRITICAL FOR THE PROCESS OF SYNAPTIC FORMATION; SO AGAIN, FORMING THOSE CONNECTIONS IN BRAIN NETWORKS RELIES TO A LARGE EXTENT ON SIGNALLING THROUGH THIS RECEPTOR AND WE KNOW THAT EXPOSURE TO LEAD AND TO ARSENIC INHIBITS INTRACELLULAR SIGNALLING THROUGH THE

MNDAR RECEPTOR, IT ALSO RESULTS IN ALTERED EXPRESSION OF MNDAR SUBUNITS SO THAT THE RECEPTORS ARE PROTEINS WITHIN CELL MEMBRANES THAT ARE COMPOSED OF VARIOUS SUBUNITS, EXPOSURE TO LEAD WILL ALTER THE COMPOSITION OF THOSE RECEPTORS IN SUCH A WAY THAT THE NORMAL KIND OF SIGNALLING PROCESSES THAT LEAD TO FORMATION OF BRAIN NETWORKS IS DISRUPTED.

SO WE KNOW THAT IF YOU BLOCK OR IMPAIR OR DISRUPT NNDAR RECEPTOR AND NNDAR RECEPTOR FUNCTION, THAT WILL IMPAIR SYNAPTOGENESIS AND IT WILL IMPAIR THE MAINTENANCE OF CONNECTIONS WITHIN BRAIN NETWORKS.

SO WE KNOW THAT LEAD HAS THAT EFFECT FROM NUMEROUS STUDIES ON NNDA RECEPTORS AND WE KNOW THAT PROCESS OF SYNAPTOGENESIS AND SYNAPTIC FORMATION IS ALTERED IN CHILDREN WITH AUTISM.

Q WOULD IT BE FAIR TO SAY THAT THE BIOLOGICAL PATHWAYS INVOLVED IN AUTISM, DO THEY OVERLAP TO A GREAT EXTENT WITH HOW METALS -- THE PROCESSES OF METALS AFFECTING THE BRAIN?

A YEAH. SO THE VARIOUS, YOU KNOW, THE PATHWAYS THAT SORT OF CONTRIBUTE TO THE EMERGENCE OF SYMPTOMS OF AUTISM ARE THE SAME PATHWAYS THAT ARE DISRUPTED BY EXPOSURE TO METALS DURING THE PERIOD OF BRAIN NETWORK DEVELOPMENT SO, YOU KNOW, SYNAPTOGENESIS AND NETWORK FORMATION.

THE OTHERS ARE -- THE OTHER PROCESSES I MENTIONED ARE OXIDATIVE STRESS, SO THAT'S CAUSED BY AN IMBALANCE IN OXYGEN FREE RADICALS THAT HAS DELETERIOUS

EFFECTS ON CELLULAR FUNCTION, IT CAN LEAD TO DNA DAMAGE, DISRUPTION IN CELL MEMBRANE FUNCTION AND ALTERATIONS IN MITOCHONDRIAL ENERGY METABOLISM. WE KNOW THAT THOSE PROCESSES ALSO ARE DISRUPTED IN AUTISM AND THE DEGREE OF DESTRUCTION CORRELATES WITH THE SEVERITY OF SYMPTOMS.

INTERESTINGLY, YOU KNOW, SOME STUDIES HAVE SHOWN THAT, YOU KNOW, THERE ARE HIGHER LEVELS OF INFLAMMATION AND OXIDATIVE STRESS IN PARENTS AND MOTHERS OF CHILDREN WITH AUTISM, WHICH SUGGESTS THAT THOSE PROCESSES ARE, YOU KNOW, PLAYING A ROLE PRENATALLY AS WELL, BUT THE EXTENT TO WHICH THEY CAN INJURE THE DEVELOPING BRAIN DOES NOT, YOU KNOW, SORT OF DEPEND ON TIMING IN THAT WAY, YOU KNOW, IN THE SAME WAY THAT THEY -- THAT OXIDATIVE STRESS CAN CAUSE DAMAGE TO THE DNA AND CELL MEMBRANES PRIOR TO BIRTH, THE SAME THING CAN BE OCCURRING POSTNATALLY IN THE FACE OF AN EXPOSURE TO SOMETHING THAT WILL INDUCE STRESS.

Q NOW, TALKING ABOUT ONE OF THE METALS, SPECIFICALLY MERCURY, DEFENSE COUNSEL DURING HIS OPENING STATEMENT SAID THAT WE'VE BEEN DOWN THIS ROAD BEFORE WITH VACCINES AND MERCURY.

DOCTOR, IS IT YOUR UNDERSTANDING THAT THE MERCURY FOUND IN VACCINES IS THE SAME MERCURY THAT IS PRESENT THROUGH ENVIRONMENTAL FOOD SOURCES AND ENVIRONMENT GENERALLY?

A NO. MY UNDERSTANDING IS THAT IT'S A DIFFERENT FORM OF MERCURY THAN, YOU KNOW, IN FOODS AND ENVIRONMENTAL SOURCES. WE'RE TALKING ABOUT METHYL

MERCURY, AND FURTHERMORE, THE TIMING OF EXPOSURE IS A LITTLE BIT DIFFERENT.

SO YOU KNOW, VACCINES ARE GIVEN AT, LET'S SAY, THE TWO YEARS OF AGE OR AT LEAST THE ONES ALLEGED TO CAUSE AUTISM ARE GIVEN 18 MONTHS TO TWO YEARS OF AGE SO AT THE TIME THAT SYMPTOMS EMERGE WHEN REGRESSION IS HAPPENING.

BUT I THINK AS WE'VE TALKED ABOUT THAT BY THE TIME THAT HAPPENS, THE PROCESSES THAT LEAD TO THAT HAVE ALREADY UNFOLDED, AND I THINK THAT THE CRITICAL WINDOW IS REALLY THE PERIOD BETWEEN BIRTH AND AROUND TWO YEARS OF AGE THAT, YOU KNOW, AN EXPOSURE AT TWO YEARS OF AGE MAY CAUSE -- I MEAN, IN THIS CASE IT'S A DIFFERENT FORM OF MERCURY, AND I THINK IT'S, YOU KNOW, ALREADY KIND OF UNRELATED ON THAT BASIS.

BUT ALSO WITH RESPECT TO SPECIFICALLY TO AUTISM THAT I THINK, YOU KNOW, YOU DON'T CAUSE AUTISM AT THE VERY TIME THAT AUTISM IS DIAGNOSED. IT HAS TO BE SOMETHING TO WHICH YOU WERE EXPOSED TO BEFOREHAND.

Q DOCTOR, DO YOU -- OR HAVE YOU EVER OPINED THAT THE TYPE OF MERCURY FOUND IN VACCINES CAN CAUSE AUTISM?

A NO, I HAVEN'T.

Q OKAY. WHY HAVEN'T YOU OPINED THAT?

A I DON'T BELIEVE THAT THERE'S ANY EVIDENCE THAT THAT'S THE CASE.

Q NOW, DOCTOR, I JUST WANTED TO FINISH OFF A COUPLE OF LAST POINTS. I WANTED TO JUST GO BACK TO THE NIH DOCUMENT. THEY SAY IN HERE THAT NEARLY HALF OF THE

CHILDREN WITH AUTISM HAVE AVERAGE OR ABOVE AVERAGE INTELLECTUAL ABILITY.

DO YOU SEE THAT, DOCTOR?

A YES, I DO.

Q I JUST WANT TO PAUSE THERE FOR A SECOND BECAUSE IF IT'S TRUE THAT EXPOSURE TO METALS CAN AFFECT INTELLECTUAL DEVELOPMENT, PARTICULARLY LEAD CAN HAVE AN EFFECT ON IQ, AND SO FORTH, HOW DOES THAT MAKE SENSE THAT NEARLY HALF OF ASD CHILDREN HAVE AN AVERAGE OR ABOVE AVERAGE INTELLECTUAL ABILITY? CAN YOU RECONCILE THAT FOR US?

A YES, CERTAINLY.

SO, FIRST OF ALL, NOT ALL CASES OF CHILDREN WITH AUTISM ARE GOING TO HAVE LEAD EXPOSURE, AND SO I THINK, YOU KNOW, IF HALF HAVE AVERAGE OR ABOVE AVERAGE INTELLECTUAL ABILITY, IT ALSO MEANS THAT HALF HAVE AVERAGE OR BELOW AVERAGE -- OR HAVE BELOW AVERAGE INTELLECTUAL ABILITY.

Q UM-HMM.

A AND SO, YOU KNOW, THERE IS A SUBSTANTIAL PROPORTION OF CHILDREN WHO HAVE AUTISM WHO ALSO HAVE INTELLECTUAL DISABILITY. ALSO, YOU KNOW, WE'RE DEALING WITH A KIND OF A BINARY -- THE CUTOFF HERE IS BINARY, SO YOU KNOW, INTELLECTUAL DISABILITY OR NOT. WELL, THAT DOESN'T MEAN THAT THERE'S NOT SOME IMPACT ON INTELLECTUAL ABILITY AND COGNITIVE CONSCIOUS, SO WE KNOW FROM LATER CHILDHOOD STUDIES OF LEAD EXPOSURE THAT LEAD RESULTS IN A LOSS OF IQ POINTS, LET'S SAY, ANYWHERE IN

THE RANGE OF 1 TO 10 POINTS OR MORE DEPENDING ON HOW MUCH LEAD YOU'RE EXPOSED TO AND OVER WHAT PERIOD OF TIME.

SO YOU KNOW, IF HYPOTHETICALLY IN THE ABSENCE OF LEAD EXPOSURE YOUR IQ MIGHT HAVE BEEN 115 AND NOW IT'S 110, YOU'RE NOT INTELLECTUALLY DISABLED, BUT IT DOES HAVE AN IMPACT ON YOUR LIFE AND YOUR ABILITY TO FUNCTION.

Q AND LASTLY, DOCTOR, THE DEFENDANTS HAVE SAID THAT ANY STUDIES THAT ADDRESS THE EFFECT OF METALS ON DEVELOPMENT OF ASD SYMPTOMS SHOULD BE DISCOUNTED BECAUSE THAT'S SYMPTOMS OF ASD, THAT'S NOT ASD.

IS THAT AN APPROPRIATE DISTINCTION?

A I MEAN, SYMPTOMS OF ASD ARE ASD, IT'S A SYMPTOM-BASED DIAGNOSIS.

NOW, THE OTHER THING THAT I WOULD SAY ABOUT LEAD JUST TO FINISH MY PREVIOUS THOUGHT IS THAT, YOU KNOW, CERTAIN TYPES OF BRAIN FUNCTIONS MAY BE MORE LIKELY TO BE AFFECTED BY IT THAN OTHERS; SO FOR EXAMPLE, EXECUTIVE FUNCTION, COGNITIVE CONTROL FUNCTIONS THAT DEPEND ON THE PREFRONTAL CORTEX, WHICH IS ACTUALLY THE PART OF THE BRAIN THAT IS LAST TO DEVELOP SO THE CONNECTIVITY WITHIN SORT OF THAT FRONT PART OF THE BRAIN, THE PREFRONTAL CORTEX, DEVELOPS LATER THAN CONNECTIVITY IN THE BACK PART OF THE BRAIN THAT IS RESPONSIBLE FOR SORT OF BASIC LEVEL VISION AND HEARING, AND SO FORTH.

AND IT'S THAT PREFRONTAL CORTEX THAT IS

RESPONSIBLE, YOU KNOW, FOR ATTENTION, EMOTIONAL CONTROL, EXECUTIVE CONTROL AND INHIBITION, AND SO FORTH, AND THOSE PROCESSES ARE NOT NECESSARILY DIRECTLY RELATED TO IQ, SO WE ALL KNOW THAT THERE MAY BE, YOU KNOW, INDIVIDUALS WHO ARE -- HAVE EXTREMELY HIGH IQ'S, BUT HAVE DIFFICULTY WITH REGULATING THEIR EMOTION OR MAY HAVE -- MAY MEET CRITERIA FOR ADHD.

SO THAT'S A, YOU KNOW, HAS TO DO WITH DIFFERENTIAL EFFECTS ON DIFFERENT BRAIN AREAS AND THAT MIGHT BE RELATED TO THE SORT OF WINDOW OF SUSCEPTIBILITY WITH RESPECT TO WHEN THOSE BRAIN AREAS ARE DEVELOPING.

Q LASTLY, DOCTOR, DEFENSE COUNSEL IN OPENING STATEMENT THAT SAID THAT YOU EXPLICITLY REJECT CAUSATION BETWEEN METALS AND ASD.

FIRST OF ALL, HAVE YOU BEEN ASKED TO LOOK AT CAUSATION BETWEEN METALS AND ASD IN THIS LITIGATION?

A THAT HAS NOT BEEN MY CHARGE. I HAVE NOT REJECTED THAT CLAIM, BUT MY -- MY UNDERSTANDING IS THAT THE PURPOSE OF MY TESTIMONY IS NOT TO SPEAK TO CAUSATION.

Q OKAY. AND YOU HAVEN'T REVIEWED THE VAST BODY OF EPIDEMIOLOGICAL DATA ADDRESSING EXPOSURE TO METALS AND ASD SPECIFICALLY IN THIS CASE; CORRECT?

A I HAVE LOOKED AT IT.

Q DOCTOR, THAT'S -- GIVE ME ONE SECOND.

THAT'S ALL I HAVE FOR YOU. THANK YOU SO MUCH FOR YOUR TIME. I'M GOING TO PASS THE WITNESS.

THE WITNESS: THANK YOU.

THE COURT: OKAY. EXAMINATION FROM THE DEFENSE, PLEASE.

MR. PETROSINELLI: YES, YOUR HONOR. IT LOOKS LIKE THEY WENT ABOUT 55 MINUTES. I WILL BE SHORTER THAN THAT, BUT I ASSUME WE SHOULD GO TO ABOUT NOON AND THEN WE'LL BREAK FOR LUNCH.

THE COURT: I HAVE TO BREAK FOR LUNCH TO GIVE MY STAFF A BREAK, YES.

MR. PETROSINELLI: OF COURSE. YES, I WILL PROCEED.

THE COURT: THANK YOU.

CROSS EXAMINATION

MR. IMBROSCIO:

Q LET ME -- FIRST OF ALL, GOOD MORNING. IT'S NICE TO SEE YOU AGAIN, SIR.

A LIKEWISE.

Q I WANT TO TRY TO BEGIN WITH SOME POINTS THAT I DON'T THINK WE'RE GOING TO HAVE DISAGREEMENT ON AND PICK UP RIGHT WHERE YOU LEFT OFF.

YOU ARE NOT OFFERING AN OPINION IN THIS LITIGATION THAT EXPOSURE TO HEAVY METALS CAUSES AUTISM; RIGHT?

A CORRECT.

Q YOU'VE LOOKED AT THE EPI, BUT YOU'RE NOT GOING TO OFFER THAT OPINION.

SAME WITH ADHD; RIGHT?

A YES.

Q OKAY.

NOW, TO BE CLEAR, YOU'RE CURRENTLY A CLINICIAN AND NOT AN EPIDEMIOLOGIST; RIGHT?

A I AM -- THAT'S CORRECT. I'M NOT AN EPIDEMIOLOGIST.

Q AND WE'RE GOING TO BE TALKING ABOUT YOUR BIOLOGIC PLAUSIBILITY OPINIONS PROBABLY AFTER THE LUNCH BREAK.

BUT JUST TO BE CLEAR, YOU WOULD AGREE THAT BIOLOGIC PLAUSIBILITY DOES NOT DISPENSE WITH THE NEED TO ESTABLISH A VALID EPIDEMIOLOGICAL ASSOCIATION; CORRECT?

A IN WHAT CONTEXT?

Q WELL, LET ME ASK YOU AGAIN.

DO YOU AGREE, QUOTE, "THAT BIOLOGIC PLAUSIBILITY DOES NOT DISPENSE WITH THE NEED TO ESTABLISH A VALID EPIDEMIOLOGICAL ASSOCIATION IN THIS CONTEXT," HEAVY METALS AND AUTISM?

A YEAH, I DO THINK WE -- YOU NEED TO ESTABLISH EVIDENCE FROM A VARIETY OF SOURCES, INCLUDING EPIDEMIOLOGIC EVIDENCE.

Q ANOTHER WAY TO MAYBE SAY IT IS THAT BIOLOGIC PLAUSIBILITY, THOSE KINDS OF ARGUMENTS MAY HELP RULE OUT BUT NOT NECESSARILY RULE IN CAUSALITY IN ASSOCIATIONS.

WOULD YOU AGREE WITH THAT?

A I THINK THAT'S FAIR.

Q OKAY.

NOW, YOU TALKED A LOT ABOUT THIS.

YOU DON'T DISPUTE THE GENERAL PROPOSITION THAT

GENETICS PLAYS A SIGNIFICANT ROLE IN THE DEVELOPMENT OF AUTISM; RIGHT?

A NO, I WOULD NOT.

Q AND I THINK IN YOUR REPORT YOU CITE SOME ARTICLES THAT SUGGEST THAT CONCORDANCE MIGHT BE AS HIGH AS 83 PERCENT, BUT YOU AT LEAST IN YOUR REPORT CITED SOME OF THOSE ARTICLES; CORRECT?

A YES.

Q OKAY.

YOU UNDERSTAND THAT AUTISM IS ONE OF THE MOST, IF NOT THE MOST, HERITABLE DISEASE; IS THAT YOUR UNDERSTANDING?

A IT -- WELL, PSYCHIATRIC OR BEHAVIORAL DISEASES, YES.

Q OKAY. BEAR WITH ME.

NOW, YOU TALKED A LITTLE BIT ABOUT AUTISM ON DIRECT. LET ME JUST ASK YOU A LITTLE BIT MORE ABOUT YOUR BACKGROUND.

YOU SAID CURRENTLY YOU'RE A CLINICIAN AT A PRIVATE CLINIC; CORRECT? CORTICA?

A CORRECT, YES.

Q AND WHEN YOU WERE IN ACADEMIA, IS IT FAIR TO SAY THAT YOUR FOCUS WAS NOT ON AUTISM RESEARCH; RIGHT?

A NOT SPECIFICALLY.

Q AND YOU WERE AT UCSF. YOU LEFT UCSF IN 2017; RIGHT?

A THAT IS CORRECT.

Q AND UCSF, THEY HAVE GOT AN AUTISM CENTER THERE.

YOU WEREN'T PART OF IT; CORRECT?

A I WAS NOT PART OF IT, BUT I COLLABORATED WITH THE AUTISM RESEARCHERS IN UCSF.

Q YOU WERE NOT IN THAT GROUP, CORRECT, SIR?

A YEAH, I WAS NOT IN THE GROUP. THAT GROUP IS IN THE DEPARTMENT OF PSYCHIATRY. I WAS IN NEUROLOGY.

Q AND THROUGHOUT YOUR CAREER IN ACADEMIA UP UNTIL THE TIME YOU LEFT UCSF, YOU ACTUALLY HAD NOT DONE ANY PUBLICATIONS, PAPERS OR PRESENTATIONS ON ASD; RIGHT?

A NOT SPECIFICALLY ON ASD.

Q AND SITTING HERE TODAY AS OF THIS MOMENT, YOU'VE NOT WRITTEN ANY PAPERS ON THE CAUSES OF ASD; CORRECT?

A NO, I DON'T BELIEVE SO.

Q OKAY. AND --

A WELL, I MEAN, I HAVE CONTRIBUTED TO GENETIC STUDIES LOOKING AT GENES THAT ARE IMPLICATED IN ASD.

Q WELL, LET ME ASK YOU THIS QUESTION: ARE YOU -- ARE THERE ANY PAPERS THAT YOU'VE WRITTEN THAT HAVE ANYTHING TO DO WITH THE CAUSES OF AUTISM?

A WELL, SO I HAVE BEEN A CO-AUTHOR ON PAPERS THAT LOOK AT SPECIFIC GENETIC ALTERATIONS THAT MAY BE IMPLICATED IN AUTISM.

Q THOSE PAPERS DIDN'T DEAL WITH AUTISM SPECIFICALLY, DID THEY, SIR?

A WELL, SO THEY WERE MORE FOCUSED ON THE GENETIC ALTERCATIONS, PER SE, AND NOT ON AUTISM; BUT, IN FACT, THE CHILDREN WHO ARE REPORTED IN THOSE PAPERS DID HAVE

AUTISM.

Q DO YOU REMEMBER ON DECEMBER 15TH YOU AND I TALKED, YOU WERE DEPOSED?

A YES.

Q DO YOU REMEMBER BEING ASKED THIS QUESTION:

"YEAH, WELL, THERE -- ARE THERE ANY PAPERS THAT YOU'VE WRITTEN THAT HAVE ANYTHING TO DO WITH THE CAUSE OF AUTISM?"

"ANSWER: NO."

DO YOU REMEMBER ME ASKING THAT QUESTION, YOU GIVING THAT ANSWER?

A I DON'T REMEMBER, BUT I BELIEVED -- I BELIEVE IT IF YOU TELL ME THAT. IT'S A PARTICULAR PAPER THAT HAS TO DO WITH IT THAT I'M THINKING OF THAT HAS TO DO WITH THE TRAP 7 MUTATION THAT MAY NOT HAVE COME TO MIND WHEN I WAS ANSWERING.

THE COURT: LET'S MOVE ON.

MR. PETROSINELLI: YES, YOUR HONOR.

Q AND TO BE CLEAR, AT CORTICA YOU'RE NOT DOING ANY RESEARCH OR STUDIES ON POTENTIAL CAUSES OF AUTISM; RIGHT?

A NO, I'M NOT.

Q OKAY. AND YOU MADE REFERENCE TO -- YOU HAVE PUBLISHED A FEW PAPERS DEALING WITH NOVEL TREATMENTS OF AUTISM; CORRECT?

A CORRECT. I DON'T KNOW THAT THOSE ARE PUBLISHED, BUT THERE ARE SOME CONFERENCE PRESENTATIONS.

Q YEAH, I MISSPOKE. YOU'RE RIGHT.

YOU PRESENTED SOME PAPERS ABOUT I THINK SOME OF THE CRANIAL ELECTROTHERAPY STIMULATION TREATMENT OF THE BRAIN; CORRECT?

A YEAH, I PRESENTED SOME PAPERS AT CONFERENCES OF THAT AND ALSO ABOUT THE UTILITY OF DEVELOPMENTAL THERAPIES LIKE SPEECH AND OCCUPATION THERAPY IN THE TREATMENT OF AUTISM.

Q OKAY. DOCTOR, WOULD YOU AGREE WITH ME THAT THE NOTION OF EXPOSURE TO HEAVY METALS CAUSING AUTISM IS A NOTION THAT'S NOT IN WIDE CURRENCY?

A I THINK IT IS A NOTION THAT HAS -- I THINK IT IS IN WIDE CURRENCY. I'M NOT SURE THAT, YOU KNOW, IT IS SOMETHING THAT IS UNIVERSALLY AGREED, BUT I DON'T THINK THAT IT'S FAIR TO SAY THAT IT IS SOMETHING THAT IF YOU SPOKE TO A CLINICIAN ABOUT IT, THEY WOULD SAY, OH, THEY HAVE NEVER HEARD ANYTHING LIKE THAT BEFORE.

Q ALL RIGHT.

WELL, DO YOU REMEMBER, AGAIN, BACK TO YOUR DEPOSITION -- CAN YOU PULL THIS UP, EXHIBIT 8, PAGE 240, LINES 4 TO 10.

DOCTOR, YOU WERE ASKED THIS QUESTION:

"AND SO BY DEFINITION AT LEAST CURRENTLY, IT'S NOT GENERALLY ACCEPTED IN THE SCIENTIFIC COMMUNITY THAT AUTISM -- HEAVY METALS CAUSE AUTISM?"

AND YOU SAID, "IT'S NOT A NOTION THAT'S IN WIDE CURRENCY."

THOSE WERE YOUR WORDS AT THE DEPOSITION.

A YEAH, SO HERE WE'RE REFERRING TO THE SCIENTIFIC COMMUNITY. BUT, YEAH, SO I THINK IF YOU ASKED CLINICIANS WHO TREAT AUTISM OR PARENTS OR FAMILIES, AND AGAIN, YOU KNOW, IT'S NOT NECESSARILY ACCEPTED THAT AS A FACT THAT HEAVY METALS CAUSE AUTISM, BUT I THINK THAT THE NOTION THAT THERE MIGHT BE A RELATIONSHIP IS NOT NOVEL, LET'S SAY THAT.

Q OKAY. THANK YOU.

SO AT LEAST, AS YOU SAID, WITHIN THE SCIENTIFIC COMMUNITY THAT'S NOT BEEN ESTABLISHED?

A YES.

Q OKAY.

NOW, DOCTOR, YOU MENTIONED YOU TRAINED AT HARVARD AND YOU SPENT TIME IN ACADEMIA AND YOU NOW TREAT KIDS WITH AUTISM.

I THINK YOU TOLD ME THAT THE IDEA THAT HEAVY METALS IN BABY FOOD MIGHT BE CAUSING AUTISM, THAT WAS SOMETHING THAT WAS NOT ON YOUR RADAR, AT LEAST AT THE TIME OF YOUR DEPOSITION OR BEFORE YOU BECAME INVOLVED IN THIS CASE; RIGHT?

A YEAH, I HAD NOT BEEN AWARE OF THE SPECIFIC ISSUE OF BABY FOOD UNTIL I CAME ACROSS THE CONGRESSIONAL REPORT.

Q OKAY.

AND YOU WERE NOT AWARE OF ANY CLAIM, ANY PUBLICATION THAT MADE THAT CLAIM THAT HEAVY METALS IN BABY FOOD CAUSED AUTISM; RIGHT?

A NO, I'M NOT.

Q NOW, I WANT TO, BEFORE THE LUNCH BREAK IN ABOUT A FEW MINUTES, TALK VERY BRIEFLY ABOUT YOUR WORK AT CORTICA, AND I THINK YOU MAY HAVE ANSWERED SOME OF THESE ALREADY, BUT IT SOUNDS LIKE, I THINK YOU TOLD ME IN YOUR DEPOSITION ABOUT 60 TO 70 PERCENT OF YOUR TIME IS SPENT IN CLINICAL CARE?

A THAT'S ABOUT RIGHT.

Q AND ABOUT ROUGHLY HALF THE PATIENTS YOU SEE ARE ALREADY DIAGNOSED WITH AUTISM?

A THAT SOUNDS RIGHT.

Q YEAH.

AND THEN FOR THOSE WHO HAVEN'T BEEN DIAGNOSED, YOU SOMETIMES MAKE THOSE DIAGNOSES, OBVIOUSLY IF IT'S APPROPRIATE; RIGHT?

A YES.

Q AND AGAIN, I THINK YOU SAID THIS, BUT LET ME JUST ASK IT PRECISELY.

THERE IS A DIFFERENCE BETWEEN AUTISM AND GENERALIZED NEURODEVELOPMENTAL SYMPTOMS; CORRECT?

A WELL, AUTISM IS A SPECIFIC CONSTELLATION OF SYMPTOMS, SO NOT ALL THE CHILDREN WITH NEURODEVELOPMENTAL ISSUES WILL HAVE A DIAGNOSIS OF AUTISM.

Q AND I THINK YOU MADE REFERENCE TO THE DSM 5.

TELL THE JUDGE WHAT DSM 5 VERSION IS.

A YEAH, SO THE DSM IS THE DIAGNOSTIC AND STATISTICAL MANUAL OF MEDICAL DISORDERS, 5 REFERS TO FIFTH VERSION OF THAT MANUAL AND THAT IS BASICALLY THE

COMPENDIUM THAT LAYS OUT THE DIAGNOSTIC CRITERIA FOR VARIOUS CONDITIONS, INCLUDING AUTISM, ALSO MAJOR DEPRESSION, GENERALIZED ANXIETY DISORDER, SO ANYTHING THAT IS SORT OF FELT BY THE AMERICAN PSYCHIATRIC ASSOCIATION TO BE WITHIN THEIR WHEELHOUSE IS DEFINED IN THE DSM 5.

Q OKAY. YEAH, THAT'S HELPFUL.

SO I JUST WANT TO -- SINCE YOU DIDN'T GET INTO THE DETAIL THERE, I WANT TO JUST RUN THROUGH IT PRETTY QUICKLY, THEN WE'LL TAKE THE LUNCH BREAK.

CAN YOU -- AND, IAN, CAN YOU PLEASE PULL UP, YEAH, SLIDE 5.

SO WHAT I'VE -- YOU'RE CERTAINLY FAMILIAR WITH THE DSM 5, YOU USE IT EVERY DAY; CORRECT?

A YES.

Q AS IT RELATES TO AUTISM?

A WELL, CORRECT. I USE THESE CRITERIA EVERY DAY, YEAH.

Q YEAH, FAIR ENOUGH.

AND SO THERE ARE -- AS I UNDERSTAND IT THERE ARE FIVE TOP LINE CATEGORIES FOR AUTISM -- FOR AN AUTISM DIAGNOSIS THAT WE'VE JUST EXTRACTED HERE.

A YES.

Q "PERSISTENT DEFICITS IN COMMUNICATION INTERACTION, RESTRICTIVE, REPETITIVE BEHAVIORS, AND THEN THE SYMPTOMS IN EARLY DEVELOPMENT PERIOD, SYMPTOMS THAT CAN CAUSE CLINICALLY SIGNIFICANT IMPAIRMENT AND DISTURBANCES THAT

AREN'T BETTER EXPLAINED BY INTELLECTUAL DISABILITY."

THAT'S A FAIR SUMMARY OF THE DSM 5 CATEGORIES; RIGHT?

A YES.

Q OKAY.

LET'S GO TO THE NEXT SLIDE.

SO I JUST WANT TO BREAK THOSE DOWN.

UNDER CATEGORY 1, THERE ARE ACTUALLY THREE -- NEXT SLIDE -- THERE ARE ACTUALLY THREE SUB COMPONENTS. I WON'T READ THEM ALL.

BUT TO QUALIFY FOR AN AUTISM DIAGNOSIS, YOU NEEDED TO MEET EACH OF THESE THREE SUB COMPONENTS WITHIN PART 1. SO EMOTIONAL RECIPROCITY, NONVERBAL COMMUNICATION BEHAVIORS, AND, YOU KNOW, DEVELOPING AND UNDERSTANDING RELATIONSHIPS; TRUE?

A THAT'S TRUE.

Q AND THEN IF YOU'VE GOT THOSE THREE AREAS OF PERSISTENT DEFICITS IN SOCIAL COMMUNICATION, YOU GO TO STEP 2 -- NEXT SLIDE -- WHERE YOU'VE GOT TO HAVE TWO OF THESE FOUR CATEGORIES OF BEHAVIORS; CORRECT?

A YES.

Q AND I WON'T READ ALL OF THOSE, BUT IF A CHILD HAS TWO OR MORE OF THOSE, THEN THEY WOULD MEET THIS SECOND CATEGORY OF DSM 5; CORRECT?

A CORRECT.

Q OKAY.

AND THEN TO SKIP AHEAD TO THE THIRD ONE NOW AND

THE REST OF THEM.

SO THREE REALLY -- AND YOU SAID THIS -- THE SYMPTOMS HAVE TO BE PRESENT, NOT NECESSARILY THE DIAGNOSIS, BUT THE SYMPTOMS HAVE TO BE PRESENT IN THE EARLY DEVELOPMENTAL PERIOD; CORRECT?

A RIGHT.

Q AND I THINK YOU SAID THREE IS SORT OF THE GENERAL -- THREE YEARS OF AGE -- IS THE GENERAL THRESHOLD BY WHICH THE SYMPTOMS SHOULD HAVE TO HAVE MANIFESTED EVEN IF SOMEONE DIDN'T PICK UP ON THEM.

IS THAT FAIR?

A YEAH. THREE IS NOT AN ABSOLUTE THRESHOLD. IT COULD BE, YOU KNOW, FOUR OR FOUR AND A HALF.

Q YEAH.

I THINK THE DSM 4, WHICH I THINK YOU ARE PROBABLY FAMILIAR WITH, I THINK THEY DID HAVE THREE YEARS OLD AND NOW THEY'VE CHANGED IT TO EARLY DEVELOPMENT PERIOD; RIGHT?

A CORRECT.

Q OKAY.

AND THEN THE SYMPTOMS HAVE TO BE SIGNIFICANT. THEY HAVE TO CAUSE CLINICALLY SIGNIFICANT IMPAIRMENT, YOU KNOW, FOR THESE -- FOR THIS CHILD; CORRECT?

A YES.

Q AND FINALLY, THE SYMPTOMS HAVE TO NOT BE BETTER EXPLAINED BY INTELLECTUAL DISABILITY OR GLOBAL DEVELOPMENTAL DELAY; CORRECT?

A YES.

Q AND I THINK YOU SAID THIS. A CHILD COULD HAVE ONE OR MORE OF THESE SYMPTOMS AND NOT NECESSARILY QUALIFY AS HAVING AUTISM; RIGHT?

A RIGHT. WELL, UNLESS THEY MEET ALL OF THESE CRITERIA AS THEY DON'T BY DEFINITION HAVE AUTISM.

Q AND WE TALKED ABOUT DECREASED IQ AND I HAD SOME CDC NUMBERS I'LL JUST SKIP THROUGH.

YOU AGREE THAT A FAIR NUMBER OF CHILDREN, MORE THAN HALF WITH AUTISM, HAVE EITHER HIGHER OR NORMAL IQ; CORRECT?

A YES.

Q OKAY.

REALLY QUICKLY, LAST POINT I'LL MAKE BEFORE THE LUNCH BREAK.

YOU'RE FAMILIAR WITH SOME OF THE SCREENING QUESTIONNAIRES FOR AUTISM, LIKE THE SOCIAL COMMUNICATION QUESTIONNAIRE, THE SOCIAL RESPONSIVENESS SCALE.

YOU'RE FAMILIAR WITH THOSE GENERALLY, ARE YOU NOT, SIR?

A YES.

Q AND THOSE QUESTIONNAIRES OR SCREENING TOOLS, THEY ARE NOT DIAGNOSTIC INSTRUMENTS; CORRECT?

A NOT GENERALLY, ALTHOUGH THEY CAN BE USED TO SUPPORT A CLINICAL DIAGNOSIS.

Q FAIR ENOUGH.

THEY ARE SCREENING INSTRUMENTS TO IDENTIFY PERSONS WHO HAVE AT LEAST SOME OF THESE CHARACTERISTICS OF AUTISM; CORRECT?

A YES.

MR. PETROSINELLI: SO, YOUR HONOR, I WAS GOING TO MAYBE BREAK HERE, THIS IS PROBABLY A GOOD NATURAL BREAKING POINT, BUT THREE MINUTES BEFORE. IS THAT OKAY?

THE COURT: PERFECT. WE WILL RESUME AT 1:30, PLEASE.

MR. PETROSINELLI: THANK YOU, YOUR HONOR.

THE COURT: ALL RIGHT. THANK YOU, DOCTOR. THANKS EVERYBODY.

MR. ESFANDIARY: THANK YOU, YOUR HONOR.

THE COURT: 1:30, PLEASE.

MR. PETROSINELLI: AND I ASSUME THAT THERE'S A RULE IN PLACE, YOUR HONOR, WHERE THEY CANNOT TALK TO THE WITNESS DURING THE EXAMINATION. I DON'T KNOW WHAT THE COURT'S RULES ARE ON THAT.

THE COURT: WELL, I DON'T HAVE ANY ORDER TO THAT EFFECT.

MR. WISNER: WE HAVE NO INTENTION OF TALKING TO THE WITNESS BEYOND MAYBE MAKING SURE HE GETS FED.

THE COURT: OKAY.

MR. PETROSINELLI: NO OBJECTION TO THE DIETARY DISCUSSION, YOUR HONOR.

THE COURT: ALL RIGHT. TERRIFIC. THANKS.

MR. PETROSINELLI: THANK YOU.

{LUNCHEON RECESS}

CASE NUMBER: 21STCV22822
CASE NAME: NC VS. HAIN, ET AL.
LOS ANGELES, CALIFORNIA MONDAY, JANUARY 31, 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: GOOD AFTERNOON. THIS IS JUDGE HOGUE SPEAKING.

MR. PETROSINELLI: LET ME KNOW WHEN YOU'RE READY.

THE COURT: I'M READY.

MR. PETROSINELLI: OKAY. I WAS WAITING FOR A CUE FROM YOU.

Q OKAY. THANK YOU. WELCOME BACK, DR. SHAPIRO.

A YEAH, HI.

Q BEFORE THE BREAK WE WERE TALKING ABOUT SOME OF THE SCREENING MECHANISMS. I WANT TO TALK ABOUT THAT.

BUT JUST SO I UNDERSTAND YOUR TESTIMONY, DID I HEAR YOU TO SAY THAT JUST BECAUSE YOU'RE POSITIVE ON ONE OF THOSE SCREENING MECHANISMS, THAT DOESN'T EQUATE WITH A DIAGNOSIS OF AUTISM; CORRECT?

A THAT'S TRUE. AUTISM IS A CLINICAL DIAGNOSIS SO

YOU NEED TO PUT TOGETHER MULTIPLE SOURCES OF INFORMATION.

Q UNDERSTOOD.

OKAY. SO IN CORTICA, YOU DO HAVE AN INTAKE QUESTIONNAIRE THAT YOU USE IN -- WITH PROSPECTIVE PATIENTS; CORRECT?

A CORRECT.

Q AND YOUR COUNSEL WAS GRACIOUS ENOUGH TO SHARE IT WITH ME. I JUST WANT TO ASK YOU A FEW QUESTIONS ABOUT IT.

I IMAGINE YOU'RE FAMILIAR WITH IT AND PROBABLY LOOKED AT IT A LOT; RIGHT?

A YES.

Q OKAY.

AND IT'S DESIGNED TO BE COMPREHENSIVE; CORRECT?

A WELL, IT'S DESIGNED TO BE COMPREHENSIVE, BUT NOT EXHAUSTIVE.

Q FAIR ENOUGH. FAIR ENOUGH.

AT LEAST -- I KNOW IT'S ADMINISTERED ELECTRONICALLY, BUT AT LEAST WHEN I PRINTED IT OUT, IT WAS 30 PAGES LONG.

SO HERE'S WHAT I'D LIKE TO DO, FIRST I WANT TO PULL UP THE CDC'S STATEMENT OF RISK FACTORS THAT MR. ESFANDIARY SHOWED YOU.

CAN YOU PULL IT UP. IT'S SLIDE 8.

DO YOU RECALL GOING OVER THIS LIST WITH MR. ESFANDIARY?

MR. ESFANDIARY: WE DID NOT GO OVER THIS.

THE WITNESS: I --

MR. PETROSINELLI: I'M SORRY. IT WAS USED IN OPENING.

Q WE TALKED ABOUT THIS IN YOUR DEPOSITION; RIGHT?

A I BELIEVE SO, YES.

Q OKAY.

A I'VE SEEN THIS BEFORE.

Q OKAY. FAIR ENOUGH.

SO I WANT TO WALK THROUGH THIS AND MAYBE LINE IT UP AGAINST YOUR QUESTIONNAIRE.

SO FOR INSTANCE, THE FIRST LINE IT SAYS:

"MOST SCIENTISTS AGREE THAT GENES ARE ONE OF THE RISK FACTORS THAT CAN MAKE A PERSON MORE LIKELY TO DEVELOP ASD."

YOU AGREE WITH THAT; CORRECT?

A YES.

Q AND LET'S GO TO SLIDE 9 IF WE COULD.

AND SO, IN FACT, YOUR INTAKE FORM ASKED ABOUT WHETHER THE PATIENT HAS SEEN A GENETICIST AND ANY GENETIC RESULTS THEY HAVE SEEN, THAT THEY HAVE GOTTEN; CORRECT?

A YES, WE DO ASK ABOUT THAT.

Q OKAY. NEXT SLIDE.

THE CDC SAYS, "CHILDREN WHO HAVE A SIBLING WITH ASD ARE AT A HIGHER RISK OF HAVING AUTISM."

YOU AGREE WITH THAT; RIGHT?

A YES.

Q AND YOUR INTAKE FORM ASKS ABOUT FAMILY HISTORY

INCLUDING HISTORY OF SIBLING; CORRECT?

A YES.

Q ALL RIGHT. NEXT SLIDE.

YOUR QUESTIONNAIRE ASKS ABOUT CERTAIN GENETIC AND CHROMOSOMAL CONDITIONS, AND AGAIN, YOUR INTAKE FORM TALKS ABOUT THAT AND SEEKS THAT INFORMATION; CORRECT?

A YES.

Q AND NEXT SLIDE.

THEN IT TALKS ABOUT CERTAIN MEDICINES TAKEN DURING PREGNANCY VALPROIC ACID AND THALIDOMIDE HAVE BEEN LINKED AND YOUR INTAKE FORM REASONABLY ASKS WHAT MEDICINES THE BIRTH MOTHER MIGHT HAVE TAKEN; CORRECT?

A WE DO ASK THAT, YES.

Q OKAY.

AND THE NEXT SLIDE, PLEASE.

IT SAYS THAT THERE'S SOME EVIDENCE THAT THE CRITICAL PERIOD FOR DEVELOPING AUTISM OCCURS BEFORE, DURING AND IMMEDIATELY AFTER BIRTH.

THAT'S SOMETIMES CALLED THE PERINATAL PERIOD; CORRECT?

A YES.

Q AND YOUR INTAKE FORM ASKS, AMONG OTHER THINGS, WERE THERE ANY PROBLEMS WITH PREGNANCY, LABOR OR BIRTH; CORRECT?

A CORRECT.

Q AND THEN FINALLY, THE CDC RISK FACTOR LISTS CHILDREN BORN TO OLDER PARENTS ARE AT A HIGHER RISK.

YOU AGREE WITH THAT; CORRECT?

A CORRECT.

Q AND ONE OF THE FIRST THINGS YOU ASK ON YOUR INTAKE FORM IS, WHAT WAS THE MOTHER'S AGE, THE BIOLOGICAL MOTHER, AND THE FATHER'S AGE AT THE TIME OF BIRTH; CORRECT?

A IT'S -- I DON'T KNOW IF IT'S ONE OF THE FIRST THINGS, BUT IT'S DEFINITELY ON THERE.

Q YEAH, SURE.

LET ME JUST DO A QUICK THING OF TERMINOLOGY HERE JUST SO I HAVE IT.

SO THE WORD "ENVIRONMENTAL FACTORS" HAS BEEN USED A LOT.

SO I UNDERSTAND HOW IT'S USED BY YOU AND IN THE LITERATURE, THE THINGS WE JUST WENT OVER, LIKE AGE OF THE MOTHER OR SIBLINGS, THOSE ARE ACTUALLY TECHNICALLY CONSIDERED ENVIRONMENTAL FACTORS. IT MEANS NON GENETIC; RIGHT?

A SIBLING, NO. BUT THE AGE OF THE PARENTS ARE -- IS CONSIDERED AN ENVIRONMENTAL OR NONGENETIC RISK FACTOR. BUT THE SIBLING FAMILY HISTORY SPEAKS TO THE GENETIC RISK FACTORS.

Q FAIR ENOUGH.

I GUESS MY POINT IS MORE SIMPLE IS, AS A LAY PERSON I HEAR "ENVIRONMENTAL FACTOR," I THINK ABOUT THINGS FLOATING AROUND IN THE ENVIRONMENTAL OR THINGS -- IT'S USED MORE BROADLY THAN THAT WHEN IT'S USED IN THIS CORRECT; CORRECT?

A YEAH. GENERALLY, IT MEANS NONGENETIC IN THIS

CONTEXT.

Q THAT'S HELPFUL. THANK YOU.

WE TALKED ABOUT THIS IN YOUR DEPOSITION, BUT TO BE CLEAR, YOUR QUESTIONNAIRE DOESN'T MENTION ANYTHING ABOUT HEAVY METALS; CORRECT?

A IT DOES NOT.

Q OKAY. DOES IT -- WELL, LET'S SKIP THAT.

BEAR WITH ME FOR A SECOND, YOUR HONOR.

YOU DON'T ASK YOUR PROSPECTIVE PATIENTS WHETHER THEY HAVE EATEN FRUITS OR VEGETABLES OR GRAINS AS SOME SCREENING MECHANISM FOR POTENTIAL HEAVY METALS; CORRECT?

A I THINK WE ASK GENERALLY ABOUT DIET, BUT WE DON'T ASK SPECIFICALLY ABOUT THAT WITH THAT INDICATION.

Q AND, IN FACT, YOU'VE NEVER WARNED A PATIENT OR A PATIENT'S FAMILY NOT TO EAT CERTAIN KINDS OF FOODS BECAUSE OF THE RISK OF HEAVY METALS; CORRECT?

A WELL, I DO COUNSEL -- I MEAN, I -- I HAVEN'T WARNED FAMILIES NOT TO EAT BABY FOODS BECAUSE OF RISK OF HEAVY METALS. I HAVE TALKED ABOUT THE IMPORTANCE OF DIET AND THE PREFERENCE FOR FOODS THAT ARE, YOU KNOW, FREE OF PESTICIDES AND CONTAMINANTS AND THAT SORT OF THING.

Q OKAY. WELL, LET'S TALK ABOUT THE NUTRITIONAL ISSUES.

IT'S FAIR TO SAY THAT MANY CHILDREN WITH AUTISM HAVE PROBLEMS RELATING TO EATING, INCLUDING FOOD SELECTIVITY, RITUALS AROUND EATING AND CERTAIN OTHER COMPULSIVE EATING HABITS; CORRECT?

A THAT IS TRUE.
Q OKAY.
AND ONE OF THOSE EATING PROBLEMS IS SOMETHING CALLED PICA OR PICA, I DON'T KNOW HOW -- THE RIGHT WAY TO PRONOUNCE. IT IS THAT TRUE?
A YEAH, I USUALLY SAY PICA, BUT --
Q OKAY.
A -- SOME PEOPLE MAY PRONOUNCE IT DIFFERENTLY.
BUT THAT'S TRUE. IT'S NOT SO MUCH AN EATING PROBLEM AS INGESTING OR MOUTHING NONEDIBLE OBJECTS.
Q FAIR ENOUGH.
I WAS USING THAT, I THINK, BROADLY.
SO PICA -- I'LL USE YOUR PRONUNCIATION -- PICA IS WHEN A CHILD EATS NON FOOD ITEMS, DIRT, PAINT CHIPS, VARIOUS OTHER THINGS; CORRECT?
A YES, CORRECT.
Q OKAY.
AND I THINK YOU MENTIONED THAT ON YOUR DIRECT.
AS TO THE ABNORMAL EATING PATTERNS OF FOOD, SOMETIMES KIDS WITH AUTISM WILL ONLY EAT CERTAIN TYPES OF FOODS AND NOT OTHERS; CORRECT?
A YES.
Q AND THAT FOOD SELECTIVITY ISSUE CAN SOMETIMES CREATE MALNUTRITION PROBLEMS WHERE THEY DON'T GET MAYBE CERTAIN NUTRIENTS THAT THEY SHOULD OTHERWISE BE GETTING; RIGHT?
A YEAH, IT CAN LEAD TO CERTAIN NUTRITIONAL DEFICITS.

Q AND I BELIEVE ON YOUR WEBSITE YOU POINT OUT THE PROSPECT THAT MAYBE A PATIENT MIGHT NEED NUTRITIONAL SUPPLEMENTS OR OTHER MEDICATIONS TO HELP ON THESE DEFICIENCIES; CORRECT?

A YEAH, I DIDN'T AUTHOR THE WEBSITE, BUT I WOULD GENERALLY AGREE WITH THAT.

Q YEAH, OKAY.

AND THEN FINALLY, THESE -- KIDS WITH AUTISM CAN SOMETIMES HAVE METABOLIC DIFFERENCES, AND I THINK YOU ALLUDED TO THIS IN HOW THEY -- I THINK WHAT YOU SAID HOW THEY PROCESSED HEAVY METALS; TRUE?

A THAT HAS BEEN SUGGESTED IN SOME RESEARCH, YES.

Q YEAH.

OKAY. NEXT TOPIC: QUICKLY, WE TALKED A LITTLE BIT ABOUT THE CDC EARLIER. I JUST WANT TO RUN THROUGH TWO MORE OR THREE MORE QUICKLY.

CAN WE GO TO SLIDE 15, PLEASE, IAN.

SO THE AMERICAN ACADEMY OF PEDIATRICS -- WHAT I'M GOING TO DO IS I'M GOING TO RUN THROUGH JUST A FEW OF THEM QUICKLY.

CAN YOU PULL THAT UP.

THE AMERICAN ACADEMY OF PEDIATRICS, THEY PUBLISHED A PAPER ON AUTISM.

AND THAT'S EXHIBIT 8. RIGHT? NO, I'M SORRY. 51. 651.

I DON'T THINK THIS IS CONTROVERSIAL.

YOU AGREE, DOCTOR, THAT THE AMERICAN ACADEMY OF PEDIATRICS, THEY DON'T LIST HEAVY METALS AS A RISK

FACTOR FOR AUTISM; CORRECT?

A DOES NOT SEEM TO BE LISTED HERE, YES.

Q YEAH.

AND IT SAYS, "THE POTENTIAL ENVIRONMENTAL FACTORS THAT MAY BE RELATED TO INCREASED PURPORTED PREVALENCE OF ASD IS AN INTERACTIVE STUDY THAT AS YET IS WITHOUT FIRM CONCLUSION." YOU WOULD AGREE WITH THAT; RIGHT?

A I AGREE THAT IT'S AN AREA OF ACTIVE STUDY, YEAH.

Q YOU DISAGREE WITH THE "WITHOUT FIRM CONCLUSION"?

A WELL, I THINK IT -- AGAIN, IT DEPENDS ON WHAT SPECIFICALLY YOU'RE REFERRING TO.

Q OKAY.

A BUT AS A BROAD AREA, I WOULD SAY THERE'S NOT ONE SPECIFIC OR A LIST OF SPECIFIC ENVIRONMENTAL RISK FACTORS THAT ARE WELL ESTABLISHED.

Q OKAY.

MR. ESFANDIARY: I'D JUST LIKE TO INTERPOSE AN OBJECTION TO THE EXTENT THAT MR. IMBROSCIO HASN'T CLARIFIED WHETHER THE WITNESS HAS SEEN THE DOCUMENT, IT SEEMS TO BE IMPEACHMENT BY EXTRINSIC EVIDENCE.

THE COURT: WELL, HE CAN DO THAT. I HAVE ANOTHER CONCERN, THOUGH, WHICH IS THAT EVERYBODY'S MARKING AND SHOWING ME EXHIBITS AND WE'RE NOT OFFERING THEM INTO THE RECORD, SO AT THE END OF THE HEARING OR HEARINGS, YOU ALL NEED TO SOMEHOW PUT THOSE INTO COURT

SO IT'S VERY CLEAR WHAT WAS USED OR NOT USED.

MR. ESFANDIARY: YOUR HONOR, AT THE END OF EACH DAY WE'RE GOING TO ENTER INTO THE RECORD OFFICIALLY, THE EXHIBITS THAT WE USED DURING THE DAY.

THE COURT: OKAY. BUT WE'LL NEED COPIES OF THEM TOO.

MR. PETROSINELLI: YEAH, WE TALKED ABOUT THAT. WE HAVE AN AGREEMENT.

THE COURT: ALL RIGHT. GOOD.

MR. PETROSINELLI:

Q SO LET'S GO TO THE NEXT SLIDE.

THIS IS THE AMERICAN PSYCHIATRIC ASSOCIATION, AND I THINK I SHOWED THIS TO YOU IN YOUR DEPOSITION.

IT'S EXHIBIT 635. THANK YOU.

DO YOU RECALL SEEING THIS IN YOUR DEPOSITION?

A YES.

Q ALL RIGHT. AND TO BE CLEAR, THE AMERICAN PSYCHIATRIC ASSOCIATION, THEY DON'T LIST HEAVY METALS AS A RISK FACTOR FOR AUTISM; CORRECT?

A NOT TO MY KNOWLEDGE.

Q OKAY.

AND LET'S GO TO EXHIBIT 674.

I THINK YOU WERE SHOWN A PUBLICATION FROM THE NATIONAL INSTITUTES OF HEALTH, ONE OF THE SUBDIVISIONS, BUT I WANT TO SHOW YOU THIS IS THE NIH, THE BIG NIH, THEIR PUBLICATION ON AUTISM SPECTRUM DISORDER, THE FACT SHEET.

THAT'S EXHIBIT 674.

LET'S GO TO PAGE 3, IAN.

A SO ACTUALLY, THIS IS A DIFFERENT SUBDIVISION. THIS IS THE NATIONAL INSTITUTE OF NEUROLOGIC DISORDERS AND STROKE, SO IT'S ANOTHER SUB-INSTITUTE.

Q I APOLOGIZE. YOU'RE ABSOLUTELY RIGHT ABOUT THAT. SORRY, I MISSED THAT.

IAN, COULD WE BLOW UP THAT SECTION ON WHAT CAUSES AUTISM.

SO AS I THINK WE HAVE -- YOU'VE AGREED IN YOUR DEPOSITION, NIH DOESN'T LIST HEAVY METALS AS A FACTOR -- AS A RISK FACTOR FOR AUTISM; CORRECT?

A CORRECT. SO THIS PARTICULAR NIH FACT SHEET DOES NOT LIST HEAVY METALS, BUT THE OTHER ONE WHICH WE SAW EARLIER DOES.

Q WELL, IT LISTS IT AS SOMETHING THAT MAY BE LINKED TO RESEARCH THAT'S ONGOING; CORRECT?

A THAT'S RIGHT.

Q I THINK IT CITED THE ARORA STUDY AS THE SINGLE STUDY CITED; CORRECT?

A YES, THAT -- AT LEAST THAT STUDY.

Q OKAY. WELL, THE RECORD WILL SPEAK TO WHAT IT SHOULD CITE.

A YEAH.

Q THE NIH SUBDIVISION HERE SAYS, "ENVIRONMENTAL FACTORS MAY ALSO PLAY A ROLE IN GENE FUNCTION AND DEVELOPMENT, BUT NO SPECIFIC ENVIRONMENTAL CAUSES HAVE YET BEEN IDENTIFIED."

THAT'S AT LEAST WHAT THIS DIVISION OF NIH SAYS

ABOUT OTHER ENVIRONMENTAL RISK FACTORS; CORRECT?

A THAT'S WHAT IT SAYS. BUT IT ALSO CONTRADICTS THE OTHER DOCUMENTS WE JUST REVIEWED WHICH LIST, FOR EXAMPLE, EXPOSURE TO GALPORATE AND FLORDIMIDE AS RISK FACTORS.

Q YEAH.

ALL RIGHT. LET'S MOVE ON.

NOW, HERE -- I -- NOW I WANT TO SPEND THE REST OF OUR TIME TALKING ABOUT YOUR OPINIONS IN THIS CASE THAT YOU'VE OFFERED IN YOUR REPORT.

JUST SO I CAN SET THE FRAMEWORK: YOUR OPINION IS ESSENTIALLY THAT THERE ARE NEUROBIOLOGICAL PATHWAYS OF HEAVY METALS THAT ARE IMPLICATED -- EXCUSE ME -- LET ME STRIKE THAT AGAIN. I WANT TO GET THIS EXACTLY RIGHT.

THERE ARE NEUROBIOLOGICAL PATHWAYS OF HEAVY METAL TOXICITY THAT ARE SIMILAR TO MECHANISMS THAT HAVE BEEN CONNECTED TO SOME OF THE SYMPTOMS OF AUTISM.

IS THAT A FAIR SUMMARY OF YOUR ESSENTIAL OPINION HERE?

A WELL, I -- YEAH, I THINK THAT -- I THINK THAT MY OPINION IS LITTLE BIT STRONGER THAN THAT, WHICH IS THAT THE MECHANISMS OF HEAVY METAL TOXICITY OVERLAP SUBSTANTIALLY WITH THE PATHOGENETIC MECHANISMS OF AUTISM.

Q RIGHT.

AND THAT'S WHAT I WANT TO TALK ABOUT TO YOU ABOUT.

FIRST, YOU WOULD AGREE THAT THERE ARE MANY

THEORIES ABOUT THE MECHANISMS THAT ARE IMPLICATED WITH AUTISM; CORRECT?

A YES, I -- AS A GENERAL STATEMENT, YES.

Q OKAY.

AND YOU'RE NOT HERE TO SAY THAT BECAUSE HEAVY METALS IMPLICATE PATHWAY X AND PATHWAY X IS ALSO IMPLICATED WITH AUTISM, THAT THEREFORE HEAVY METALS ARE A DEMONSTRATED CAUSE OF AUTISM, RIGHT? THAT'S NOT WHY YOU'RE HERE?

A YEAH, I'M NOT OFFERING AN OPINION ON CAUSATION.

Q OKAY.

AND I THINK YOU SAID THIS ON DIRECT.

YOU WOULD AGREE THERE'S NO BIOLOGICAL SIGNATURE OF AUTISM THAT WOULD ALLOW US TO CONNECT ANY ONE OF THESE MECHANISMS TO AUTISM; TRUE?

A WELL, THAT -- THE WAY YOU PHRASED THAT, I DON'T AGREE WITH IT.

SO THERE'S NO SPECIFIC BIOMARKER FOR AUTISM AND THERE'S NO -- THERE'S NO BIOLOGICAL TEST THAT CAN TELL YOU YOU HAVE AUTISM OR DON'T.

BUT THERE ARE BIOLOGICAL SIGNATURES IN AUTISM, SO GENE EXPRESSION PROFILES, PROFILES OF -- MARKERS OF INFLAMMATION THAT CAN, YOU KNOW, DISTINGUISH AUTISM FROM NON AUTISTIC POPULATIONS RELATIVELY RELIABLY AND SOME OF THOSE ACTUALLY -- SOME OF THOSE GENE EXPRESSION CHANGES AND INFLAMMATORY ACTIVATION OF INFLAMMASONE CAN ALSO BE TRIGGERED BY HEAVY METAL EXPOSURE.

Q OKAY.

AND JUST SO I UNDERSTAND THIS: AS YOU KNOW, DR. GESCHWIND IS ONE OF OUR EXPERTS. HE'S AT UCLA.

YOU'RE FAMILIAR WITH DR. GESCHWIND; RIGHT?

A YES.

Q AND I BELIEVE YOU SAID HE ACTUALLY INTERVIEWED YOU FOR MEDICAL SCHOOL AT SOME POINT IN TIME; RIGHT?

A I -- I -- YEAH, I THINK IT WAS FOR MEDICAL SCHOOL, I'M PRETTY SURE.

Q OKAY. NO WORRIES.

YOU WOULD AGREE THAT HE'S ONE OF THE LEADING RESEARCHERS WHEN IT COMES TO AUTISM AND GENETICS AND THE LIKE; TRUE?

A HE'S VERY WELL KNOWN IN THAT AREA.

Q FAIR ENOUGH.

AND JUST SO I UNDERSTAND, THE WORK THAT YOU DID IN ACADEMIA, IT ACTUALLY WAS NOT LOOKING INTO THESE MECHANISMS OF AUTISM, RIGHT, THAT'S NOT -- THAT WASN'T YOUR RESEARCH AREA OF EX -- OF SPECIALTY; CORRECT?

A MY RESEARCH WAS ON BRAIN DEVELOPMENT MORE GENERALLY AND PARTICULARLY ON THE DEVELOPMENT OF COGNITION AND LANGUAGE.

Q OKAY.

SO WE TALK ABOUT THESE MECHANISMS THAT YOU'VE DISCUSSED.

IN FACT, MANY OF THESE MECHANISMS THAT YOU DISCUSS ARE ACTUALLY THINGS THAT CAN HAPPEN IRRESPECTIVE OF METAL EXPOSURE; CORRECT?

A THEY DON'T REQUIRE METAL EXPOSURE.

Q OKAY.

AND JUST SO I MAKE SURE I HAVE THIS.

YOU'RE NOT HERE TODAY TO SAY THAT ANY ONE OF THESE PARTICULAR MECHANISMS IS IN FACT A DEMONSTRATED MECHANISM THAT CONNECTS HEAVY METALS WITH AUTISM; TRUE?

A WELL, I'M SAYING THAT THEY ARE DEMONSTRATED MECHANISMS THAT AREN'T INVOLVED IN AUTISM AND IN THE BRINGING ABOUT THE CHANGES IN THE BRAIN AND THE NERVOUS SYSTEM FUNCTION THAT CAUSE AUTISM AND THERE ARE ALSO CHANGES THAT CAN BE TRIGGERED BY A HEAVY METAL EXPOSURE.

Q SO THESE ARE -- THESE ARE HYPOTHESES OF HOW THIS MIGHT BE GOING ON IN YOUR VIEW; CORRECT?

A ESSENTIALLY, THEY ARE --

Q OKAY.

A -- THERE'S THESE BIOLOGICAL PATHWAYS ARE THE SAME.

Q AND SO AS I UNDERSTAND YOUR REASONING, FIRST YOU REVIEWED SOME ARTICLES ON THE BIOLOGICAL EFFECTS OF HEAVY METAL FROM ANIMAL STUDIES OR EXPERIMENTAL HUMAN STUDIES, RIGHT, THAT WAS SORT OF STEP ONE; TRUE?

A WELL, THE HUMAN STUDIES ARE -- I MEAN, WE DON'T EXPERIMENT ON HUMANS. BUT OBSERVATIONAL HUMAN STUDIES, YES.

Q YEAH, THAT'S WHAT I MEANT. I'M SORRY. I WAS NOT CLEAR THERE.

AND THE STUDIES THAT YOU LOOKED AT LOOKING AT THE BIOLOGICAL EFFECTS OF HEAVY METALS, TO BE CLEAR, THESE AREN'T STUDIES THAT YOU YOURSELF HAVE CONDUCTED;

CORRECT?

A I DID NOT CONDUCT THOSE STUDIES.

Q AND AS WE SAID, THAT WAS NOT YOUR AREA OF RESEARCH IN ACADEMIA; TRUE?

A YOU MEAN THE PHYSIOLOGIC STUDIES OF HEAVY METAL EXPOSURE?

Q YEAH.

A THAT WAS NOT MY AREA OF RESEARCH.

Q YEAH, YEAH.

AND THEN THE SECOND STEP WAS YOU REVIEWED SOME OTHER STUDIES THAT LOOKED AT AUTISM AND POTENTIAL PATHWAYS IMPLICATED IN AUTISM; CORRECT?

A YES.

Q AND THEN KIND OF WHAT YOU DID, I THINK YOU USED THE WORD SUBSTANTIAL OVERLAP, BUT YOU POINTED OUT THERE ARE SOME COMMONLY CITED MECHANISMS THAT ARE IMPLICATED IN BOTH; CORRECT?

A RIGHT.

Q OKAY.

AND THOSE INCLUDED, IF I GET THEM ALL DOWN FROM YOUR REPORT, INFLAMMATORY ACTIVATION, CELEPROCTOSIS, OXIDATIVE STRESS AND MITOCHONDRIAL DISFUNCTION, THOSE ARE AT LEAST FOUR OF THE ONES THAT YOU'VE MENTIONED EITHER TODAY OR IN YOUR REPORT; CORRECT?

A THOSE ARE SOME OF THEM, YES.

Q YEAH.

AND BECAUSE THERE'S THIS SIMILARITY, THIS OVERLAP, THAT'S ESSENTIALLY THE BASIS OF YOUR BIOLOGIC

PLAUSIBILITY OPINION; CORRECT?

A YEAH. I MEAN, I WOULD SAY THERE'S SORT OF A COMMON PATHWAY THAT IS FIGURED BOTH BY GENETIC CHANGES AND BY A CERTAIN ENVIRONMENTAL INFLUENCE INCLUDING HEAVY METALS.

Q AND JUST SO WE'RE CLEAR, THE BIOLOGIC PATHWAY MECHANISMS, THEY ARE NOT SPECIFIC TO HEAVY METAL EXPOSURE, THEY ARE GENERAL BIOLOGIC PROCESSES THAT OCCUR AS A RESULT OF DIFFERENT ENVIRONMENTAL INSULTS, OF PHYSIOLOGICAL ABNORMALITIES OR GENETIC VARIATIONS; TRUE?

A WELL, I WOULD SAY THERE ARE NUMEROUS CAUSES. I WOULDN'T SAY THAT, YOU KNOW, THEY ARE EXTREMELY COMMON OR NORMAL. SO, YOU KNOW, SEVERE INFECTIONS FOR EXAMPLE, MIGHT CAUSE EXPOSURE TO PHOSPHATES OR OTHER PESTICIDES, THAT ARE VARIOUS AGENTS THAT CAN CAUSE THESE CHANGES APART FROM HEAVY METALS, BUT -- SO I'M NOT -- I AGREE IN THE SENSE THAT IT'S NOT SPECIFIC TO HEAVY METAL TOXICITY.

Q AND THAT'S ALL THAT I WAS GETTING AT.

THESE MECHANISMS THAT YOU'RE TALKING ABOUT, NOT SPECIFIC TO HEAVY METAL TOXICITY.

OKAY. ONE MOMENT.

SO THESE ARE THINGS THAT CAN HAPPEN IN THE BODY IRRESPECTIVE OF METAL EXPOSURE; TRUE?

A WELL, I MEAN, THEY DON'T HAPPEN WITHOUT A TRIGGER, BUT THE TRIGGER DOESN'T HAVE TO BE METAL EXPOSURE.

Q YEAH, FAIR ENOUGH.

AND YOU CAN'T POINT ME TO A SINGLE STUDY THAT SAYS THESE HEAVY METALS TRIGGER ANY OF THESE MECHANISMS AND THEREFORE MAY CAUSE ASD? YOU --

A I'M NOT AWARE OF A SINGLE STUDY THAT PUTS IT TOGETHER IN THAT WAY.

Q THAT'S WHAT YOU'RE DOING HERE; CORRECT?

A ESSENTIALLY.

Q YEAH.

AND I LOOKED AT SOME OF THE STUDIES YOU CITED ON PAGE 16 AND 17 OF YOUR REPORT. I WON'T READ THEM ALL FOR THE COURT REPORTER BECAUSE THEY WILL BE LENGTHY.

BUT NONE OF THEM ACTUALLY MENTION AUTISM SPECIFICALLY; CORRECT?

A THAT'S PROBABLY TRUE. I WOULD NEED TO REVIEW THEM TO BE SURE.

Q OKAY.

AND BY THE SAME TOKEN THESE MECHANISMS AREN'T SPECIFIC TO HEAVY METALS. THESE MECHANISMS ARE ALSO NOT SPECIFIC TO ASD DEVELOPMENT EITHER; CORRECT?

A MANY OF THE ONES WE TALKED ABOUT ARE NOT SPECIFIC TO ASD.

Q YEAH.

AND, IN FACT, SOME OF THESE PATHWAYS THAT YOU'VE IDENTIFIED IMPLICATED IN PARKINSON'S AND ALZHEIMER'S FOR SURE; CORRECT?

A YEAH, THAT'S CORRECT. AND THAT HAS TO DO WITH THE -- SORT OF THE TIMING WITH RESPECT TO BRAIN DEVELOPMENT AND MATURATION, SO THEY ARE CLEARLY

PROCESSES THAT ARE INVOLVED IN NEURODEGENERATION AND ABNORMAL NERVE CELL FUNCTION, BUT IF THE ONSET IS LATE IN LIFE, THEY CAN LEAD TO NEURODEGENERATIVE DISORDERS. IF IT'S EARLY IN LIFE, THEY CAN LEAD TO NEURODEVELOPMENTAL DISORDERS.

Q AND YOU MENTIONED NM -- NMDA, THAT'S BEEN IMPLICATED IN STROKE AND SCHIZOPHRENIA AND EPILEPSY; CORRECT?

A WELL, THEY ARE ABNORMALITIES IN NMDA RECEPTOR FUNCTION IN THOSE CONDITIONS. IN STROKE IT'S MORE OF AN -- IT'S A, YOU KNOW, THAT'S NOT THE PRIMARY ETIOLOGIC -- THAT IS NOT WHAT KICKS OFF THE PROCESS IN STROKE, BUT CERTAINLY AN NMDA RECEPTOR DYSFUNCTION IS A FEATURE OF OTHER PSYCHIATRIC DISORDERS --

Q YEAH.

A -- AND EPILEPSY.

Q SURE.

AND --

A AND THEY TO SOME EXTENT EXPLAIN THE GENETIC OVERLAP BETWEEN SCHIZOPHRENIA AND AUTISM SO THERE'S SORT OF SHARED GENETIC RISK BETWEEN THOSE DISORDERS.

Q ONE FINAL MECHANISM I WANT TO MENTION BRIEFLY IS YOU MENTIONED PROTEIN KINASE C, SOMETIMES CALLED PKC AS ONE POTENTIAL MECHANISM GOING ON HERE IN YOUR REPORT.

A RIGHT. THE ALTERATION OF PROTEIN KINASE C SIGNALLING, YES.

Q YEAH.

AND TO BE CLEAR, THAT PATHWAY HAS BEEN

IMPLICATED IN CERTAIN CANCERS, RENAL DISEASE, CARDIOVASCULAR DISEASE, AMONG OTHERS; TRUE?

A THAT'S TRUE. SOME OF THESE PATHWAYS ARE, YOU KNOW, RATHER GENERAL, AND IT DEPENDS, AGAIN, ON WHAT CELLS ARE EXPOSED AT WHAT TIME DURING DEVELOPMENT THEY ARE EXPOSED, AND, YOU KNOW, WHAT THE REST OF THE SUBSTRATE IS.

Q AND AS I UNDERSTAND IN YOUR REPORT YOU DON'T OPINE ON WHETHER AND HOW THE EFFECT OF THESE SPECIFIC BIOLOGICAL MECHANISMS YOU DESCRIBE, HOW THEY VARY BETWEEN POTENTIAL PRENATAL AND POST-NATAL ENVIRONMENT; TRUE?

A I AM NOT -- I'M NOT SURE WHAT EXACTLY YOU'RE REFERRING TO.

Q YEAH. THAT'S A FAIR -- THAT WAS NOT A GREAT QUESTION.

AS I READ YOUR REPORT, DOCTOR, YOU DESCRIBE THESE PATHWAYS, BUT YOU DON'T TEASE OUT WHICH ONES ARE PRE-NATAL PATHWAYS WHICH ONES MAY BE IN THE EARLY DEVELOPMENT PHASE AS YOU SAID.

A YEAH, SO THAT'S A GOOD QUESTION. I DON'T GO INTO MUCH DETAIL ON THAT IN THE REPORT.

SO THAT THERE ARE A COUPLE OF, I THINK, CLARIFICATIONS THAT MIGHT BE RELEVANT. SO THAT THERE ARE SORT OF GENERAL -- MORE GENERAL PROCESSES AND MORE SPECIFIC PROCESSES, SO THINGS LIKE DISRUPTION OF MITOCHONDRIAL FUNCTION, OXIDATIVE STRESS, INFLAMMATION, THOSE ARE SYSTEMIC ISSUES THAT CAN OCCUR, YOU KNOW, PRE-

OR POST-NATALLY AND IN FACT, YOU KNOW, THERE'S A BODY OF RESEARCH LOOKING AT INFLAMMATION AND OXIDATIVE STRESS, I THINK I EVEN REFERRED TO THIS EARLIER, IN THE MOTHER AFFECTING RISK OF AUTISM AND DEVELOPMENTAL DISORDERS IN THE CHILD.

Q YES.

A SO THOSE ARE KIND OF SYSTEMIC CHANGES IN THE SORT OF THE DEVELOPMENTAL AREA THAT CAN AFFECT HOW THE BRAIN FORMS.

AND THEN THERE ARE RATHER SPECIFIC PROCESSES LIKE SYNAPTOGENESIS WHICH OCCUR AT A STAGE IN THE DEVELOPMENT OF BRAIN AND THE NERVOUS SYSTEM THAT IS, YOU KNOW, POTENTIALLY A VULNERABLE PERIOD WITH RESPECT TO THE DEVELOPMENT OF AUTISM AND OTHER NEURODEVELOPMENTAL CONDITIONS, SO SYNAPTOGENESIS IS SOMETHING THAT'S OCCURRING IN, YOU KNOW, MOSTLY IN POST-NATAL LIFE, AT LEAST THE FORMATION OF -- AND REFINEMENT OF FRAME NETWORKS.

AND THE FUNCTION OF NMDA RECEPTORS, AS I SAID EARLIER, IS IMPORTANT FOR ENSURING THAT THAT HAPPENS IN AN APPROPRIATE MANNER. SO IF YOU INTERFERE WITHIN NMDA RECEPTOR FUNCTION AT THIS KIND OF CRITICAL JUNCTURE FOR SYNAPTOGENESIS, YOU'LL GET A CERTAIN -- A PARTICULAR KIND OF ARRAY OF ANOMALIES.

IF YOU INTERFERE WITH THAT RECEPTOR FUNCTION AT A DIFFERENT AGE OR A DIFFERENT STAGE OF BRAIN DEVELOPMENT, YOU MAY SEE SOMETHING ELSE.

Q OKAY. THAT'S HELPFUL.

LAST TOPIC I JUST WANT TO PICK UP THE -- SOMETHING THAT YOU TALKED ABOUT ON DIRECT, THAT'S THE HALLMAYER STUDY.

AND JUST SO THE RECORD IS CLEAR, YOU DON'T DISCUSS THE HALLMAYER STUDY IN YOUR REPORT THAT YOU GAVE TO US; CORRECT?

A I DON'T THINK I DISCUSS IT SPECIFICALLY IN THE REPORT.

Q YEAH.

AND WE'VE GOTTEN, I THINK, FOUR DIFFERENT LISTS OF THE MATERIALS THAT YOU'VE RELIED ON, ONE WITH YOUR REPORT, ONE ON NOVEMBER 24TH, ONE ON DECEMBER 13TH, AND ONE FIVE DAYS AGO, LAST WEDNESDAY, JANUARY 26TH.

TO BE CLEAR, THE FIRST TIME THAT YOU'VE LISTED HALLMAYER AS SOMETHING THAT YOU'RE RELYING ON WAS LAST WEDNESDAY; CORRECT?

A THAT MIGHT BE TRUE. I WAS AWARE OF THE STUDY AND IT HAD COME UP IN DISCUSSION, AND I DON'T REMEMBER EXACTLY WHEN I PROVIDED THE REFERENCE, BUT IT WAS AT SOME POINT -- WELL, AT SOME POINT PRIOR TO THIS HEARING.

Q YEAH.

SO THAT'S WHY I WANTED TO ASK YOU. I'M JUST CURIOUS.

DID YOU GIVE THE REPORT -- THE STUDY TO MS. -- TO THE LAWYERS OR DID THEY GIVE IT TO YOU THAT REMINDED YOU ABOUT THE STUDY?

A NO, I GAVE IT --

MR. ESFANDIARY: I'M GOING TO OBJECT ON THE

GROUNDS OF PRIVILEGE HERE, PURSUANT TO THE PARTIES' AGREEMENT THAT COMMUNICATION BETWEEN THE COUNSEL AND THE EXPERTS ARE PRIVILEGED. WE HAVE A STIPULATION TO THAT EFFECT.

MR. PETROSINELLI: I DON'T WANT TO GET INTO THAT. I DON'T THINK IT IS, BUT I'LL WITHDRAW THE QUESTION.

Q IN ANY EVENT, FAIR TO SAY THAT YOU LOOKED AT THE STUDY RECENTLY IN ANTICIPATION OF YOUR TESTIMONY; CORRECT?

A WELL, I'VE BEEN FAMILIAR WITH THE STUDY FOR A WHILE. I MAY NOT HAVE CITED IT IN MY REPORT. I CITED OTHER STUDIES THAT, YOU KNOW, ESTIMATE GENETIC HERITABILITY OF AUTISM AND HALLMAYER WAS ONE THAT I WAS FAMILIAR WITH, AND I THINK IT --

Q OKAY.

A -- MAY HAVE BEEN, YOU KNOW, JUST AN OVERSIGHT IN THAT I DIDN'T MENTION IT IN MY REPORT, BUT IT'S ALONG THE LINES OF SOME OTHER STUDIES THAT I DID MENTION.

Q WELL, THAT'S WHAT I WANT TO ASK YOU ABOUT.

CAN WE PULL THAT UP, HALLMAYER. WHAT EXHIBIT IS IT?

EXHIBIT 71.

AND CAN YOU GO TO PAGE 10.

SO THERE WAS A DISCUSSION ABOUT WHAT WERE THE ENVIRONMENTAL FACTORS THAT WERE DISCUSSED IN HALLMAYER, AND I THINK THE HALLMAYER STUDY ITSELF ACTUALLY LISTS WHAT ENVIRONMENTAL FACTORS WERE FOCUSSED -- CAN YOU PULL

UP THE BOTTOM PARAGRAPH, PLEASE, IAN. THERE WE GO.

AND LOOKING AT THE MIDDLE SENTENCE.

IT SAYS, "THE NONGENETIC RISK FACTORS THAT MAY INDEX ENVIRONMENTAL INFLUENCES INCLUDE PARENTAL AGE, LOW BIRTH WEIGHT, MULTIPLE BIRTHS AND MATERNAL INFECTIONS DURING PREGNANCY."

DO YOU SEE THAT?

A YEAH, THOSE ARE THE ONES THAT ARE LISTED THERE.

Q AND THOSE ARE THE ONES THAT ARE LISTED IN CDC WEBSITE; CORRECT?

A THEY ARE -- YEAH, THERE ARE AT LEAST PARTIALLY OVERLAPPING WITH THAT.

Q AND THEY ARE THE ONES THAT YOUR INTAKE FORM AT CORTICA DESIGNS TO GET INFORMATION ABOUT; CORRECT?

A YEAH, I THINK THE INTAKE FORM DOES ASK ABOUT THOSE, MOST OF THOSE THINGS.

Q AND IT DOESN'T SAY ANYTHING ABOUT HEAVY METALS THERE; CORRECT?

A ON THE INTAKE FORM OR IN THE PAPER?

Q WELL, I'M SORRY, IN THE HALLMAYER PAPER.

A YEAH. RIGHT. THE -- YEAH.

Q OKAY.

AND THEN I GUESS LET ME ASK YOU THIS: HAVE YOU SINCE BEING PREPARED TO COME AND TESTIFY ABOUT THIS ARTICLE HERE BEFORE JUDGE HOGUE, DID YOU DO ANY WORK TO FIGURE OUT WHAT THE SCIENTIFIC COMMUNITY HAS SAID ABOUT THE HALLMAYER PAPER SINCE IT WAS PUBLISHED IN 2011?

A NOT SPECIFICALLY.

Q OKAY. WELL, LET'S PULL UP EXHIBIT 661.

THIS IS AN ARTICLE WHERE THE FIRST AUTHOR IS DR. TICK, BEATA TICK.

MR. ESFANDIARY: I'M GOING TO OBJECT TO THE EXTENT THAT YOU HAVEN'T ESTABLISHED WHETHER THE WITNESS HAS ACTUALLY RECEIVED THIS DOCUMENT BEFORE.

THE COURT: OVERRULED.

MR. PETROSINELLI: YEAH.

Q AND THEN ONE -- THANK YOU, YOUR HONOR -- ONE OF THE AUTHORS IS MICHAEL RUTTER.

DO YOU KNOW WHO DR. RUTTER IS?

A NOT PERSONALLY, BUT I'M FAMILIAR WITH THE NAME.

Q YEAH.

AND HE'S SORT OF KNOWN AS THE FATHER OF -- WHAT IS HE THE FATHER OF? FATHER THE CHILD PSYCHIATRY.

DOES THAT RING A BELL?

A I DON'T KNOW THAT I'VE HEARD THAT REFERRAL, BUT I'LL TAKE YOUR WORD FOR IT.

Q THAT'S FINE.

CAN WE BLOW UP THE BACKGROUND SECTION, PLEASE, IAN.

SO THE ISSUE HERE IN THIS STUDY IS LIKE IT WAS IN HALLMAYER, WHICH IS WHAT IS THE IMPACT OF ENVIRONMENTAL FACTORS VERSUS GENETIC FACTORS AND MAYBE JUST HIGHLIGHT THE CONCLUSION.

IN THIS STUDY THEY DEMONSTRATE THAT AUTISM, ASD, IS DUE TO STRONG GENETIC EFFECTS, B, A SHARED ENVIRONMENTAL EFFECTS BECOMES SIGNIFICANT AS A FUNCTION

OF LOWER PREVALENCE RATE, AND C, PREVIOUSLY REPORTED SIGNIFICANT SHARED ENVIRONMENTAL INFLUENCES ARE LIKELY A STATISTICAL ARTIFACT OF OVER-INCLUSION OF CONCORDANT DIZYGOTIC TWINS.

WE'LL GET TO THAT IN A MOMENT.

BUT LET'S GO TO THE CONCLUSION OF THE ARTICLE WHICH IT SAYS IT IN SOMEWHAT PLAINER ENGLISH.

IF YOU CAN BLOW UP PAGE 593 AT THE BOTTOM OF THE CONCLUSION OR ALL THE CONCLUSION.

THANK YOU, SIR.

AND THE NEXT PARAGRAPH TOO.

ALL RIGHT. DOCTOR, I HAVE IN FRONT OF YOU THE CONCLUSION FROM THE TICK STUDY. AND LET'S JUST READ IT TOGETHER.

IT SAYS IT USED AN APPROPRIATE META ANALYTIC STATISTICAL APPROACH, THEY DEMONSTRATED THAT THE ETIOLOGY OF AUTISM SPECTRUM DISORDER IN A COMBINED SAMPLE IS MORE CONSISTENT WITH STRONG GENETIC INFLUENCES.

AND JUST TO BE CLEAR, WHEN YOU TALKED ABOUT HALLMAYER, YOU SAID THE HALLMAYER DATA SEEMED TO BE -- SHOW LESS CONNECTION WITH GENETICS THAN OTHER STUDIES.

I THINK THAT'S WHAT YOU SAID; CORRECT?

A SOMETHING LIKE THAT. YES. THE HERITABILITY ESTIMATES IN THE HALLMAYER STUDY WERE LOWER THAN IN SOME OTHER STUDIES.

Q YEAH.

AND THEN IT GOES ON, THIS STUDY SAYS, "WE CAN

REJECT THE CLAIM THAT THERE IS A STRONG SHARED ENVIRONMENTAL EFFECT ON AUTISM SPECTRUM DISORDERS ACCOUNTING FOR THE MAJORITY OF VARIANCE AND ALERT TO THE DANGER OF PLACING TOO MUCH WEIGHT ON FINDINGS FROM A SINGLE STUDY SUCH AS HALLMAYER, ET AL., 2011."

THAT'S THE STUDY YOU LOOKED AT WITH MR. ESFANDIARY; CORRECT?

A THAT WAS THE HALLMAYER STUDY, YES.

Q AND THEN IT GOES ON TO SAY, "AT THE SAME TIME WE DO NOT EXCLUDE THE POSSIBILITY THAT ENVIRONMENTAL OR AT LEAST NONGENETIC EFFECTS INFLUENCE AUTISM SPECTRUM DISORDER, BUT UNLESS A SUITABLY POWERED AND WELL DESIGNED NEW STUDY COMES FORWARD, THIS CLAIM SHOULD BE PUT TO ONE SIDE FOR NOW."

THAT'S THE CONCLUSION OF THE TICK STUDY IN 2015; CORRECT?

A THAT IS WHAT THEY SAY.

Q OKAY.

MR. PETROSINELLI: I DON'T HAVE ANY FURTHER QUESTIONS, YOUR HONOR. THANK YOU.

THE COURT: ALL RIGHT.

DOES THE PLAINTIFF WANT TO FOLLOW UP WITH ANY QUESTIONS?

MR. ESFANDIARY: JUST A COUPLE OF VERY SHORT QUESTIONS, YOUR HONOR. IT WON'T TAKE VERY LONG AT ALL.

THE COURT: THANK YOU.

REDIRECT EXAMINATION

MR. ESFANDIARY:

Q DR. SHAPIRO, THANK YOU FOR BEING WITH US HERE THIS AFTERNOON. I JUST HAVE A COUPLE FOLLOW-UP QUESTIONS FOR YOU.

DO YOU REMEMBER MR. IMBROSCIO ASKING YOU WHETHER IT WAS GENERALLY ACCEPTED IN THE SCIENTIFIC COMMUNITY WHETHER METALS CAN CAUSE ASD? DO YOU REMEMBER THAT QUESTION?

A YES.

Q PUTTING ASIDE THE QUESTION OF WHETHER IT'S GENERALLY ACCEPTED, DOES IT MAKE LOGICAL SENSE BASED ON WHAT WE KNOW ABOUT HEAVY METALS AND WHAT THEY DO TO THE BRAIN?

A I THINK IT IS GENERALLY ACCEPTED IN THE SCIENTIFIC COMMUNITY THAT HEAVY METALS ARE NEUROTOXIC, AND IF YOU INTRODUCE A TOXIC AGENT TO THE BRAIN AT A CRITICAL DEVELOPMENTAL PERIOD, IT CERTAINLY MAKES SENSE THAT IT COULD LEAD TO AN EARLY DEVELOPMENTAL DISTURBANCES INCLUDING ASD.

Q MR. IMBROSCIO ALSO ASKED YOU ABOUT THE SPECIFIC MECHANISMS THAT METALS INDUCE IN THE BRAIN AND HE ASKED QUESTIONS ABOUT WHETHER THERE ARE GENERAL MECHANISMS THAT HAPPEN IN THE BRAIN IRRESPECTIVE OF THE HEAVY METAL PRESENCE. I BELIEVE YOU ALSO TALKED ABOUT THIS DURING YOUR DEPOSITION.

IS IT JUST THAT METALS OR THESE PROCESSES IN THE BRAIN HAPPEN GENERALLY OR IS IT THAT METALS CAN

CAUSE A PATHOLOGICAL AMOUNT OF THESE PROCESSES TO HAPPEN THAT OVERLAPS WITH THE SYMPTOMS OF ASD?

MR. PETROSINELLI: OBJECTION; LEADING.

THE COURT: OVERRULED.

THE WITNESS: SO THESE ARE PATHOLOGICAL PROCESSES, AND I THINK WHAT I TRIED TO SAY IN MY ANSWER EARLIER WAS THESE ARE NOT SORT OF PROCESSES THAT UNFOLD WITHOUT PROVOCATION AND WE HAVE NO IMPACT ON BRAIN DEVELOPMENT. THEY ARE, YOU KNOW, CLEARLY PATHOLOGICAL, THE MORE INTENSE THEY ARE, THE MORE PATHOLOGY THEY CAUSE.

AND THEY CAN, YOU KNOW, BE TRIGGERED BY A VARIETY OF DIFFERENT CAUSES OF WHICH METALS ARE ONE, BUT JUST BECAUSE THEY HAVE MANY POTENTIAL CAUSES DOESN'T MEAN THAT THEY ARE BENIGN.

SO, FOR EXAMPLE, A FLU-LIKE ILLNESS COULD BE CAUSED BY COVID OR FLU OR ANY NUMBER OF DIFFERENT VIRUSES OR INFECTIOUS AGENTS, IT'S NOT SPECIFIC TO A PARTICULAR INFECTIOUS AGENT, BUT IT'S NOT A BENIGN CONDITION.

MR. ESFANDIARY:

Q AND LASTLY, DOCTOR, AND WE'RE GOING TO END ON THIS: I WANT TO SHOW YOU, IF WE CAN JUST INSERT THIS HERE, DOCTOR, JUST GOING BACK TO THE HALLMAYER STUDY BRIEFLY, CAN YOU -- OOPS -- JUST GOING BACK TO THE HALLMAYER STUDY BRIEFLY.

COUNSEL JUST SHOWED YOU THE PART OF THIS DOCUMENT TALKING ABOUT NONGENETIC RISK FACTORS SUCH AS

PARENTAL AGE, LOW BIRTH WEIGHT AND PREMATURE BIRTHS.

DO YOU REMEMBER TALKING TO HIM ABOUT THAT?

A YES.

Q I JUST WANT TO TAKE A LOOK AT WHAT PAPER THE HALLMAYER STUDY CITES FOR THIS PROPOSITION VERY QUICKLY. AND IF WE GO DOWN TO THEIR CITATIONS, I BELIEVE IT'S CITATION 24 THEY CITE DR. GARDENER, DON'T THEY?

A SEEMS TO BE THE CASE.

SO, YOU KNOW, IF I COULD SAY SOMETHING ABOUT THE HALLMAYER STUDY.

Q SURE.

A AND THE PREVIOUS STUDY THAT WAS REFERENCED.

SO, AGAIN, THIS GETS TO AN ISSUE THAT WE TALKED ABOUT A LITTLE BIT EARLIER, WHICH IS THE DIFFERENCE BETWEEN HERITABILITY AS A POPULATION RISK AND INDIVIDUAL RISKS OF DEVELOPING DISORDER AND SEVERITY OF THAT DISORDER, WHICH ARE ALSO IMPORTANT.

AND I THINK THAT, YOU KNOW, I CERTAINLY WOULD AGREE WITH THE STATEMENT THAT GENETICS PLAYS A VERY STRONG ROLE IN A POPULATION BASIS IN THE PATHOGENESIS OF AUTISM AND THAT THE PURE ENVIRONMENTAL VARIABLES ARE AT PLAY, BUT THE MORE THE INFLUENCE OF GENETICS WILL BE EVIDENT. SO IF YOU KIND OF EQUALIZE THE ENVIRONMENT, THEN GENETICS IS GOING TO ACCOUNT FOR ALMOST ALL OF, YOU KNOW, WHAT'S LEFT IN TERMS OF VARIABILITY.

IF YOU HAVE MORE ENVIRONMENTAL VARIABILITY, THEN, YOU KNOW, THE GENETIC COMPONENT IS GOING TO APPEAR TO BE WEAKER.

AGAIN, AT THE POPULATION LEVEL. AT THE INDIVIDUAL LEVEL I THINK IT'S SORT OF, YOU KNOW, IT'S A DIFFERENT STORY.

SO AT THE INDIVIDUAL LEVEL YOU MAY HAVE GENETIC SUSCEPTIBILITY BASED ON, YOU KNOW, EITHER ONE, YOU KNOW, GENE THAT IS VERY A STRONG GENETIC RISK FACTOR OR A COMBINATION OF GENES THAT TOGETHER CONTRIBUTE TO RISK, BUT THE QUESTION OF WHETHER YOU'RE GOING TO DEVELOP A DISORDER AND HOW SEVERE THAT DISORDER IS IS GOING TO DEPEND ON ENVIRONMENTAL INFLUENCE.

SO I THINK WE NEED TO BE CAREFUL NOT TO CONFLATE THE POPULATION LEVEL DESCRIPTION AND THE INDIVIDUAL DESCRIPTION.

BUT IN THE HALLMAYER AND THESE OTHER STUDIES ARE POPULATION STUDIES, BUT IF YOU JUST LOOK AT THE DATA, THE FACT IS THAT THERE ARE TWIN PAIRS THAT ARE DISCORDANT FOR AUTISM, AND THAT IS NOT EXPLAINED AWAY BY A META ANALYSIS.

MR. ESFANDIARY: THANK YOU, DOCTOR. THAT'S A GREAT PLACE TO END IT. I HAVE NO FURTHER QUESTIONS.

THE COURT: ALL RIGHT.

MR. PETROSINELLI: YEAH, NO QUESTIONS, YOUR HONOR.

THE COURT: THANK YOU. WOULD YOU LIKE TO TAKE A BREAK NOW OR DO YOU WANT TO LAUNCH INTO THE NEXT WITNESS?

MR. ESFANDIARY: WE CAN TAKE A FIVE-MINUTE BREAK, YOUR HONOR.

THE COURT: OKAY. WE'LL COME BACK IN FIVE MINUTES. THANK YOU.

MR. ESFANDIARY: THANK YOU.

MR. PETROSINELLI: THANK YOU, YOUR HONOR.

(RECESS)

THE COURT: OKAY. WE'LL NEED TO SWEAR THE WITNESS IN AGAIN, MR. WISNER. MY CLERK IS COMING AROUND.

HI, DR. RITZ. MY NAME IS AMY HOGUE. IT'S NICE TO MEET YOU.

THE WITNESS: IT'S NICE TO MEET YOU, JUDGE.

THE CLERK: CAN YOU PLEASE RAISE YOUR RIGHT HAND.

THE WITNESS: OKAY. YOU NEED TO SEE ME.

THE CLERK: I SEE YOU.

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: I DO.

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

THE WITNESS: DR. BEATE RITZ. B-E-A-T-E, FIRST NAME. AND LAST NAME R-I-T-Z.

THE CLERK: THANK YOU.

DIRECT EXAMINATION

MR. WISNER:

Q GOOD AFTERNOON, DR. RITZ. THANK YOU SO MUCH FOR BEING HERE.

BEFORE WE GET STARTED, THOUGH, I JUST WANTED TO ASK THE COURT, IS THERE ANYTHING SPECIFICALLY YOUR HONOR WOULD LIKE ME TO ADDRESS BECAUSE I HAVE MY SCRIPT AND I HAVE MY OUTLINE, BUT I WANT TO MAKE SURE I GET ALL THE THINGS YOU CARE ABOUT, YOUR HONOR.

THE COURT: WELL, AS DISCUSSED, I WANT TO HEAR ABOUT IS THE UNDERLYING RESEARCH AND THE STRENGTH OF THE CONNECTION AND SUPPORT THAT IT GETS TO THE OPINIONS OF DR. RITZ.

MR. WISNER: OKAY. WE'RE DEFINITELY GOING TO COVER THAT.

THE COURT: YES.

MR. WISNER: OKAY. GREAT.

Q ALL RIGHT. WELL, DR. RITZ, THANK YOU FOR JOINING US. I UNDERSTAND YOU HAVE A ACCENT.

WHERE ARE YOU FROM?

A I'M FROM GERMANY.

Q HOW LONG HAVE YOU BEEN HERE IN L.A.?

A 30 -- 33 YEARS NOW, I GUESS.

Q OKAY. SO AND IN HOMAGE TO THE FACT THAT YOU'RE GERMAN AND THE FACT WE'RE GOING TO HAVE TO BLITZ THROUGH ALL OF THIS TESTIMONY BECAUSE THERE'S A LOT TO COVER, WE PUT TOGETHER WHAT I'M GOING TO CALL THE RITZ AUTOBAHN AND THIS IS THE ROADMAP THAT WE'RE GOING TO USE FOR YOUR

TESTIMONY TODAY; ALL RIGHT?

A SO NO SPEED LIMITS, RIGHT.

Q EXACTLY. EXACTLY.

SO WE'RE GOING TO START OF WITH YOUR QUALIFICATIONS AND EXPERIENCE AND WE'RE GOING TO TALK ABOUT SOME BASIC EPI PRINCIPLES. WE'LL PROBABLY GO THROUGH THAT QUICKER THAN I ANTICIPATED JUST BECAUSE I THINK THE COURT IS FAMILIAR WITH A LOT OF THAT ALREADY.

THEN WE'RE GOING TO TALK ABOUT YOUR METHODOLOGY THAT YOU USED. WE'RE GOING TO TALK ABOUT THE DATA ABOUT LEAD AND ASD AND THEN WE'RE GOING TO END ON THE DATA REGARDING LEAD AND ADHD; OKAY?

A GOOD.

Q ALL RIGHT. SO LET'S START OFF WITH YOUR QUALIFICATIONS.

WHERE DO YOU CURRENTLY WORK?

A WELL, I WORK AT UCLA IN THE SCHOOL OF PUBLIC HEALTH AND THE SCHOOL OF MEDICINE. I HAVE DOUBLE APPOINTMENTS.

Q WHAT DO YOU DO AT UCLA?

A WELL, I AM WHAT'S CALLED A MEMBER OF THE CENTER FOR OCCUPATIONAL AND ENVIRONMENTAL HEALTH, BUT I AM THE CURRENTLY SOLE EPIDEMIOLOGIST IN THAT CENTER, SO MY FACULTY APPOINTMENT IT IS EPIDEMIOLOGY, THAT'S WHAT I TEACH. BUT MY DESIGNATED JOB FOR THE STATE OF CALIFORNIA, BECAUSE THESE SPECIFIC FACULTY POSITIONS WERE GIVEN TO UCLA BY THE STATE OF CALIFORNIA, AS EXTRA POSITIONS ARE TO DO RESEARCH AND OUTREACH AND

INFORMATION PROVIDING FOR THE COMMUNITY OF CALIFORNIA IN TERMS OF OCCUPATIONAL AND ENVIRONMENTAL HEALTH.

Q WHAT IS OCCUPATIONAL EPIDEMIOLOGY OR ENVIRONMENTAL EPIDEMIOLOGY?

A WELL, RIGHT, SO EPIDEMIOLOGISTS OFTEN DEFINE THEMSELVES ACCORDING TO A SPECIFIC DISEASE THEY ARE STUDYING, SO YOU MIGHT HEAR THAT SOMEBODY SAYS I'M A CANCER EPIDEMIOLOGIST OR, YOU KNOW, I'M AN HIV EPIDEMIOLOGIST.

WELL, FOR OCCUPATIONAL AND ENVIRONMENTAL EPIDEMIOLOGY, IT'S ACTUALLY SPECIFIC TO THE EXPOSURES THAT WE ARE STUDYING, SO I OFTEN, WHEN I TEACH MY STUDENTS, WOULD SAY, WELL, YOU KNOW, THERE IS DEFINITELY FOR SURE ONE TYPE OF DISEASE YOU CAN PREVENT AND THAT IS OCCUPATIONAL AND ENVIRONMENTAL INDUCED DISEASE BECAUSE IF YOU TAKE THOSE TOXINS OR WHATEVER THE EXPOSURES ARE AWAY, YOU WOULD NOT SEE THE DISEASE, AND THEREFORE, IN A WAY OUR JOB IS EASIER, BUT OUR JOB IS ALSO HARDER BECAUSE WE HAVE A VERY BROAD SPECTRUM OF DISEASES WE ARE STUDYING AND OF EXPOSURES.

Q LET ME SHOW YOU EXHIBIT 3. THIS IS A COPY OF YOUR C.V.

DO YOU SEE THAT?

A YES.

Q AND I SEE HERE IN YOUR EDUCATION THAT YOU RECEIVED YOUR PH.D. AND MASTERS IN PUBLIC HEALTH IN EPIDEMIOLOGY FROM UCLA.

DO YOU SEE THAT?

A YES.

Q BUT IT LOOKS LIKE BEFORE THAT YOU HAD AN EARLIER CAREER IN MEDICINE AT THE MEDICAL SCHOOL UNIVERSITY OF HAMBURG.

DO YOU SEE THAT?

A YES.

Q CAN YOU PLEASE DESCRIBE TO THE COURT WHAT THAT BACKGROUND WAS?

A YEAH, ACTUALLY I HAVE A MEDICAL DEGREE, AN M.D. FROM THE UNIVERSITY OF HAMBURG AND A PH.D. ACTUALLY ALSO SO I BASICALLY HAVE TWO PH.D.'S IN MEDICAL SOCIOLOGY.

MY MEDICAL EDUCATION AT THE UNIVERSITY OF HAMBURG WAS VERY BROAD, BUT I DID MY SPECIALTY IN PSYCHIATRY SO I WAS A RESIDENT IN PSYCHIATRY AND I WAS A RESEARCHER AND THEN A ASSISTANT PROFESSOR IN MEDICAL SOCIOLOGY WHICH WAS AT THE TIME THE BRANCH WHERE WE WERE STUDYING WORK-RELATED AND ENVIRONMENTAL EXPOSURES AND THAT WAS PRIOR TO ME COMING TO UCLA TO GET A FORMAL TRAINING IN EPIDEMIOLOGY.

AND BY THE WAY, THAT WAS FUNDED BY THE GERMAN STATE WITH A FELLOWSHIP SPECIFICALLY TO GET PEOPLE EDUCATED IN EPIDEMIOLOGY BECAUSE THAT BRANCH OF SCIENCE AT THE TIME WAS NOT TAUGHT IN GERMANY.

Q LET ME GET THIS STRAIGHT. GERMANY PAID FOR YOUR EPIDEMIOLOGICAL TRAINING AND CALIFORNIA GETS THE BENEFIT; IS THAT RIGHT?

A YES. EXACTLY.

Q OKAY.

DOCTOR, ONE OF THE THINGS I WANT TO ASK YOU AND I THINK THIS IS IMPORTANT FOR ANY EXPERT: WHY DID YOU GET INTO EPIDEMIOLOGY? WHY GO FROM THIS CAREER IN MEDICINE FOCUSING ON PSYCHIATRY AND START LOOKING AT THE CAUSES OF DISEASES?

A YEAH, I WAS VERY FASCINATED BY THE CAUSE OF DISEASE FROM THE VERY BEGINNING OF MY MEDICAL STUDIES; IN FACT, I WOULD ALWAYS, YOU KNOW, I'M ONE OF THESE PEOPLE WHO LIKES DETECTIVE STORIES AND I'D WANT TO KNOW THE "WHO DONE IT" THAN ANYTHING ELSE. SO IN MEDICINE IT REALLY INTERESTED ME WHO DONE IT. AND I REALIZED THAT A LOT OF MEDICINE NEVER REALLY ASKED THAT QUESTION OR ASKED THE QUESTION TOO LATE, MEANING, HAD I KNOWN WHO DONE IT, I COULD HAVE PREVENTED THE OUTCOME.

OF COURSE THAT WOULD MAKE ME WITHOUT A JOB BECAUSE I WOULDN'T TREAT PEOPLE ANYMORE, BUT HONESTLY, I WOULD RATHER LOSE MY JOB BECAUSE OF THAT THAN SEE WHAT I SAW IN A LOT OF FIELDS OF MEDICINE WHERE, YOU KNOW, THE EFFECTS OF A LOT OF THINGS WERE JUST REALLY HORRIBLE, ESPECIALLY NEUROLOGY AND PSYCHIATRY WHERE WE HAVE VERY LITTLE TREATMENT OPPORTUNITIES. YOU BASICALLY ARE WATCHING PEOPLE GET WORSE OR YOU ARE WATCHING PEOPLE BEING TAKEN CARE OF, BUT YOU REALLY CAN'T HELP THEM. IT'S NOT LIKE CANCER WHERE YOU CAN CUT SOMETHING OUT.

Q BECAUSE OF YOUR TRAINING AND BACKGROUND SPECIFICALLY IN MEDICINE AS IT RELATES TO PSYCHIATRY AND NEUROLOGICAL DISEASE, HAS THE STUDY OF THE CAUSE OF THOSE DISEASES PLAYED A PRIMARY ROLE IN YOUR RESEARCH AS

AN EPIDEMIOLOGIST?

A ABSOLUTELY. I VERY EARLY AT UCLA FIGURED OUT THAT ONE OR TWO OF THE MOST IMPORTANT THINGS IN ENVIRONMENTAL EPIDEMIOLOGY AT UCLA FOR ME WAS TO STUDY EXPOSURES THAT ARE VERY WIDESPREAD IN THE STATE OF CALIFORNIA, AND THAT'S AIR POLLUTION AND PESTICIDE EXPOSURES, SO I CONCENTRATED ON THOSE. AND INTERESTINGLY THE PESTICIDE EXPOSURES ARE KNOWN NEUROTOXINS AND ACTUALLY A LOT OF THEM HAVE METALS IN THEM.

AND OF COURSE AIR POLLUTION, WE ARE CURRENTLY DOING A STUDY SPECIFICALLY ON THE METAL COMPONENTS IN AIR POLLUTION BECAUSE WE BELIEVE THAT THEY ARE POSSIBLY THE MOST TOXIC.

AND WHEN YOU LOOK AT MY C.V., I ACTUALLY LED IN 2012 OF THE LARGEST STUDY IN THE U.S. STILL EXISTING, I THINK, ON AUTISM AND AIR POLLUTION.

Q LET'S LOOK AT YOUR C.V.

SO WE HAVE HERE THE AREA RELATED TO RESEARCH, AND LET'S LOOK AT PAGE 6.

SO HERE WE ARE.

IS THAT THE -- TELL ME WHEN YOU SEE THE ONE ON -- IS THIS THE AIR -- THE ONE DOWN HERE?

A YEAH, DOWN THERE IS THE ONE WITH CALIFORNIA DATA.

Q OKAY.

A THE ONE UP TOP IS ACTUALLY EVEN MORE INTERESTING IN A WAY BECAUSE IT'S A LONGER RUNNING STUDY

IN DENMARK WHERE YOU HAVE UNBELIEVABLY GOOD OPPORTUNITIES TO LINK DATA SETS AND THEY ALSO HAVE A NATIONAL BIRTH COHORT AND I'VE DONE A LOT OF STUDIES IN DENMARK BECAUSE THEY HAVE THIS WEALTH OF DATA AND THEY ALSO HAVE A NATIONAL HEALTH SYSTEM SO YOU CAN ACTUALLY GET DIAGNOSIS DONE REALLY WELL AND YOU CAN PICK OUT DISEASES FROM THESE REGISTRIES QUITE WELL.

AND THE NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES FUNDED ME TO DO THIS BIG STUDY IN DENMARK.

Q NOW, DOCTOR, THERE'S BEEN SOME DISCUSSION EARLIER TODAY ABOUT DIFFERENT PROGRAMS AT UCLA. I BELIEVE THERE IS A SPECIFIC PROGRAM THAT LOOKS AT AUTISM CALLED CART.

ARE YOU FAMILIAR WITH THAT PROGRAM?

A YES. ABSOLUTELY.

Q WHAT'S YOUR FAMILIARITY WITH THAT GROUP?

A WELL, IT'S A GROUP THAT SPECIALIZED ON -- IT'S SITUATED WITHIN NEUROLOGY, AND BY THE WAY, I HAVE A CO-APPOINTMENT OF COURSE IN NEUROLOGY AT UCLA, SO I KNOW ALL THOSE COLLEAGUES. BUT IT IS CENTERED SPECIFICALLY FOR THE TREATMENT AND STUDIES OF AUTISM. IT IS MORE HEAVILY TREATMENT-ORIENTED THAN REALLY ETIOLOGIC RESEARCH ORIENTED, BUT IT HAS BOTH COMPONENTS.

Q AND IF WE LOOK BACK AT YOUR C.V. HERE, I SEE THAT -- I MEAN, IT'S A FAIRLY LONG C.V., IT'S 50 PAGES LONG SO I WOULD ACTUALLY HAVE TO SPEND ALL DAY IN IT, BUT I SEE RIGHT HERE THAT THERE WAS AN AUTISM

EPIDEMIOLOGY INVITED SPEAKER AT THE ANNUAL CART MEETING AT UCLA IN 2014.

DO YOU SEE THAT?

A YES.

Q SO CAN YOU PLEASE -- SO WOULD IT BE FAIR TO SAY, THEN, THAT THIS PROGRAM ACTUALLY INVITED YOU TO COME AND PRESENT ON AUTISM AND EPIDEMIOLOGY TO THEIR PROGRAM?

A YES. THEY HAVE A REGULAR SPEAKER SERIES THAT I ALSO ATTEND WHENEVER I CAN, AND IN 2014 THEY RECOGNIZED ME AS ONE OF THE EPIDEMIOLOGISTS IN AUTISM AND ENVIRONMENT AND I GAVE THAT INVITED SPEECH.

Q WERE YOU INVITED BY DR. GESCHWIND?

A YES.

Q OKAY. ALL RIGHT.

ON PAGE 49 OF YOUR C.V. THERE IS -- LET ME GO TO IT -- THERE IS A BUNCH OF LETTERS AND OTHER PUBLICATIONS.

DO YOU SEE THAT?

A YES.

Q AND DOWN HERE AT THE BOTTOM, THERE'S A PUBLICATION NUMBER 10 AND IT APPEARS TO BE PROJECT TENDR, "TARGETING ENVIRONMENTAL NEURODEVELOPMENTAL RISKS AND THE TENDR CONSENSUS STATEMENT."

DO YOU SEE THAT?

A YES, I SEE THAT.

Q WHAT IS TENDR, DOCTOR?

A WELL, IT'S A GROUP OF SCIENTISTS, I BELIEVE WE

ARE BETWEEN 60 AND A HUNDRED DEPENDING ON WHEN YOU COUNT, WHO HAVE COME TOGETHER, WE'RE ALL FUNDED BY THE NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, ACTUALLY THE FORMER DIRECTOR DR. BONBAUM IS ONE OF THE CO-AUTHORS OF THIS STATEMENT. WE COME TOGETHER ON A REGULAR BASIS WITH SOME FUNDING FROM FOUNDATIONS IN ORDER TO DISCUSS WHAT WE KNOW ABOUT THE SCIENCE IN NEURODEVELOPMENT, ESPECIALLY THE SCIENCE WHERE WE HAVE -- WHERE WE CAN ENCOURAGE PREVENTATIVE ACTION WHICH ARE ENVIRONMENTAL FACTORS AND, YOU KNOW, OCCUPATIONAL RISK FACTORS, BEHAVIORAL RISK FACTORS, AND WE EVALUATE THE SCIENCE AND THEN COME UP WITH A CONSENSUS STATEMENT THAT WE PUBLISH IN A PEER-REVIEWED JOURNAL, IN THIS CASE THIS ONE WAS PUBLISHED IN ENVIRONMENTAL HEALTH PERSPECTIVES, WHICH IS THE OFFICIAL JOURNAL PUBLISHED BY THE NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES.

Q NOW, JUST FOR THOSE OF US WHO AREN'T FAMILIAR WITH THE VARIOUS ALPHABET SOUP OF AGENCIES, WHAT IS THE NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH, NIEH?

A NIEHS IS THE NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES AND IT IS SPECIFICALLY TASKS JUST LIKE I AM IN THE COEH AT UCLA IN THAT CENTER TO INVESTIGATE ENVIRONMENTAL CAUSES OF DISEASE, AND ENVIRONMENT IN THIS CASE REALLY EXCLUDES BEHAVIORS LIKE SMOKING BUT INCLUDES EVERYTHING ELSE THAT WE CAN CALL ENVIRONMENTAL.

Q NOW, I WANT TO TAKE A LOOK AT THAT VERY DOCUMENT THAT'S LISTED RIGHT HERE.

YOU SEE THAT WAS PUBLISHED IN 2016?

A YES.

Q WOULD YOU RECOGNIZE A COPY OF THAT DOCUMENT IF YOU SAW IT TODAY?

A YES.

Q ALL RIGHT. I'M SHOWING YOU WHAT HAS BEEN MARKED AS EXHIBIT 32 IN THE RECORD.

DOCTOR, DO YOU RECOGNIZE THIS DOCUMENT?

A YES.

Q IS THIS THAT CONSENSUS STATEMENT THAT WE WERE JUST DISCUSSING?

A YES, IT IS.

Q ALL RIGHT. NOW, IF WE GO DOWN TO THE BOTTOM THE BACK OF IT THERE IS A LIST OF VARIOUS AUTHORS.

DO YOU SEE THAT?

A YES.

Q YOU HAVE A GROUP OF SCIENTISTS; RIGHT?

A YES.

Q AND YOU HAVE SCIENTISTS FROM ALL OVER. YOU HAVE UC DAVIS, HARVARD, NIEHS, BERKELEY, CINCINNATI COLLEGE OF MEDICINE, UNIVERSITY OF ROCHESTER MEDICAL SCHOOL.

DO YOU SEE ALL THAT?

A YES.

Q AND THEN THIS SORT OF BROAD GROUP OF SCIENTISTS ALL COMING TOGETHER AS PART OF THIS TENDR GROUP, IS THAT SOMETHING THAT YOU FREQUENTLY SEE IN THE AREA OF ENVIRONMENTAL EPIDEMIOLOGY?

A IT'S ACTUALLY RATHER UNUSUAL. AND WHAT IS EVEN MORE UNUSUAL IS THAT IT'S DIFFERENT DISCIPLINES ACTUALLY TALKING TO EACH OTHER, SO EPIDEMIOLOGISTS AND YOU SEE A FEW PEOPLE HERE WHO HAVE THE TITLE TOXICOLOGY AND NEUROSCIENCE, AND THAT IS REALLY THE UNUSUAL PART, BUT SOMETHING THAT THE NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES HAS BEEN FOSTERING OVER THE LAST DECADE THAT WE ACTUALLY TALK TO BASIC SCIENTISTS WHO DO ANIMAL STUDIES, TOXICOLOGY STUDIES, AND WE GO ALL THE WAY FROM HUMAN RESEARCH TO CELL MODELS.

AND EVEN MORE IMPORTANT WE ALSO HAVE HEALTH PROFESSIONALS AND PROVIDERS, AND YOU'RE POINTING THAT OUT RIGHT HERE, SO WE HAVE ACTUALLY REPRESENTATIVES OF THE CLINICAL SCIENCES WHO CARE ABOUT CHILDREN'S HEALTH IN THIS CASE, ESPECIALLY CHILDREN'S NEURODEVELOPMENTAL HEALTH.

Q NOW, OBVIOUSLY YOU ARE ONE THE SIGNATORIES ON THIS.

DO YOU SEE THAT?

A YES.

Q OKAY. AND IF WE GO DOWN TO THE NEXT PAGE, MORE SCIENTISTS, AND THEN THERE'S A GROUP OF CHILDREN'S HEALTH AND DISABILITY ADVOCATES.

DO YOU SEE THAT?

A YES.

Q AND THAT'S THE THIRD GROUP OF INTERESTING INDIVIDUALS WHO PARTICIPATE IN THIS WHO KEEP US HONEST AND ON TARGET IN TERMS OF REALLY CARING ABOUT WHAT'S

HAPPENING TO THE AFFECTED POPULATION AND THEY ARE REALLY ADVOCATES FOR THE FAMILIES AND FOR, YEAH, THE COMMUNITIES.

Q THAT'S WHAT I WAS GOING TO GET AT.

THESE ARE GROUPS THAT REPRESENT THE AUTISM COMMUNITY.

IS THAT FAIR?

A THAT'S CORRECT. NOT JUST AUTISM, BUT, YOU KNOW, GENERAL NEURODEVELOPMENT AND HEALTH OF CHILDREN, HEALTHY DEVELOPMENT OF THE BRAIN, BASICALLY.

Q AND THEN DOWN HERE THERE'S A SECTION THAT SAYS, "ORGANIZATIONS THAT ENDORSE OR SUPPORT THE TENDR CONSENSUS STATEMENT."

DO YOU SEE THAT?

A YES.

Q AND THERE'S BEEN SOME DISCUSSION ABOUT THIS INSTITUTION. THERE'S THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS.

DO YOU SEE THAT?

A YES. ACOG.

Q YEAH.

AND DID YOU SEE THAT THEY SPECIFICALLY HAVE SUPPORT THE USE OF THIS DOCUMENT AS AN EDUCATIONAL TOOL? DO YOU SEE THAT?

A YES. AND THAT'S ACTUALLY HOW SOME OF THESE DOCUMENTS ARE SPECIFICALLY MEANT TO BE USED.

Q CAN YOU EXPLAIN?

A SO WHAT WE ARE DOING AS SCIENTISTS IS OFTEN WE

SIT IN OUR SO-CALLED IVORY TOWER, WE DO OUR RESEARCH, WE COMMUNICATE THAT TO OUR COLLEAGUES, BUT WE ARE NOT COMMUNICATING IT MORE BROADLY TO THE PUBLIC OR TO STAKEHOLDERS. AND IN THIS CASE STAKEHOLDERS COULD BE, FOR EXAMPLE, COLLEAGUES WHO WORK WITH FAMILIES AND WORK WITH WOMEN AND CHILDREN AND WHO NEED TO FIND OUT MORE ABOUT THE CAUSES OF CERTAIN DISEASES AND THE WAY HOW WE CAN PREVENT THEM AND WHO ALSO CAN THEN EDUCATE THOSE AFFECTED ABOUT, YOU KNOW, POSSIBLE PREVENTIVE MEASURES OR POSSIBLE ACTIONS THEY COULD BE TAKING.

Q SO IF WE GO UP TO THE TOP OF THE PAPER, THIS IS ON THE FIRST PAGE, AND WE LOOK AT THE PARAGRAPH DOWN HERE AT THE BOTTOM.

A YES.

Q THERE'S A SECTION THAT READS, "PRIME EXAMPLES OF NEURODEVELOPMENTALLY TOXIC CHEMICALS."

A RIGHT.

Q AND IT GOES ON TO SAY, "THE FOLLOWING LIST PROVIDES PRIME EXAMPLES OF TOXIC CHEMICALS THAT CAN CONTRIBUTE TO LEARNING BEHAVIORAL OR INTELLECTUAL IMPAIRMENT AS WELL AS THE SPECIFIC NEURODEVELOPMENTAL DISORDERS SUCH AS ADHD OR AUTISM SPECTRUM DISORDER."

DO YOU SEE THAT?

A YES.

Q NOW, WE SEE DOWN HERE SOME STUFF THAT YOU KIND OF MENTIONED ALREADY. WE'VE GOT PESTICIDES. WE HAVE AIR POLLUTION. FLAME RETARDANTS.

DO YOU SEE THAT?

A YES.

Q AND THEN --

A ACTUALLY MY STUDY IS ONE OF THOSE.

Q THAT'S RIGHT. THAT'S RIGHT.

AND THEN IF WE LOOK ON THE NEXT PAGE, THEY SPECIFICALLY MENTION LEAD AND MERCURY.

DO YOU SEE THAT?

A YES.

Q AND SOME OF THESE PEOPLE THAT ARE HIGHLIGHTED HERE LIKE, FOR EXAMPLE, DR. LAMPIER, THESE ARE PEOPLE WHO ARE ACTUALLY PART OF TENDR; CORRECT?

A THAT'S CORRECT. AS WELL AS DR. KARGAR WHO IS UNDER MERCURY.

Q OH, YES. THANK YOU.

AND SO I MEAN, TO BE CLEAR, DOCTOR, THIS DOCUMENT THAT YOU SIGNED AND APPARENTLY OTHER PEOPLE DID AS WELL, THIS WAS ISSUED BEFORE YOU WERE INVOLVED IN THIS LITIGATION; IS THAT RIGHT?

A YES, IN 2016.

Q OKAY.

SO, I MEAN, I GUESS ONE OF THE THINGS THAT I'M TRYING TO GET AT IS THERE'S BEEN SOME DISCUSSION, SOME FIGHTING REALLY, ABOUT WHETHER OR NOT THERE IS AN AUTISM COMMUNITY AND WHETHER OR NOT HEAVY METALS HAS A POTENTIAL ETIOLOGICAL FACTOR AND WHETHER THAT IS ACCEPTED OR NOT.

FROM YOUR PERSPECTIVE WHO WORKS SPECIFICALLY IN

ENVIRONMENTAL EPIDEMIOLOGY, SPECIFICALLY IN NEURODEVELOPMENTAL DISABILITY ISSUES AND SPECIFICALLY IN EPIDEMIOLOGY, WHAT IS YOUR VIEW ABOUT WHETHER OR NOT THE RELATIONSHIP BETWEEN HEAVY METALS AND ASD AND ADHD IS SOMETHING THAT IS GENERALLY ACCEPTED?

A IT'S ABSOLUTELY ACCEPTED AND THAT'S WHAT THIS TENDR STATEMENT IS ALL ABOUT.

IN FACT, WHEN WE CAME TOGETHER TO WRITE THIS STATEMENT, WE ALL THOUGHT, OH, WE HAVE TO GO AFTER THE NEXT REALLY IMPORTANT EXCITING NEUROTOXIN, AND REALLY THE METALS ARE AN OLD HAT, WE KNOW SO MUCH ABOUT THEM, RIGHT, IT WAS ALMOST LIKE UNDER, OKAY, YES, OF COURSE METALS, BUT WE ALREADY KNOW THIS, NOW LET'S MOVE ON TO THIS EXCITING NEW PESTICIDE.

Q ALL RIGHT. WELL, LET'S GO BACK TO YOUR AUTOBAHN.

WE'VE COVERED YOUR QUALIFICATIONS AND EXPERIENCE I THINK PRETTY WELL.

LET'S GET INTO SOME EPI 101 ISSUES.

I UNDERSTAND WE'VE PREPARED A DEMONSTRATIVE TO SORT OF HELP WALK THROUGH SOME OF THESE CONCEPTS.

THIS IS EXHIBIT 140.

DO YOU SEE THE SCREEN IN FRONT OF YOU, DOCTOR?

A YES.

Q ALL RIGHT. NOW, WE DON'T NEED TO SPEND TOO MUCH TIME ON THIS. I'M SURE THE COURT IS FAMILIAR GENERALLY WITH SOME OF THESE STUDIES.

BUT THERE WERE SOME THINGS SAID ABOUT THE

HIERARCHY OF STUDIES DURING THE OPENING STATEMENTS, AND I KIND OF WANT TO EXPLORE THAT WITH YOU SINCE THIS IS LITERALLY WHAT YOU TEACH.

SO, FIRST OF ALL, WITH IS A COHORT STUDY?

A WELL, A COHORT STUDY IS A STUDY OF HUMANS IN WHOM I ASSESS EXPOSURE RIGHT AT THE ONSET AT BASELINE, AND THEN I FOLLOW PEOPLE, I CATEGORIZE THEM ACCORDING TO EXPOSED/UNEXPOSED OR I HAVE A MEASURE OF THE LEVEL OF EXPOSURE, AND THEN I FOLLOW THEM FOR THE OUTCOME OF INTEREST.

SO IF IT'S CANCER, I ASSESS THEM FOR CANCER. IF IT'S AUTISM, IT MIGHT BE A FIRST COHORT AND I FOLLOW THAT UP FOR AUTISTIC -- THE AUTISM DIAGNOSIS LATER ON.

Q DOCTOR -- OH.

A BUT WHAT IS -- YEAH, WHAT IS IMPORTANT IS THAT I ASSESS MY EXPOSURES RIGHT AT THE OUTSET.

Q WHY? WHY IS THAT IMPORTANT?

A BECAUSE THAT ESTABLISHES TEMPORALITY VERY CLEARLY AND SO WE HAVE -- WE DON'T HAVE TO USE ANY -- ANY OTHER TYPES OF MEASURES REALLY BECAUSE, YOU KNOW, EVERYTHING WE MEASURE IN TERMS OF EXPOSURE THEN AT THE BEGINNING IS DEFINITELY PRIOR TO THE ONSET OF THE DISEASE BECAUSE I'M MEASURING IT BEFORE THE DISEASE EVEN OCCURRED.

HOWEVER, THERE ARE PROBLEMS WITH THIS IF THE EXPOSURE IS ACTUALLY A CUMULATIVE EXPOSURE, THEN I HAVE TO KEEP MEASURING.

SO ONE SINGLE MEASURE AT BASELINE IN A COHORT

MAY OR MAY NOT BE SUFFICIENT AND MAY NOT TELL ME THE WHOLE STORY.

Q NOW, LET'S SAY, FOR EXAMPLE, YOU TAKE A MEASUREMENT HERE AT THE ONSET OF THE STUDY. I'LL MARK THIS WITH SOME RED LINES.

DO YOU SEE THAT?

A YES.

Q OKAY.

AND THERE YOU HAVE A MEASURE OF WHO WAS EXPOSED TO, LET'S SAY, LEAD AND WHO ISN'T, OKAY.

A (INDICATING).

Q AND THEN, LET'S SAY, AS YOU MOVE ALONG, THERE IS EXPOSURES, YOU KNOW, LATER ON AT DIFFERENT POINTS, MAYBE THROUGH FOOD OR THE ENVIRONMENT OR WHATEVER; OKAY?

A YES.

Q IF YOU DON'T CAPTURE THOSE EXPOSURES, WHAT HAPPENS TO YOUR DATA ON THE END?

A SO THIS IS A QUESTION OF ADEQUATE EXPOSURE ASSESSMENT, AND IF I DON'T BELIEVE THAT THE ONLY EXPOSURE OF INTEREST FOR THE OUTCOME IS THE ONE THAT I MEASURE AT BASELINE, IF, IN FACT, THERE ARE DIFFERENT SENSITIVE PERIODS DURING WHICH THE EXPOSURE IS PARTICULARLY IMPORTANT, I MAY ACTUALLY, IF I DON'T CONTINUE TO MEASURE THE EXPOSURES THROUGHOUT THE FOLLOW UP UNTIL THE DIAGNOSIS HAPPENED, THEN I MAY ACTUALLY HAVE MISSED THE MOST IMPORTANT EXPOSURES.

Q OKAY. WELL, COHORT STUDY. SO IF YOU'RE GOING TO LOOK AT PEOPLE AND FOLLOW THEM FOR A LONG TIME, YOU

HAVE TO HAVE A REALLY BIG GROUP OF PEOPLE TO STUDY A RARE DISEASE.

A ABSOLUTELY. THAT'S WHY IT'S ACTUALLY QUITE RARE TO SEE THESE KIND OF STUDY FOR RARE DISEASES, AND AUTISM IS CERTAINLY A RARE DISEASE, LUCKILY.

Q ALL RIGHT. WELL, LET'S LOOK AT CASE CONTROL STUDIES.

WHAT ARE THOSE?

A WELL, IN THIS CASE WE'RE ACTUALLY STARTING WITH CASES. SO THIS IS MORE OR LESS THE MORE EFFICIENT WAY OF DOING THE SAME KIND OF RESEARCH THAT WE'RE DOING WHEN WE DO A COHORT STUDY, BUT YOU'RE STARTING WITH PEOPLE WHO ARE ALREADY DIAGNOSED. AND WHY IS THAT MORE EFFICIENT? BECAUSE YOU CAN GO TO A CLINIC OR YOU CAN GO TO SOME REGISTRY OR SOME WAY OF FINDING CASES AND THEY HAVE ALREADY DIAGNOSED THE CASES FOR YOU, THEY HAVE FOUND THE CASES FOR YOU, AND NOW YOU HAVE TO KIND OF GO BACK IN TIME, YOU WALK YOUR WAY BACKWARDS AND YOU SAY AT WHAT POINT IN THE LIFE SPAN OF THESE INDIVIDUALS DID EXPOSURES OCCUR?

AND YOU MAY HAVE RECORDS THAT TELL YOU ABOUT THIS AND THAT'S VERY GOOD. OR YOU MAY HAVE BLOOD SAMPLES THAT ARE STORED SOMEWHERE THAT SOMEBODY USED.

AND YOU DO THE SAME THING FOR WHAT WE CALL THE CONTROL SUBJECTS, WHO ARE BASICALLY A SAMPLE OF PEOPLE WHO DON'T HAVE THE DIAGNOSIS, BUT OTHERWISE, IF THEY HAD GOTTEN THE DIAGNOSIS, WOULD HAVE ALSO BEEN PICKED UP IN THE SAME SYSTEM THAT GAVE YOU THE CASES.

AND THEN YOU WALK BACK IN TIME WITH THE CONTROLS IN THE SAME WAY. YOU FIND THE SAME RECORDS FOR THEM, AND YOU BASICALLY DETERMINE THE EXPOSURE DISTRIBUTION IN THE CONTROLS AS KIND OF THE REFERENCE SET BECAUSE THE CONTROLS NEVER GOT DIAGNOSED, MEANING, WHATEVER THEIR EXPOSURES WERE DID NOT HARM THEM, AND NOW YOU'RE COMPARING THIS REFERENCE EXPOSURE TO THE EXPOSURE IN THE CASES, AND YOU THEN DETERMINE WHETHER THE EXPOSURE IN THE CASES WAS HIGHER OR LOWER.

Q NOW, DOCTOR, IS IT ALWAYS THE CASE THAT A COHORT STUDY IS BETTER THAN A CASE CONTROL STUDY?

A ABSOLUTELY NOT.

I KNOW THAT PEOPLE WHO ARE NOT EDUCATED AS EPIDEMIOLOGISTS EVEN ENVIRONMENTAL HEALTH SCIENTISTS AND PHYSICIANS WHO ARE VERY SMART PEOPLE OFTEN HAVE SAID THIS STORY THAT, YOU KNOW, COHORT STUDIES ARE THE BEST OBSERVATIONAL, COHORT STUDIES ARE THE BEST STUDIES DESIGNED IN EPI AND THEN, YOU KNOW, DOWNGRADING YOU'RE GOING TO CASE CONTROL STUDIES, CROSS SECTIONAL STUDIES, TIME SERIES, ET CETERA; ACTUALLY I USE A SLIDE IN MY TEACHING WHERE I SHOW A PICTURE LIKE THAT OF THIS, YOU KNOW, FUNNEL KIND OF AND --

Q A PYRAMID.

A YEAH. AND THEN I EXPLAIN TO MY STUDENTS WHY THAT IS THE WRONG WAY OF THINKING ABOUT STUDY DESIGN BECAUSE STUDY DESIGNS HAVE ADVANTAGES AND DISADVANTAGES.

AND, FOR EXAMPLE, IN A CASE CONTROL STUDY, I CAN GET BETTER DATA THAN IN A COHORT STUDY BECAUSE I CAN

SPEND MORE EFFORT AND MORE MONEY ON MUCH SMALLER GROUPS OF PEOPLE. IT'S A MUCH MORE EFFICIENT STUDY DESIGN THAN A COHORT STUDY.

IF YOU IMAGINE THAT I HAVE TO COLLECT DATA FROM A HUNDRED THOUSAND PEOPLE AND NOT ONLY COLLECT DATA AT BASELINE, BUT I THEN HAVE TO FOLLOW THEM OVER MANY, MANY, MANY YEARS, THAT'S REALLY EXPENSIVE, SO ALL I MIGHT BE ABLE TO AFFORD IS A QUESTIONNAIRE THAT PEOPLE FILL OUT BY THEMSELVES.

IN A CASE CONTROL STUDY, I CAN SIT DOWN WITH THESE PEOPLE, I CAN TAKE BLOOD SAMPLES, I CAN TAKE A LOT OF TIME RECONSTRUCTING EXPOSURE HISTORIES. I CAN ASK THEM ABOUT RECORDS THAT EXIST. I CAN GO BACK TO RECORD SYSTEMS. I CAN MAKE A LOT MORE EFFORT TO ACTUALLY CHARACTERIZE EXPOSURES IN A MUCH BETTER WAY.

SIMILARLY, THESE CASES WERE ALREADY DIAGNOSED. THEY USUALLY COME FROM VERY CREDIBLE SOURCES. THEY COME FROM MEDICAL CENTERS. THEY COME FROM REGISTRIES THAT ARE CERTIFIED. SO THERE'S A LOT OF EFFORT THAT WENT INTO CASE ASCERTAINMENT AND CASE DIAGNOSING AND GETTING IT RIGHT.

AND IN A COHORT STUDY WHERE YOU HAVE TO LIKE FOLLOW UP OVER AND OVER AGAIN, YOU REALLY NEED TO SET UP THIS KIND OF DIAGNOSTIC SYSTEM ON YOUR OWN AND MAKE SURE THAT EVERY COHORT MEMBER IS SUBJECTED TO IT, AND THAT MAY NOT BE POSSIBLE SO YOU NEED TO USE LESS VALID OR LESS SENSITIVE MEASURES THAN WHAT YOU GET IN A CASE CONTROL STUDY.

Q WOULD IT BE FAIR TO SAY THAT SOMETIMES CASE CONTROL STUDIES ARE BETTER AND SOMETIMES COHORT STUDIES ARE BETTER, IT JUST DEPENDS?

A ABSOLUTELY. AND WHAT I USUALLY TEACH MY STUDENTS IS THAT WE WANT -- IDEALLY, WE WANT BOTH TYPES OF STUDY AND WE WANT TO SEE WHETHER THEY AGREE AND HOW THEY AGREE AND, YOU KNOW, EVALUATE FOR WHAT THEY ARE.

Q NOW, DOCTOR, HOW LONG HAVE YOU BEEN TEACHING YOUR EPIDEMIOLOGY PH.D. STUDENTS AT UCLA THE FALLACY OF THIS HIERARCHY? HOW LONG HAVE YOU BEEN DOING THAT FOR?

A WELL, I'VE BEEN TEACHING SINCE 1995, AND I THINK THIS HIERARCHY I'VE BEEN TEACHING FOR THE LAST 20 YEARS BECAUSE THERE WAS ONE PAPER THAT REALLY EXPLAINED THIS VERY NICELY AND I THOUGHT IT WAS A GREAT EXAMPLE.

Q NOW, REGARDING THE APPROACH YOU TOOK IN THIS CASE, DID YOU APPLY THAT SAME INTELLECTUAL RIGOR, LOOKING AT EACH STUDY ON ITS OWN MERITS AND NOT JUST CATEGORIZING THEM ON A HIERARCHY?

A ABSOLUTELY. I MEAN, THAT'S WHAT WE EPIDEMIOLOGISTS ARE REALLY TAUGHT. WE ARE TAUGHT TO BE EXTREMELY CRITICAL. WE ARE TAUGHT TO FIND THE FAULT IN EVERYTHING AND WE ARE BARELY EVER TAUGHT TO SEE THE POSITIVE BECAUSE WE ARE ALWAYS DOUBTING FIRST AND IT NEEDS A LOT OF DATA TO OVERCOME THAT.

Q NOW, SINCE WE'RE SITTING HERE ON A CASE CONTROL, I JUST WANT TO ASK ABOUT THE NATURE OF THESE STUDIES.

LET'S SAY, FOR EXAMPLE, THERE IS WE'LL SAY,

WE'LL CALL THEM GENES; OKAY?

A OKAY.

Q AND LET'S SAY GENES CAN CAUSE WHETHER OR NOT SOMEONE DEVELOPS A DISEASE OR DOES NOT DEVELOP A DISEASE.

DOES THAT CONSIDERATION BOTHER YOU IN THE CONTEXT OF THIS STUDY?

A ABSOLUTELY NOT.

Q WHY?

A WELL, BECAUSE IN THE END GENES ARE ALL BLUEPRINTS AND GENES ARE THERE TO, YOU KNOW, GENERATE THE ORGANISMS WE ARE AND PROGRAMMING US FOR THE ENVIRONMENT THAT WE ARE ENCOUNTERING, SO OUR GENETICS IS BASICALLY WHAT SETS US UP TO ENCOUNTER WHAT WE LIVE THROUGH IN EVERY SENSE.

SO WE COULD BE GENETICALLY SUSCEPTIBLE TO CERTAIN TYPES OF EXPOSURES OR WE MAY HAVE A LOT OF GENETIC RESILIENCE TO OTHER TYPES OF EXPOSURES, AND IN FACT, THAT'S CALLED THE STUDY OF GENE ENVIRONMENT INTERACTION THAT I'VE BEEN ENGAGING IN FOR THE LAST 20 YEARS TRYING TO EXACTLY LOOK AT, YOU KNOW, HOW DO THESE TWO COMPONENTS COME TOGETHER BECAUSE WE ALL KNOW NOT EVERYBODY WHO SMOKES GETS LUNG CANCER, RIGHT.

Q RIGHT.

A THERE'S A LARGE SUB GROUP OF HEAVY SMOKERS WHO DO, BUT IT'S 10 PERCENT OF ALL HEAVY SMOKERS.

Q YEAH, THOSE ARE ALWAYS THE PEOPLE THAT, YOU KNOW, SMOKERS TELL YOU, WELL, MY GRANDFATHER SMOKED FOR

40 YEARS AND WAS PERFECTLY HEALTHY, RIGHT?

A EXACTLY.

Q ALL RIGHT. SO I DON'T WANT TO GO THROUGH ALL THESE OTHER STUDY DESIGNS. WE DON'T REALLY HAVE TIME FOR THAT. AND IF WE NEED TO GET INTO IT, WE WILL. BUT I DO WANT TO TALK BRIEFLY ABOUT HOW TO INTERPRET STATISTICAL SIGNIFICANCE AND WHAT DO YOU EVERY AS AN EPIDEMIOLOGIST.

SO WHAT ARE WE LOOKING AT HERE?

A WELL, WE'RE LOOKING AT A GRAPH WITH A STUDY RESULT THAT WE CALL A SUMMARY ESTIMATE. WE WOULD CALL -- SO THAT SUMMARY ESTIMATE IS THE DOT IN THE MIDDLE.

AND BASICALLY THAT ESTIMATE TELLS YOU SOMETHING ABOUT WHAT THE DISEASE RISK IN THE EXPOSED IS COMPARED TO THE UNEXPOSED AND THAT WOULD BE A RISK RATIO. THE RISK IN THE EXPOSED OVER THE RISK IN THE UNEXPOSED. OR THE DISEASE RATE IN THE EXPOSED OVER THE DISEASE RATE IN THE UNEXPOSED.

AND SINCE THAT'S A RATIO MEASURE, IF IT'S ABOVE ONE, IT MEANS THAT THE RISK OF DISEASE IS HIGHER IN THOSE EXPOSED THAN UNEXPOSED, AND IF IT'S BELOW ONE, IT WOULD BE LOWER.

SO THAT'S ALL OUR CENTRAL ESTIMATE HERE, OUR SUMMARY ESTIMATE IN THE MIDDLE OF THE DOT.

AND THEN WE HAVE THESE LINES, THESE WHISKERS GOING OUT THERE, AND THAT'S WHAT WE USUALLY -- I DON'T KNOW WHAT YOU USED HERE, BUT THE CONVENTION IS THAT IT'S A 95 PERCENT CONFIDENCE INTERVAL, AND AT THE END OF IT

YOU FIND THE CONFIDENCE LIMITS. IN THIS CASE IT WOULD BE SOMETHING LIKE 1.423 AND YOUR CENTRAL ESTIMATE WOULD BE 2.

SO THIS STUDY WOULD TELL ME THAT WHATEVER THE EXPOSURE WAS THERE'S PROBABLY A TWO-FOLD INCREASED RISK IN THE EXPOSED OVER THE UNEXPOSED WITH A 95 PERCENT CONFIDENCE INTERVAL OF 1.423 EXCLUDING THE 1 WHICH IS THE NULL VALUE BECAUSE IF THIS RATIO, THE NUMBER ON TOP AND THE BOTTOM IS THE SAME, THEN THE RATIO MEASURE IS 1.

Q NOW, DOCTOR, WHEN YOU SAY THE STATISTICAL SIGNIFICANCE, WHAT DOES THAT ACTUALLY MEAN?

A THAT MEANS THAT THE 95 PERCENT CONFIDENCE INTERVAL ACTUALLY EXCLUDES THAT NULL VALUE THAT I SET WHICH IS THE 1, AND THAT IF I WERE TO DO THIS KIND OF STUDY AGAIN, THIS EXPERIMENT AGAIN, THAT A HUNDRED MORE OR 99 MORE TIMES, THEN IN 95 PERCENT OF THE -- 95 PERCENT OF THE RESULTS WOULD BE WITHIN THAT FRAMEWORK OF 1.423, WOULD LEND MY ESTIMATE IN THAT RANGE.

Q NOW, WHAT IF YOU HAVE ANOTHER RESULT THAT LIKE WE HAVE HERE, SAME POINT ESTIMATE, BUT THE CONFIDENCE INTERVAL JUST PASSES NULL? IS THAT CONSIDERED A STATISTICALLY SIGNIFICANT RESULT?

A NO, THIS -- ACCORDING TO THE P VALUE OF LESS THAN .05 OR THE 95 PERCENT CONFIDENCE INTERVAL, IN THIS CASE STATISTICIANS AND EPIDEMIOLOGISTS WOULD AGREE THAT YOU CALL THIS STUDY NOT STATISTICALLY SIGNIFICANT.

YOU CAN SEE THAT THE POINT ESTIMATES ARE EXACTLY THE SAME. THEY TELL YOU EXACTLY THE SAME STORY

THAT, YOU KNOW, THE EXPOSURE INCREASED THE RISK OF TWO-FOLD BECAUSE THAT'S THE DISEASE RISK IN THE EXPOSED OVER THE UNEXPOSED, BUT THESE WHISKERS ARE WIDER. WHY ARE THEY WIDER? VERY SIMPLY THE STUDY MAY HAVE BEEN SLIGHTLY SMALLER.

SO THE STUDY OF NUMBER 1 MAY HAVE ENROLLED 200 CASES IN CONTROLS AND THE STUDY NUMBER 2 100 CASES AND CONTROLS AND I'M GETTING THESE WIDER CONFIDENCE INTERVAL LIMITS BECAUSE I DON'T HAVE ENOUGH INFORMATION TO EXCLUDE THE SMALL CHANCE THAT 2 ISN'T 2, THAT IT'S TRULY SOMEWHERE CLOSER TO 1.

Q AND THE FACT THAT THIS CROSS THAT BLUE LINE RIGHT THERE, DOES THAT MEAN YOU IGNORE IT?

A ABSOLUTELY NOT. AND THAT'S ACTUALLY SOMETHING I ALSO TEACH MY STUDENTS, JUST TAUGHT IT TWO WEEKS AGO, THAT YES, IF YOU SEE NUMBER -- STUDY NUMBER 2 AND THE ONLY STUDY IN THE WORLD, YOU SCRATCH YOUR HEAD AND SAY INTERESTING, SUGGESTIVE, I'D BETTER GO AND DO ANOTHER BIGGER STUDY.

IF YOU, HOWEVER, SEE STUDY NUMBER 2 AFTER YOU SEE STUDY RESULTS NUMBER 1, THEN YOU SAY, AHH, GREAT, IT'S CONSISTENT AND NOW I CAN ADD THE TWO STUDIES TOGETHER AND CONCLUDE THAT GIVEN THAT THEY ARE CONSISTENT AND GIVEN THAT THEY ARE BOTH TELLING ME THE SAME STORY, MY STUDY NUMBER 2 IS KIND OF CONFIRMATIVE OF STUDY NUMBER 1.

Q WHAT IF WE ADDED A THIRD STUDY HERE? NOW THIS ONE'S MUCH SMALLER POINT ESTIMATE, MUCH SMALLER

CONFIDENCE INTERVAL, BUT TO THE RIGHT OF 1, WHAT DOES THAT TELL YOU AS AN EPIDEMIOLOGIST?

A WELL, FIRST OF ALL, IT'S CONSISTENT WITH AN EFFECT, HOWEVER, THE EFFECT SIZE IS MUCH SMALLER. THIS MUST BE A MUCH LARGER STUDY BECAUSE OTHERWISE WE WOULDN'T HAVE THIS VERY TIGHT CONFIDENCE INTERVAL. AND IT TELLS ME THAT MY TWO-FOLD RISK ESTIMATE WAS POSSIBLY AN OVERESTIMATION AND THAT THE TRUE RISK IS MAYBE SOMEWHERE BETWEEN 1.4 AND 1.5 AS MY CONFIDENCE INTERVAL OF STUDY 3 SUGGESTS, BUT THAT OVERALL THERE IS AN INCREASE THIS RISK AND OVERALL ALL THREE STUDIES ARE INCREDIBLY CONSISTENT WITH AN ADVERSE EFFECT OF THIS EXPOSURE.

Q DOCTOR, BEFORE YOU COULD SAY THIS IS CONSISTENT OR CONFIRMATORY OR EVEN MAKE A CONCLUSION ABOUT CAUSATION, WOULD YOU NEED TO INDIVIDUALLY LOOK AT THE STRENGTHS AND WEAKNESSES OF EACH OF THESE STUDIES TO SEE IF THEY WERE BEING CAUSED BY ANY SYSTEMIC BIAS?

A ABSOLUTELY. THAT'S, YOU KNOW, THAT'S WHERE WE AS EPIDEMIOLOGISTS START. WE LOOK AT THESE DATA AND THEN WE SAY, OH, HOW WAS THE STUDY DONE? WHY IS STUDY 1 AND 2 SUGGESTING A TWO-FOLD RISK INCREASE AND STUDY 3 ONLY A 1.4 FOLD?

FOR EXAMPLE, I SAY, WELL, EXPOSURE OR RISK IN THE EXPOSED. WHEN I SAY THAT, I DIDN'T TELL YOU WHAT IS THE EXPOSURE. THE EXPOSURE COULD BE HIGH. THE EXPOSURE COULD BE LOW. SO IF I NOW LOOK AT STUDY 1 AND 2 AND I SEE THAT THE EXPOSURE WAS ACTUALLY TWO-FOLD OR

THREE-FOLD HIGHER IN THOSE STUDY SUBJECTS THAN IN STUDY NUMBER 3, THEN IT'S EVEN MORE CONSISTENT.

IF I DON'T SEE THAT, THEN I HAVE TO SAY, WELL, WHAT ELSE WAS IT THAT GAVE ME A TWO-FOLD WHEN MAYBE THE TRUTH IS CLOSER TO THE THIRD STUDY.

Q NOW, LET'S SAY, I THROW IN A NEW SCENARIO, RIGHT, WHERE WE HAVE THE SAME CONFIDENCE INTERVALS JUST ALL SHIFTED OVER SO THAT NONE OF THEM ARE STATISTICALLY SIGNIFICANT.

THE APPROACH YOU JUST DESCRIBED LOOKING AT THE STRENGTHS AND WEAKNESSES OF THE STUDIES AND THINKING ABOUT BIASES OR WHATNOT, WOULD YOU APPLY THAT SAME APPROACH REGARDLESS OF THE RESULTS THAT YOU'RE SEEING?

A ABSOLUTELY. BY THE WAY, STUDY 3 IS STILL STATISTICALLY SIGNIFICANT, IT'S JUST ON THE LEFT SUGGESTING NEGATIVE EFFECTS. SO -- NEGATIVE ASSOCIATION.

SO WHAT YOU WOULD SAY HERE IS STUDY 1 AND 2 SUGGESTED NO ASSOCIATION, BUT NOW A MUCH LARGER STUDY, STUDY 3 SUGGESTS A NEGATIVE ASSOCIATION SO YOU HAVE TO DEFINITELY LOOK INTO WHAT THE DIFFERENCES ARE BETWEEN STUDY NUMBER 1 AND 2 AND WHY THEY WOULD NOT SEE THE SAME OUTCOME -- ASSOCIATION OUTCOME AS IN STUDY 3.

Q IF WE'RE TALKING ABOUT SOMETHING LIKE HEAVY METALS THAT HAVE BEEN STUDIED PRETTY RIGOROUSLY FOR DECADES AND YOU SEE A RESULT THAT IT'S HIGHLY PROTECTIVE OF SOME INJURY THAT IT'S KNOWN TO PROBABLY CAUSE, HOW DO YOU DEAL WITH THAT?

A WELL, THIS KIND OF RESULT ARE NOT UNUSUAL ESPECIALLY WHEN -- I STUDY A LOT OF PREGNANCY-RELATED OUTCOMES AND WE KNOW THAT THERE IS ONE ACTUALLY WEIRD BIAS THAT WE CALL THE LIFE FIRST BIAS WHERE IF YOU REALLY HAVE HIGH -- VERY HIGH EXPOSURE IN PREGNANCY, THAT CHILD NEVER COMES TO BE BORN ALIVE. WE HAVE EARLY ABORTION. AND IN THOSE KIND OF STUDIES YOU CAN SEE EXACTLY THIS KIND OF EFFECT WHERE ALL OF A SUDDEN A HIGHLY TOXIC EXPOSURE THAT IN ANIMAL STUDIES IN OTHER HUMAN STUDIES HAS BEEN PROVEN TO BE QUITE TOXIC SO YOU WOULDN'T ASSUME THAT A VITAMIN IS HELPFUL AND YOU SHOULD FEED IT TO PREGNANT WOMEN.

THAT IN THIS CASE YOU WOULD SEE A STUDY NUMBER 3 RESULT BECAUSE THE MOST AFFECTED INDIVIDUALS, THE MOST AFFECTED CHILDREN, FETUSES ARE ACTUALLY LOST BEFORE THEY COME TO A LIVE BIRTH, SO -- AND THOSE ARE ALSO THE ONES WHO LATER WOULD BE DIAGNOSED WITH THE DISORDER, AND YOU SYSTEMATICALLY LOST EXACTLY THESE INDIVIDUALS. AND THAT HAS ACTUALLY BEEN DESCRIBED VERY NICELY IN THE EPI LITERATURE AS THE SO-CALLED LIFE FIRST BIAS OF PREGNANCY EXPOSURES.

Q AND WOULD IT BE FAIR TO SAY, THEN, DOCTOR, THAT WHEN YOU'RE LOOKING AT SOMETHING LIKE A PROTECTIVE EFFECT FOR HEAVY METALS, THAT YOU DON'T LEAVE YOUR KNOWLEDGE ABOUT THE MECHANISMS AND BIOLOGY OF THE METALS AT THE DOOR, THAT YOU HAVE TO BRING THAT INTO THE ANALYSIS?

A ABSOLUTELY. THAT'S -- EVERY EPIDEMIOLOGIST

WOULD NOT DO THEIR JOB IF THEY WOULDN'T READ THE LITERATURE, IF THEY WEREN'T EDUCATED ENOUGH ABOUT WHAT PREVIOUS STUDIES HAVE SHOWN, WHAT BIOLOGY TELLS YOU; IN FACT, YOU KNOW, IT'S A LITTLE SAD THAT NOT MORE PEOPLE WITH A MEDICAL AND BIOLOGIC DEGREE TAKE UP EPIDEMIOLOGY BECAUSE I THINK IT'S ABSOLUTELY IMPORTANT THAT WE KNOW ABOUT THESE KIND OF MECHANISTIC AND TYPE OF CONTEXTS AND THAT WE PUT EVERYTHING, AS A SCIENTIST AT LEAST, PUT EVERYTHING INTO THE CONTEXT OF BIOLOGIC PLAUSIBILITY AND OF EVERYTHING ELSE WE KNOW ABOUT THE AGENTS.

Q NOW, ONE OF THE THINGS THAT I WANT TO ASK YOU ABOUT IS ACTUALLY I'M GOING TO GO BACK TO THIS CASE CONTROL STUDY. AND THIS IS REALLY IMPORTANT BECAUSE THIS HAS BEEN THE FOCUS OF THE DEFENDANTS' OPENING STATEMENT, AND THIS IS THE CONCEPT OF THE REVERSE CAUSATION.

ARE YOU FAMILIAR WITH THAT CONCEPT, DOCTOR?

A ABSOLUTELY.

Q WHAT IS REVERSE CAUSATION?

A SO REVERSE CAUSATION WOULD BE IF THE EXPOSURE DID NOT CAUSE THE OUTCOME, BUT THE OUTCOME CAUSED THE EXPOSURE OR THE LEVEL OF EXPOSURE.

SO THE WAY THAT I USUALLY EXPLAIN THAT IN MY CLASSROOM IS THAT IF YOU WANT TO KNOW WHETHER COFFEE DRINKING, AND I LOVE COFFEE, CAUSES MYOCARDIAL INFARCTION AND YOU STUDY PEOPLE WITH MYOCARDIAL INFARCTION YOU MAY REALIZE THAT THEY DRINK LESS COFFEE. AND NOW, WHY, RIGHT, COMPARED TO OTHER PEOPLE WHO

HAVEN'T HAD A MI. AND MORE LIKELY THAN NOT, THEY HAVE EITHER FIGURED OUT THAT THEY START HAVING HEART -- A RACING HEART OR THEIR DOCTOR HAD TOLD THEM, WELL, YOU KNOW, CAFFEINE INCREASES YOUR BLOOD PRESSURE OR CARDIOVASCULAR DISEASE, INCREASES YOUR RISK OF MI, MAYBE YOU SHOULD NOT DRINK COFFEE.

SO IN THIS CASE BEING DIAGNOSED WITH CARDIOVASCULAR DISEASE HAVING HAD AN MI ACTUALLY CAUSES THE EXPOSURE LEVEL AND NOT THE OTHER WAY AROUND, SO YOU HAVE -- YOU DRINK LESS COFFEE BECAUSE YOU'RE A CASE.

Q AND WHEN YOU'RE -- LET'S TALK ABOUT IT IN THE CONTEXT OF SOME OF THESE HEAVY METAL STUDIES.

NOW, I UNDERSTAND THAT A LOT OF STUDIES -- AND WE'RE GOING TO GET INTO THEM IN A MINUTE MORE SPECIFICALLY -- BUT A LOT OF THEM, NOT ALL, BUT SOME OF THEM LOOK AT CHILDREN WITH AUTISM AND CHILDREN WITHOUT AUTISM AFTER THEY HAVE BEEN DIAGNOSED AND THEN TAKE THEIR BIOMARKERS, WHETHER IT BE BLOOD, URINE, HAIR, WHATEVER IT BE, AT THAT TIME.

YOU'RE FAMILIAR WITH THOSE TYPES OF STUDIES?

A YES. ABSOLUTELY.

Q YOU KNOW, WHEN YOU WERE THINKING ABOUT THE EPIDEMIOLOGICAL EVIDENCE IN THIS CASE, DID YOU CONSIDER AND REALLY THINK THROUGH WHETHER OR NOT THE AUTISM WAS CAUSING THESE CHILDREN TO HAVE HIGHER LEVEL OF THESE METALS VERSUS THE HEAVY METALS CAUSING THEM TO HAVE AUTISM?

A ABSOLUTELY. THAT'S THE FIRST THING YOU THINK

ABOUT, YOU KNOW, IS THERE ANY KIND OF BEHAVIOR THAT AUTISM MAY ACTUALLY CAUSE OR, YEAH, ENGAGE IN KIDS WITH AUTISM OR AUTISM SPECTRUM DISORDER ENGAGE IN THAT COULD ACTUALLY CAUSE THE EXPOSURE TO BE INCREASED.

SO DO -- ARE THEY VERY THIRSTY AND THEY DRINK LEAD FROM LEAD PIPES FOR SOME REASON? OR YOU KNOW, ARE THEY HAVING MORE HAND/MOUTH BEHAVIOR AND THAT HAND/MOUTH BEHAVIOR EXPOSES THEM TO MORE LEAD BECAUSE THERE'S LEAD IN THE PAINT OR THERE'S LEAD IN THE SOIL?

Q NOW, DOCTOR, ARE YOU FAMILIAR WITH SOMETHING CALLED PICA?

A YES.

Q AND PICA, THAT'S A MANIFESTATION OF CHILDREN PUTTING INEDIBLE OBJECTS IN THEIR MOUTH?

A YES, THAT'S WHAT IT'S USUALLY DEFINED AS, AND BETTER, YOU KNOW, CHEWING ON DIRT.

Q OKAY.

A AND WHATEVER.

Q SURE. SURE.

NOW, DID YOU -- LET'S BREAK IT DOWN BY METAL. LET'S FIRST TALK ABOUT LEAD.

A UM-HMM.

Q WHEN YOU LOOKED AT LEAD IN AUTISM, DID YOU CONSIDER WHETHER OR NOT WHAT YOU WERE SEEING IN THE DATA WAS SIMPLY AUTISTIC CHILDREN PUTTING LEAD INTO THEIR MOUTH AND THAT'S WHY THEY HAD ELEVATED LEVELS AS OPPOSED TO HAVING HISTORICAL LEVELS OF EXPOSURE THAT LED TO THEIR AUTISM?

A RIGHT. SO THAT'S OF COURSE SOMETHING YOU NEED TO CONSIDER.

IN THIS CASE YOU WOULD HAVE TO HAVE AN ENVIRONMENT IN WHICH THERE ACTUALLY IS A EXPOSURE THAT YOU CAN INCREASE THROUGH PICA; MEANING, THESE KIDS ALL HAVE TO LIVE IN ENVIRONMENTS WHERE THERE'S LOTS OF LEAD DUST OR LOTS OF THINGS THAT CONTAIN LEAD THAT THEY ACTUALLY CAN PUT IN THEIR MOUTH AND CHEW ON, AND HOPEFULLY, YOU KNOW, THAT MIGHT BE THE CASE IN SOME COMMUNITIES WHERE WE HAVE HIGH LEAD LEVELS DUE TO, LET'S SAY, A BATTERY RECYCLING FACILITY AROUND THE CORNER OR, YOU KNOW, SOME KIND OF COMMUNITY BUILT ON A TOXIC WASTE DUMP OR SOME KIND OF COMMUNITY WHERE A LOT OF LEAD PAINT HAS BEEN USED IN THE HOUSES. THOSE ARE COMMUNITIES WHERE YOU'RE WORRIED ABOUT THIS.

BUT THEN HOPEFULLY, THERE ARE ALSO STUDIES THAT ARE DONE IN COMMUNITIES WHERE IT'S HIGHLY UNLIKELY THAT THESE ARE THE ONLY OR THE MAJOR SOURCES OF EXPOSURE BECAUSE WE DO KNOW THERE ARE VERY DIFFERENT SOURCES OF EXPOSURE FOR LEAD, RIGHT, COULD BE DIET. IT COULD BE WATER.

Q YEAH.

SO HOW DO YOU THEN GO ABOUT TRYING TO DETERMINE IF -- SO, FOR EXAMPLE, IF YOU'RE DOING A STUDY AND YOU SEE THAT THE AUTISTIC HAVE MUCH HIGHER LEVELS OF BLOOD, URINE AND HAIR LEAD AS WE SEE IN THE DATA HERE, HOW CAN YOU DETERMINE IF THAT'S A FUNCTION OF, YOU KNOW, IF THE PRIOR EXPOSURE CAUSING THE DISEASE OR IF IT'S JUST A

FUNCTION OF THEM PUTTING STUFF IN THEIR MOUTH?

A WELL, ONE WAY OF AT LEAST GETTING CLOSER TO THIS WOULD BE TO CONDUCT A STUDY IN WHICH YOU INVESTIGATE ABOUT THESE KIND OF BEHAVIORS THAT WOULD EXPOSE THE CHILDREN.

SO YOU ASK THE PARENTS TO DESCRIBE THESE KIND OF BEHAVIORS IN THEIR KIDS AND TELL YOU HOW MUCH THEY ARE ACTUALLY DOING THIS. AND IF YOU DON'T KNOW WHETHER -- THAT THEN ALSO THIS KIND OF BEHAVIOR ACTUALLY EXPOSES THEM TO LEAD, THEN YOU MEASURE THEIR BLOOD LEAD, AND THEN YOU COMPARE THE BLOOD LEAD IN ALL OF THE KIDS WITH THIS KIND OF EXPOSURE TO THE BLOOD LEAD IN THE KIDS WITHOUT THAT KIND OF EXPOSURE, AND IF IT'S PRETTY SIMILAR, THEN IT PROBABLY WASN'T THE BEHAVIOR.

Q SO, FOR EXAMPLE, IF YOU GET A GROUP OF AUTISTIC CHILDREN AND SOME OF THEM HAD PICA AND SOME OF THEM DIDN'T AND YOU LOOKED AT TO SEE WHAT THEIR LEAD LEVELS WERE AND SEE IF THE KIDS WITH PICA HAD HIGHER LEAD LEVELS THAN THE KIDS WITHOUT PICA. WOULD THAT BE A FAIR WAY OF DOING IT?

A RIGHT. THAT'S HOW WOULD YOU DO IT.

Q WHAT ABOUT LOOKING AT HISTORICAL EXPOSURE DATA?

A THAT'S ALWAYS A GOOD IDEA.

Q HOW --

A SO --

Q GO AHEAD.

A -- SO IF YOU HAVE BLOOD SPOTS OR IF YOU HAVE -- THAT OF COURSE WOULD BE BIOMARKER, BUT IF YOU HAD LIKE

MEASUREMENTS IN THE SOIL, MEASUREMENTS IN THE AIR, MEASUREMENTS OF THE WATER THAT WOULD ALSO BE QUITE HELPFUL.

AND I THINK THE STUDIES THAT ARE REALLY INTERESTED IN, YOU KNOW, THESE KIND OF QUESTIONS, THEY OFTEN ARE WORRIED ABOUT SOURCES, SPECIFIC SOURCES, SO YOU CAN ACTUALLY GO BACK AND SEE WHAT THE AUTHORS THOUGHT THE MAJOR SOURCE FOR THE EXPOSURE WAS.

FOR EXAMPLE, IF IT WAS LEAD IN THE WATER, THEN IT WOULD BE HIGHLY UNLIKELY THAT PICA MAKES ANY DIFFERENCE.

Q OKAY. BECAUSE BOTH PEOPLE WOULD BE EXPOSED?

A YES.

Q OKAY.

A WATER EXPOSES EVERYONE.

Q OKAY. AS THE JUDGE TAKES A DRINK OF WATER. GOOD TIMING, DR. RITZ.

THE COURT: CHEERS.

THE WITNESS: HOPEFULLY THERE'S NOT LEAD IN IT.

MR. WISNER: YOUR HONOR, WE'VE BEEN GOING FOR A LITTLE BIT. DO YOU THINK TAKING A FIVE-MINUTE BREAK NOW AND THEN FINISHING UP MAKES SENSE?

THE COURT: YEAH. I THINK THAT MAKES SENSE.

LET'S TAKE TEN MINUTES, PLEASE, SO ABOUT 3:30.

MR. WISNER: OKAY.

THE COURT: THANK YOU.

THE WITNESS: THANK YOU.

(RECESS)

THE COURT: OKAY. IT LOOKS LIKE WE'RE ALL READY TO GO AGAIN. THANK YOU.

MR. WISNER: THANK YOU, YOUR HONOR. MAY I PROCEED?

THE COURT: YES, PLEASE.

MR. WISNER: GREAT.

Q ALL RIGHT. DOCTOR, WE SPENT SOME TIME SORT OF GOING OVER SOME EPI 101 PRINCIPLES. I WANT TO GET INTO YOUR SPECIFIC METHODOLOGY AND THEN GET INTO LEAD AND ASD.

SO LET'S MOVE ON TO METHODOLOGY.

NOW, I WANT TO SHOW YOU YOUR -- WELL, LET'S NOT SHOW YOUR REPORT JUST YET. LET'S JUST ASK YOU SOME QUESTIONS.

CAN YOU PLEASE DESCRIBE TO THE COURT WHAT METHODOLOGY YOU USED TO ASSESS THE CAUSAL ASSOCIATION, IF ANY, BETWEEN LEAD AND ASD AND ADHD?

A WELL, I DO WHAT YOU USUALLY WOULD DO IN ORDER TO GET YOURSELF ACQUAINTED WITH THE LITERATURE, WHICH IS SCOURED THE LITERATURE FOR THE KIND OF EPIDEMIOLOGY PAPERS THAT REFERRED TO THE SUBJECT MATTER AND THEN KIND OF SORT THEM AND READ THEM. AND WHILE YOU'RE READING THEM, ASSESSING THEM FOR WEAKNESSES AND STRENGTHS. AND THEN FINALLY, YOU KNOW, PUTTING THEM ALL TOGETHER, RE-READING THEM USUALLY AND THEN COMING UP WITH AN EVALUATION OF THE OVERALL LITERATURE IN EPIDEMIOLOGY, AND THEN GOING BACK TO -- I AT LEAST LIKE TO DO THAT TO SOME OF THE BASIC SCIENCE LITERATURE ON THE SUBJECT AND

THE EXPOSURE AND THEN SEE HOW THAT FITS TOGETHER.

Q NOW, I UNDERSTAND THAT YOU RELIED ALMOST EXCLUSIVELY ON PEER-REVIEWED LITERATURE, IS THAT RIGHT?

A YES.

Q WHY? WHY DO YOU DO THAT?

A WELL, THEY DO A LITTLE BIT OF THE WORK FOR YOU, MEANING, I'VE BEEN, YOU KNOW, AN EDITOR FOR SEVERAL JOURNALS AND I'M A REVIEWER OF PAPERS, LIKE I THINK I GET ONE A DAY SENT TO ME TO REVIEW AND I SAY NO TO MOST OF THEM. BUT I DO PICK AND CHOOSE THE PAPERS THAT INTEREST ME, OF COURSE, OR WHERE I THINK I, YOU KNOW, A GOOD EPIDEMIOLOGIST HAS TO ACTUALLY READ THIS BECAUSE IT'S AN IMPORTANT SUBJECT, AND SO I KNOW WHAT KIND OF CRITERIA A REVIEWER AND AN EDITOR WOULD APPLY TO THESE STUDIES AND YOU READ THEM WITH A VERY CRITICAL EYE BUT ALSO AN EYE TO WHAT'S POSSIBLE AND WE ARE AN APPLIED SCIENCE. WE CANNOT TOX CHILDREN WITH METALS AND WAIT FOR THEM TO HAVE NEURO DEVELOPMENTAL DEFECTS. THAT'S NOT WHAT WE DO. AND SO WE HAVE TO LIVE WITH WHAT'S GIVEN TO US. WE HAVE TO LIVE WITH THE OBSERVATIONAL KIND OF DATA THAT'S PRESENTED AND WE HAVE TO TAKE IT AT FACE VALUE AND SAY, OKAY, THIS IS MAYBE THE BEST WE CAN DO IN THIS INSTANCE.

BUT IF I LOOK AT DIFFERENT STUDIES AND, YOU KNOW, WITH CASE CONTROL STUDY AND A COHORT STUDY AND A CROSS SECTIONAL STUDY AND A CASE REPORT, THEY ARE ALL TELLING ME KIND OF SAME STORY, THEN I'M MUCH MORE CONFIDENT THAT THIS IS A STORY THAT HAS SOME TRUTH TO

IT.

Q NOW, AFTER YOU'VE DONE THAT LITERATURE REVIEW, ARE YOU FAMILIAR WITH THE BRADFORD HILL CRITERIA OR FACTORS?

A YES. ABSOLUTELY.

Q OKAY.

NOW, IF WE LOOK HERE AT, WE'RE LOOKING AT YOUR REPORT, THIS IS EXHIBIT 3.

AND RIGHT HERE AFTER YOU REVIEWED ALL THAT LITERATURE, YOU WRITE, "THE AVAILABLE EPIDEMIOLOGICAL LITERATURE DEMONSTRATES A CONSISTENT ASSOCIATION BETWEEN LEAD EXPOSURE AND THE DEVELOPMENT OF CHILDHOOD ASD.

I WILL NOW TURN TO THE BRADFORD HILL CRITERIA TO MAKE AN ASSESSMENT CAUSALITY."

DO YOU SEE THAT?

A YES.

Q IS IT IN YOUR EXPERIENCE THAT THE FACTORS OR CONSIDERATIONS THAT BRADFORD HILL, SIR BRADFORD HILL CREATED, HELPED GUIDE YOU IN ASSESSING WHETHER THE ASSOCIATION OF WHAT YOU'RE SEEING IS IN FACT CAUSAL?

A YES, THAT'S GENERALLY WHAT IS ACCEPTED IN SCIENCE AND ESPECIALLY IN EPIDEMIOLOGY AS THE PROPER WAY TO GO ABOUT THIS. IT'S NOT A CHECKLIST. IT'S ACTUALLY APPLYING YOUR EXPERTISE, YOUR SCIENCE, KNOWLEDGE IN A VERY CONSISTENT AND ALSO A VERY TRANSPARENT MANNER.

SO WHY BRADFORD HILL IS STILL, YOU KNOW, THE KIND OF STANDARD BEARER FOR CAUSALITY IN OUR SCIENCE IS

BECAUSE HE MADE IT CLEAR WHAT KIND OF "CRITERIA" YOU'RE USING AND YOU HAVE TO ACTUALLY TELL YOUR COLLEAGUES WHAT YOU THINK ABOUT THESE DIFFERENT GUIDELINES CRITERIA AND HOW THEY FIT TOGETHER OVERALL IN COMING UP WITH YOUR EVALUATION IN THE END.

Q DOCTOR, CAN TWO EPIDEMIOLOGISTS WHO ARE EMINENTLY QUALIFIED APPLY THE SAME BRADFORD HILL FACTORS AND REACH DIFFERENT CONCLUSIONS?

A IT HAS HAPPENED. BUT IF -- YOU KNOW, IF THE LITERATURE IS VERY DIVERSE, DIVERGENT AND, I MEAN, PEOPLE HAVE BIASES, THEY BELIEVE IN CERTAIN SUBJECT MATTER; FOR EXAMPLE, PEOPLE WHO STUDY A CERTAIN SUBJECT THEIR WHOLE LIFE, THEY HAVE A VERY STRONG BIAS ABOUT WHAT MIGHT BE CAUSING THIS OUTCOME BECAUSE THEY HAVE BEEN WORKING ON IT SO HARD AND I DON'T FAULT THEM FOR IT, AND THEN YOU NEEDED A LOT OF DATA TO OVERCOME THAT BIAS. BUT OTHERWISE IF YOU STEP BACK FROM YOUR OWN BIAS, IF YOU EVALUATE THE LITERATURE IN ITS ENTIRETY, I WOULD HOPE THAT TWO EPIDEMIOLOGISTS WOULD COME TO THE SAME CONCLUSIONS USING THESE KIND OF GUIDELINES.

Q NOW, DOCTOR, I UNDERSTAND THERE'S NINE DIFFERENT BRADFORD HILL FACTORS. I DON'T WANT TO GO THROUGH ALL OF THEM. I DON'T THINK THERE'S BEEN ANY CHALLENGE OR ARGUMENT THAT THEY ARE ALL AT ISSUE. I THINK THERE'S REALLY BEEN TWO THAT WE'RE GOING TO FOCUS ON.

THE FIRST IS GOING TO BE THE FACTOR OF TEMPORALITY, AND THE OTHER ONE IS GOING TO BE THE FACTOR

OF CONSISTENCY; OKAY?

A YES.

Q ALL RIGHT. I'M GOING TO SHOW YOU EXHIBIT 159. DO YOU RECOGNIZE THIS DOCUMENT?

A YES, IT'S THE ORIGINAL ONE.

Q THE ORIGINAL ONE. THIS IS THE BRADFORD HILL ARTICLE; IS THAT RIGHT?

A CORRECT. YES, UM-HMM.

Q AND IT LOOKS LIKE THIS WAS FROM A MEETING IN JANUARY 1965; RIGHT?

A RIGHT.

Q SO IT'S SORT OF IN THE ANNALS OF EPIDEMIOLOGY.

A RIGHT.

Q SO AS WE GO INTO THIS HE IDENTIFIES THE FIRST ONE. THERE'S THE STRENGTH OF ASSOCIATION.

DO YOU SEE THAT?

A UM-HMM. YES, I SEE IT.

Q AND THEN HE GOES ON. AND LET'S LOOK AT CONSISTENCY FIRST.

SO WHAT HE WRITES HERE IS, "CONSISTENCY: NEXT ON MY LIST OF FEATURES TO BE SPECIALLY CONSIDERED I WOULD PLACE THE CONSISTENCY OF THE OBSERVED ASSOCIATION. HAS IT BEEN REPEATEDLY OBSERVED BY DIFFERENT PERSONS IN DIFFERENT PLACES, CIRCUMSTANCES AND TIMES?"

DO YOU SEE THAT?

A YES, AND THAT'S ACTUALLY REALLY IMPORTANT BECAUSE IF -- REPEATING STUDIES IN THE SAME POPULATION,

DOING IT IN THE SAME WAY, THAT'S USUALLY WHAT WE THINK ABOUT WHEN HE WE DO EXPERIMENTS AND COMPARE EXPERIMENTS, WE ARE THINKING, OH, YOU HAVE TO DO THEM IN EXACTLY THE SAME WAY, YOU HAVE TO GET THEM JUST RIGHT TO SHOW YOU THE RIGHT RESULT, RIGHT.

ACTUALLY IN EPIDEMIOLOGY IT'S MUCH MORE IMPRESSIVE IF PEOPLE ALL OVER THE WORLD HAVE USED DIFFERENT METHODS AND FOUND THE SAME THING.

AND THAT -- THE REASON FOR THAT IS THAT WE CAN'T CONTROL THE ENVIRONMENT, WE CAN'T -- WE'RE NOT PUTTING HUMANS IN CAGES AND FEEDING THEM LEAD. WE JUST HAVE TO OBSERVE THEM, SO THERE ARE BIASES. WE ALL KNOW THERE ARE LOTS OF BIASES WE HAVE TO WORRY ABOUT IN OBSERVATIONAL STUDIES. I TEACH THAT. AND WE ARE VERY GOOD AT PICKING OUT THE BIASES.

EVERY EPIDEMIOLOGIC STUDY HAS A BIAS. THERE'S NO WAY AROUND IT. BUT IF ALL OF THE STUDIES DONE WITH DIFFERENT DESIGNS THAT WOULD HAVE DIFFERENT BIASES AND THAT WOULD BE DONE BY DIFFERENT PEOPLE ON DIFFERENT CONTINENTS IN DIFFERENT ENVIRONMENTS, IN DIFFERENT CLIMATES WITH DIFFERENT GENETIC FACTORS, ALL KIND OF SHOW YOU THE SAME RESULT, THEN YOU'RE MUCH MORE CONFIDENT. THAT'S WHAT WE CALL CONSISTENCY. NOT SOMETHING THAT'S REPEATED IN EXACTLY THE SAME WAY IN THE SAME PLACE BY THE SAME PERSON.

Q I WANT TO FOCUS IN ON EACH OF THESE.

HE SAYS DIFFERENT PERSONS?

A RIGHT.

Q DIFFERENT PLACES. DIFFERENT CIRCUMSTANCES. AND DIFFERENT TIMES.

LET'S START OFF WITH PERSONS.

WHY DOES A VARIATION OF PEOPLE IN SCIENTISTS MATTER? OR IT MAY BE THE STUDY POPULATION. I DON'T KNOW WHAT PERSONS REFERS TO.

A IT'S ACTUALLY BOTH.

Q OKAY.

A IT'S THE SCIENTISTS BECAUSE, YOU KNOW, AS I SAID, I COULD BE A VERY BIASSED INDIVIDUAL AND ALL I WANT TO SHOW YOU IS ONE THING AND, YOU KNOW, I'M JUST SHOWING THAT YOU OVER AND OVER AGAIN, AND BECAUSE OF, YOU KNOW, I'M NOT LOOKING AT THE DATA ANYMORE, I'M KIND OF GENERATING THE DATA THAT SHOWS.

SO IF IT'S JUST ONE GROUP WHO'S EVER BEEN SHOWN THAT, THEN I WOULD WORRY AND SAY, WELL, I WOULD LIKE TO SEE THAT DONE BY SOMEONE ELSE.

BUT IT'S ALSO DEFINITELY DIFFERENT INDIVIDUALS WHO ARE IN THIS STUDY BECAUSE IF IT GENERALIZES AND IF IT'S GENERALIZED BIOLOGY, I SHOULD BE ABLE TO SEE THOSE IN DIFFERENT KINDS OF PEOPLE. I SHOULD BE ABLE TO SEE AN EFFECT IN CHILDREN OF DIFFERENT RACES OF DIFFERENT ETHNICITIES. I SHOULD BE ABLE TO SEE THAT IN CHILDREN WHO LIVE IN DIFFERENT PLACES, ARE RAISED IN DIFFERENT CULTURES, SO IT MAKES ME MUCH MORE TRUSTING THE RESULTS IF THAT SHOWS CONSISTENCY.

Q ALL RIGHT. DIFFERENT PLACES.

HOW DOES THAT PLAY INTO IT?

A WELL, THAT'S GENERALLY CONSIDERED GEOGRAPHY, AND ENVIRONMENTAL EPIDEMIOLOGY THAT'S REALLY IMPORTANT BECAUSE THE GEOGRAPHY IS PARTIALLY WHAT EXPOSE PEOPLE. YOU COULD BE LIVING IN A PLACE WHERE THERE'S HIGH ARSENIC WATER CONTAMINATION OR YOU COULD BE LIVING IN A PLACE WHERE THERE'S LEAD SMELTING.

SO THESE DIFFERENT PLACES ARE IMPORTANT BECAUSE OF THEIR POTENTIAL FOR DIFFERENT EXPOSURES AND DIFFERENT EXPOSURE LEVELS BUT ALSO FOR DIFFERENT SUSCEPTIBILITIES OF THE POPULATION THAT LIVES THERE.

Q WHAT ABOUT DIFFERENT CIRCUMSTANCES? WHAT'S THAT GETTING AT?

A WELL, CIRCUMSTANCES COULD JUST MEAN THE WAY THE STUDY IS COMING ABOUT. LIKE, YOU KNOW, WHAT IS THE DESIGN? IS THERE A SPECIALTY CLINIC THAT, YOU KNOW, ALL OF A SUDDEN GETS INTERESTED IN ONE OUTCOME AND DOES THE STUDY, DO I TRUST THAT ONE STUDY THAT, YOU KNOW, WAS DONE AT A SPECIALTY CLINIC OR WOULD I LIKE TO SEE THIS REPEATED BY A GENERAL PRACTITIONER KIND OF SAMPLE? WHAT ARE THE CIRCUMSTANCES THAT LED TO THIS STUDY OR TO THAT STUDY POPULATION BEING ASSEMBLED?

Q AND THEN TIMES. WHY IS HAVING DIFFERENT STUDIES AT DIFFERENT TIMES IMPORTANT?

A WELL, FOR AIR POLLUTION IT'S OBVIOUS BECAUSE AIR POLLUTION CHANGES WITH SEASON AND CHANGES OVER TIME, BUT IT'S ACTUALLY THE CASE FOR LOTS OF ENVIRONMENTAL EXPOSURES, THEY COME AND GO, LUCKILY THEY SOMETIMES GO, BUT THEY ALSO OFTEN COME; SO YOU DEFINITELY WANT TO LOOK

OVER TIME WHAT THE EXPOSURE SOURCES ARE AND WHAT THE EXPOSURE LEVELS ARE AND ARE THEY INCREASING OR DECREASING OR IN WHAT WAY ARE THEY CHANGING OVERALL.

Q I WANT TO LOOK AT THIS PARAGRAPH HERE AT THE BOTTOM. IT FLOWS ON TO THE NEXT PAGE.

HE WRITES -- SIR BRADFORD HILL WRITES, "WE HAVE THEREFORE THE SOMEWHAT PARADOXICAL POSITION THAT THE DIFFERENT RESULTS OF A DIFFERENT INQUIRY CERTAINLY CANNOT BE HELD TO REFUTE THE ORIGINAL EVIDENCE, YET THE SAME RESULTS FROM PRECISELY THE SAME FORM OF INQUIRY WILL NOT INVARIABLY GREATLY STRENGTHEN THE ORIGINAL EVIDENCE. I MYSELF WOULD PUT A GOOD DEAL OF WEIGHT UPON SIMILAR RESULTS REACHED IN QUITE DIFFERENT WAYS; FOR EXAMPLE, PROSPECTIVELY AND RETROSPECTIVELY."

DO YOU SEE THAT?

A YES. HE'S BASICALLY EXPLAINING WHAT I JUST SAID. YOU KNOW, YOU WANT -- ACTUALLY IN MORE RECENT LITERATURE THAT IS -- THERE'S A TERM FOR THIS, IT'S CALLED TRIANGULATION, AND IT IS A WAY OF COMING TO A CAUSAL CONCLUSION AND IT'S USED FOR CAUSAL EVALUATIONS SAYING THAT NO STUDY, NO OBSERVATION IS EVER PERFECT. EVERY STUDY HAS A SLIGHT LIMITATION OR A LARGE LIMITATION IN ONE WAY OR ANOTHER.

BUT IF I COME AT THE SAME PROBLEM FROM DIFFERENT ANGLES AND I STILL HAVE THE SAME ANSWER, AS, YOU KNOW, YOU WOULD EXPECT UNDER, YOU KNOW, A CERTAIN

CIRCUMSTANCE THAT, YOU KNOW, THIS HIGH EXPOSURE SHOULD SHOW YOU MORE EFFECT AND LOW EXPOSURE SHOULD SHOW YOU LESS EFFECT, IN THIS POPULATION THAT'S MORE VULNERABLE YOU SHOULD SEE MORE DISEASE. IN A POPULATION THAT IS LESS VULNERABLE, YOU SHOULD SEE LESS DISEASE. CHILDREN WHO ARE EXPOSED AT A CERTAIN AGE WHERE, YOU KNOW, IT'S IRRELEVANT SHOULD NOT HAVE THE DISEASE, WHILE CHILDREN EXPOSED AT THE RELEVANT AGE SHOULD HAVE THE DISEASE, ET CETERA.

SO THIS IS WHAT WE USE, THESE DIFFERENT STUDIES WITH DIFFERENT OUTCOMES IN THIS CASE, BUT ACCORDING TO A HYPOTHESIS, HYPOTHESIS OF A, FOR EXAMPLE, SENSITIVE PERIOD THAT IS BEING AFFECTED, A EXPOSURE THAT REALLY NEEDS TO HIT THE RIGHT TIMING OF NEURODEVELOPMENT, FOR EXAMPLE; ALL OF THAT IS BROUGHT TOGETHER AND IS MORE THAN JUST ONE STUDY AND MORE JUST -- MORE THAN JUST ONE PIECE OF EVIDENCE.

SO YOU NEVER CONCLUDE ANYTHING ON ONE PIECE OF EVIDENCE. HOPEFULLY, YOU HAVE A LOT, AND HOPEFULLY YOU HAVE A LOT OF DIFFERENT ONES.

Q NOW, DO YOU HAVE TO HAVE PROSPECTIVE AND RETROSPECTIVE STUDIES TO HAVE CONSISTENT RESULTS?

A NOT NECESSARILY. THERE ARE SITUATIONS WHERE YOU ONLY HAVE ONE TYPE OR ONLY THE OTHER AND YOU HAVE TO ACT BECAUSE WE HAVE PUBLIC HEALTH, YOU KNOW, MINDED INDIVIDUALS IN OUR DISCIPLINE. AND IF I HAVE ANIMAL DATA AND MECHANISTIC DATA AND ONE TYPE OF EPIDEMIOLOGIC STUDY IT CAN BE ENOUGH TO BE COMPELLED TO SAY, WELL, WE

NEED TO ACT, WE CANNOT WAIT FOR THE NEXT STUDY TO HAPPEN. WE HAVE TO BE PROTECTING PUBLIC HEALTH.

Q LET'S LOOK AT WHAT YOU DID SPECIFICALLY IN YOUR REPORT.

RIGHT DOWN HERE, YOU'RE GOING TO THE BRADFORD HILL CRITERIA SPECIFICALLY AS IT RELATES TO LEAD AND ASD, AND WRITE UNDER, "CONSISTENCY: THIS CRITERION IS MET SINCE POSITIVE ASSOCIATIONS HAVE BEEN REPORTED FOR DIFFERENT POPULATIONS IN DIFFERENT GEOGRAPHIC REGIONS AND DIFFERENT TIME PERIODS AS WELL AS DIFFERENT BIOLOGICAL MATRICES WHICH STRENGTHENS THE LIKELIHOOD OF A TRUE EFFECT."

DO YOU SEE THAT?

A YES.

Q THIS PRECISE THING THAT YOU STATE HERE, DIFFERENT POPULATIONS, REGIONS, TIME PERIODS, BIOLOGICAL MATRICES, IS THIS EXACTLY THE TYPE OF CONSISTENCY ANALYSIS THAT SIR BRADFORD HILL MENTIONED BACK IN 1965?

A THAT'S WHAT I IMAGINE HE WANTED ME TO DO, YES.

Q NOW, DOCTOR, I WANT TO BE CLEAR BECAUSE DEFENSE COUNSEL HAS TOLD THIS COURT THAT YOUR DEFINITION OF CONSISTENCY IS SOMEWHERE ALONG THE LINES OF IF IT DOESN'T MEET WHAT YOU WANT IT TO -- IF THE RESULTS OF THE STUDY DON'T SHOW YOU WHAT YOU WANT, THEN IT'S NOT CONSISTENT.

FIRST OF ALL, IS THAT EVEN REMOTELY ACCURATE ABOUT HOW YOU GO ABOUT APPROACHING THE SCIENTIFIC

APPROACH AND SPECIFICALLY THE CONSISTENCY CRITERIA?

A NO, ABSOLUTELY NOT.

SO CONSISTENCY MEANS OF COURSE COMPARISON AND IT MEANS COMPARISON OF DIFFERENT WAYS OF KNOWING THINGS AND THAT MEANS DIFFERENT KINDS OF STUDIES AND IT DOESN'T MEAN THAT EVERY STUDY HAS TO SHOW EXACTLY THE SAME THING.

FOR EXAMPLE, IF I HAVE A POPULATION THAT'S VERY HIGHLY EXPOSED, I MAY EXPECT A STRONGER EFFECT THAN IN A POPULATION THAT IS LOW EXPOSED, RIGHT. SO I'M EXPECTING DIFFERENT THINGS BASED ON WHAT THE EXPOSURE LEVELS ARE. BUT THAT I SEE A STRONG EFFECT IN ONE POPULATION AND A WEAK EFFECT IN ANOTHER IS NOT INCONSISTENT. IT'S ACTUALLY CONSISTENT WITH MY EXPECTATION GIVEN THE LEVEL OF EXPOSURE.

Q I GUESS THAT'S MY QUESTION.

SO IF -- I MEAN, WHEN YOU'RE LOOKING AT WHETHER OR NOT DATA OR RESULTS ARE CONSISTENT, DO YOU FRAME WHETHER IT'S CONSISTENT BASED UPON WHAT YOU ALREADY KNOW?

A OF COURSE. YOU ALWAYS, YOU KNOW, THAT'S WHY WE GET EDUCATED IN EPIDEMIOLOGY AND THAT'S WHY, YOU KNOW, THERE'S A JOKE ABOUT HOW MANY TIMES CAN YOU DO A STATISTICAL TEST AND, YOU KNOW, HAVE TO CORRECT FOR ALL YOUR PREVIOUS STATISTICAL TESTS? THE OLDER YOU GET, THE HARDER IT IS TO SHOW ANYTHING.

BUT THAT ASIDE, ACTUALLY, YES, YOU ALWAYS AS A SCIENTIST YOU LEARN -- HOPEFULLY, YOU LEARN YOUR WHOLE

LIFE. HOPEFULLY YOU ARE FLEXIBLE ENOUGH TO CHANGE YOUR MIND. HOPEFULLY YOUR BIASES WILL BE OVERWRITTEN BY THE ACTUAL DATA THAT YOU'RE COLLECTING IF IT'S SHOWING YOU SOMETHING ELSE.

AND BASICALLY, WE CALL THIS UPDATING OUR PRIORS. SO WE HAVE A PRIOR -- PRIOR PROBABILITY THAT SOMETHING IS AN EXPOSURE, IT CAUSES AN EFFECT, THEN I GO OUT THERE, I COLLECT MORE DATA AND I UPDATE MY PRIORS; MEANING, THE DATA ACTUALLY IS MEANINGFUL AND I ACTUALLY USE IT TO CHANGE MY MIND.

Q NOW, I WANT TO SHOW YOU THIS CHART THAT WE'VE PUT TOGETHER, AND THIS IS A FAIRLY COMPLEX CHART SO LET ME WALK THROUGH IT ALL.

SO WHAT WE HAVE HERE IS EVERY STUDY WITH A BIOMARKER RESULT THAT WE COULD DIG OUT OF YOUR REPORT.

AND BEFORE WE GO INTO WHAT THIS IS SHOWING, DOCTOR, CAN I JUST ASK YOU SOMETHING: BEFORE YOU GOT INVOLVED IN THIS LITIGATION, HAD YOU EVER SYSTEMATICALLY WENT THROUGH ALL THE LITERATURE TO LOOK AT ALL OF THE DATA ON METALS AND ASD?

A NO.

Q AND WHEN YOU DID, WERE YOU SURPRISED?

A I -- I WAS NOT REALLY SURPRISED, I HAVE TO SAY, BECAUSE I'VE READ SO MUCH ABOUT LEAD AND THE BRAIN IN MY LIFE, AND, YOU KNOW, LEAD IS A KNOWN NEUROTOXIN.

WHAT I WAS SURPRISED IS THAT SO MANY STUDIES ACTUALLY STARTED TO EXIST AND SHOW THIS BECAUSE FOR THE LONGEST TIME THE GENERAL BELIEF, AND I HAD THE SAME

BELIEF, WAS THAT IT'S GENETICS THAT CAUSES AUTISM, AND IT'S LIKE ONE OF THOSE STORIES WHERE, YOU KNOW, YOU DON'T LOOK BECAUSE YOU THINK YOU KNOW THE REASON, AND THEN ALL OF A SUDDEN SOMEBODY SAYS, "BUT, BUT," YOU KNOW, AND WE START ACTUALLY LOOKING AT -- WE ARE LOOKING AT THE ENVIRONMENT AND WE ARE ACTUALLY INVESTING -- WE START INVESTING THE ENVIRONMENT.

AND MY FAVORITE FUNDING AGENCY, THE NIEHS HAS NOT INVESTED IN AUTISM STUDIES MUCH AT ALL BEFORE THE YEAR 2000, AND THAT'S WHEN, YOU KNOW, EVERYBODY BELIEVED IT'S GENETICS. AND THEN SLOWLY BUT SURELY THEY STARTED INVESTING. NOW THEY RUN WHOLE AUTISM CENTERS. I MEAN, THEY FUND AUTISM CENTERS.

AND YES, THERE'S A LOT OF DATA ACCUMULATING, AND THESE LAST 20 YEARS REALLY CHANGED MY MIND.

Q NOW, LET'S LOOK AT THIS.

SO WE HAVE THIS DATA HERE. THIS IS ALL THE POSITIVE AND STATISTICALLY SIGNIFICANT RESULTS, AND THIS IS -- LOOKS LIKE SIX BY FIVE, SO IT LOOKS LIKE THERE'S ABOUT 30 STUDIES HERE.

DO YOU SEE THAT, DOCTOR?

A YES.

Q ALL RIGHT. AND WE HAVE HERE DIFFERENT COLORS. WE HAVE THE YELLOW, THE RED, THE BROWN, THE WHITE AND THE BLUE.

DO YOU SEE THAT?

A YES.

Q AND JUST SO THAT THERE'S A KEY UP HERE. THE

BLOOD RE -- THE YELLOW REFERS TO URINE; RIGHT?

A UM-HMM YES.

Q RED IS BLOOD. BROWN IS HAIR. WHITE IS TEETH AND NAILS. AND BLUE IS AIR STUDIES OR AIR POLLUTION STUDIES.

DO YOU SEE THAT?

A YES.

Q ALL RIGHT. SO LOOKING HERE AT THIS CORPUS OF STATISTICALLY SIGNIFICANT RESULTS, I SEE THAT THERE IS A WHOLE HOST OF DIFFERENT STUDY DESIGNS.

DO YOU SEE THAT?

A YES.

Q YOU HAVE COHORT DESIGNS, YOU HAVE CASE CONTROL STUDY DESIGNS. YOU HAVE CROSS SECTIONAL DESIGNS AND YOU HAVE ECOLOGICAL STUDIES.

DO YOU SEE THAT?

A YES.

Q THE FACT THAT YOU HAVE SO MANY DIFFERENT DESIGNS AND ALL SHOWING STATISTICALLY SIGNIFICANT ELEVATED LEVELS OF LEAD IN ASD PATIENTS, WHAT, IF ANY, SIGNIFICANCE DOES THAT HAVE TO YOU?

A WELL, THAT DISTRIBUTES TO CONSISTENCY ACROSS DIFFERENT STUDY DESIGNS, AND NOT ONLY DIFFERENT STUDY DESIGNS, BUT ALSO DIFFERENT BIOLOGIC MATRICES.

Q AND I SEE HERE THAT, YOU KNOW, SOME OF THESE STUDIES ARE A LITTLE BIT OLDER. WE HAVE SOME FROM 2008 AND WE HAVE SOME FROM 2020.

DO YOU SEE THAT?

A YES.

Q WHAT, IF ANYTHING, DOES THAT PLAY INTO YOUR UNDERSTANDING OF CONSISTENCY?

A THAT ACTUALLY CONTRIBUTES AGAIN BECAUSE WE KNOW THAT OVERALL LEAD LEVELS IN THE ENVIRONMENT HAVE BEEN DECREASING EXCEPT OF COURSE IN SPECIAL ENVIRONMENTS WHERE WE HAVE LEAD PIPES AND WHERE WE HAVE LEAD SMELTERS OR LEAD CONTAMINATION OF COMMUNITIES THAT WE KNOW OF.

BUT THE OVERALL LARGEST LEAD EXPOSURE IN CHILDREN WAS PROBABLY THROUGH LEADED GASOLINE THAT LUCKILY IN THE U.S. WAS STOPPED IN THE EARLY '80S, IN EUROPE SLIGHTLY LATER, BUT WE STILL HAVE LEADED GASOLINE IN QUITE A FEW OF THE COMMUNITIES THAT THESE CHILDREN ARE LIVING IN.

Q NOW, OF THESE STUDIES, WHICH ONES DID YOU FIND -- WELL, LET ME JUST DIRECT YOU TOWARDS THEM.

I WANT TO TALK ABOUT A FEW OF THESE JUST TO GIVE SOME CONTEXT. I WANT TO TALK ABOUT THE ARORA STUDY.

DO YOU SEE THAT, DOCTOR?

A YES.

Q I ALSO WANT TO TALK ABOUT THE FILON STUDY.

A YES.

Q AND I WANT TO TALK ABOUT THE KIM STUDY, OKAY? DO YOU SEE THAT?

A YES.

Q AND ONE IS BLOOD, ONE IS HAIR, ONE IS TEETH; RIGHT?

A RIGHT.

Q TWO OF THEM ARE COHORT STUDIES OR PROSPECTIVE STUDIES, AND ONE OF THEM IS A CASE CONTROL STUDY.

DO YOU SEE THAT?

A YES.

Q ALL RIGHT. WHY DON'T WE START OFF WITH THE ARORA STUDY.

WHY DON'T WE START OFF BY YOU DESCRIBING TO THE COURT YOUR UNDERSTANDING OF WHAT THE ARORA STUDY WAS.

A YEAH, MANISH ARORA IS REALLY A STAR IN THIS FIELD IN MANY WAYS BECAUSE HE IS PIONEERING THESE NEW TECHNOLOGIES THAT HE APPLIES TO TEETH AND TO STUDY METALS IN TEETH, AND NOT ONLY TO STUDY METALS IN TEETH, BECAUSE THAT'S BEEN DONE BEFORE, PEOPLE HAVE GROUND UP TEETH FOR A LONG TIME TO LOOK WHAT'S IN THERE, BUT HE ACTUALLY DOES SOME KIND OF MEASUREMENTS WHERE HE KNOWS EXACTLY DURING WHAT TIME OF THE DEVELOPMENTAL PERIOD THAT PART OF THE TOOTH WAS ACTUALLY FORMED, AND THEREFORE, INCLUDES EXPOSURES LIKE LEAD IN THE TOOTH MATERIALS. SO HE CAN ACTUALLY STAGE REALLY WELL WHAT'S HAPPENED AT WHAT TIME PERIOD OF DEVELOPMENT IN CHILDREN, AND THAT'S OF COURSE IN THE TEETH THAT THE KIDS THEN SHED BETWEEN AGE 6 AND 10 OR 12.

AND THE OTHER REALLY IMPORTANT PART ABOUT THE STUDY WAS THAT HE USED THE SWEDISH TWIN REGISTRY AND THAT'S ANOTHER REALLY AMAZING RESOURCE THAT SWEDEN HAS THE KORALINSKA INSTITUTE IS RUNNING.

AND BASICALLY WHAT THEY ARE DOING IS THEY

REGISTER ALL THE TWINS THAT ARE BORN IN SWEDEN, AND BECAUSE THEY HAVE A NATIONAL HEALTH SYSTEM, THEY CAN ACTUALLY FIND THE ONES DIAGNOSED WITH CERTAIN DISORDERS EASILY AND THEN THEY CAN ENROLL THEM IN SPECIAL STUDIES. AND THAT'S WHAT THIS STUDY DID. THEY FOUND THE AUTISTIC DIAGNOSED CHILDREN AND THEY ENROLLED THEM IN THIS STUDY AND ASKED THEM TO HELP THEM BY GIVING THEM THEIR SHED TEETH.

AND SO THAT'S A INCREDIBLY INTERESTING DESIGN BECAUSE BASICALLY YOU HAVE MONOZYGOTIC AND DIZYGOTIC TWINS, MEANING THE INTRAUTERINE ENVIRONMENT WAS EXACTLY THE SAME AND THEN THE EARLY LIFE ENVIRONMENT PROBABLY WAS THE SAME AS WELL. AND YOU HAVE THESE VERY DETAILED MEASURES OF THE EXPOSURES IN THESE CHILDREN ACCORDING TO THIS TOOTH MARKER.

AND THAT'S WHAT HE APPLIED, AND HE FOUND THAT DEFINITELY LEAD IN THE LATE PREGNANCY BUT EVEN MORE IN EARLY INFANCY WAS MUCH HIGHER IN THE AUTISTIC CHILDREN THAN THE SIBLINGS.

Q NOW, LET'S TAKE A LOOK AT THAT STUDY VERY QUICKLY.

IT STATES HERE IN THE INTRODUCTION, IT SAYS, "FETAL AND EARLY CHILDHOOD EXPOSURE TO TOXIC METALS AND DEFICIENCIES OF NUTRITIONAL ELEMENTS HAVE BEEN LINKED WITH SEVERAL ADVERSE DEVELOPMENTAL OUTCOMES FREQUENTLY ASSOCIATED WITH ASD, INCLUDING INTELLECTUAL DISABILITY IN LANGUAGE, ATTENTIONAL AND BEHAVIORAL

PROBLEMS."

THEN HE GOES ON TO TALK ABOUT, "ANIMAL STUDIES HAVE DEMONSTRATED THAT THE EFFECTS OF VARIOUS METALS ON BRAIN DEVELOPMENT COULD BE MEDIATED THROUGH DISREGULATION OF NEUROTRANSMISSION AND ALTERATIONS IN THE FRONTAL AND SUBCORTICAL BRAIN STRUCTURES SEVERAL OF WHICH HAVE ALSO BEEN IMPLICATED IN ASD."

AND SO HE SAYS, "THEREFORE ENVIRONMENTAL AND DIETARY EXPOSURES TO METAL ARE IMPORTANT ETIOLOGICAL FACTORS IN ASD."

LET ME JUST MAKE SURE I UNDERSTAND WHAT THAT MEANS.

"THEREFORE" -- WHAT DOES THAT SENTENCE MEAN?

"THEREFORE ENVIRONMENTAL AND DIETARY EXPOSURES TO METALS ARE POTENTIALLY IMPORTANT ETIOLOGICAL FACTORS."

WHAT DOES THAT MEAN?

A WELL, WHAT HE'S REFERRING TO HERE IS THE EXPERIMENTAL LITERATURE THAT ACTUALLY CAN LOOK AT MECHANISMS IN THE BRAIN, RIGHT. WE CAN OPEN UP ANIMALS' BRAINS AND WE CAN LOOK AT WHAT IS HAPPENING DURING NEURODEVELOPMENT WHEN WE EXPOSE THESE ANIMALS TO METALS AND THAT'S ACTUALLY BEEN DONE EXTENSIVELY, AND SO WE KNOW A LOT ABOUT THESE METALS AND THAT'S WHY I WASN'T SO SURPRISED WHEN I SAW FINALLY THESE STUDIES WHEN I WAS ASKED TO LOOK AT THEM BECAUSE WE KNOW SO MUCH ABOUT WHAT IS ACTUALLY HAPPENING WITH METALS IN THE BRAIN OF

ANIMALS AND WHAT KIND OF DISREGULATION THERE IS.

SO HE'S GOING BACK AS AN EXPERIMENTAL SCIENTIST, AND A REALLY GOOD ONE, HE SAYS, WELL, THIS GIVES ME ENOUGH CLUE TO SAY I HAVE TO LOOK INTO THIS MORE CLOSELY AT ENVIRONMENT BECAUSE THAT'S WHERE THE METAL COMES FROM THERE'S NO, YOU KNOW, WE -- LEAD IS NOT IN THE BODY UNLESS IT GETS IN THERE THROUGH THE ENVIRONMENT, AND POSSIBLY DIETARY EXPOSURES ARE ONE WAY OF GETTING THESE METALS INTO YOUR BODY PROBABLY RELEVANT FOR ASD.

Q YOU GO ON TO STATE OVER HERE, AGAIN, IN THIS INTRODUCTION THAT, "THEY TESTED THE HYPOTHESIS THAT

PRENATAL AND EARLY LIFE EXPOSURE TO METAL TOXICANTS OR DEFICIENCIES OF ESSENTIAL ELEMENTS DURING CRITICAL DEVELOPMENTAL WINDOWS ARE ASSOCIATED WITH ASD."

IT READS, "OUR PRIMARY FOCUS WAS ON LEAD AN ESTABLISHED NEUROTOXICANT THAT HAS BEEN IMPLICATED IN ASD."

DO YOU SEE THAT?

A YES, UM-HMM. YEAH, HE BASICALLY SAYS THAT WE ALREADY KNOW THAT IT'S IMPLICATED IN ASD, BUT WHAT I REALLY WANT TO DO IS KNOW THE TIMING OF THESE EVENTS, AND THEREFORE, THE TEETH ARE A GREAT MATRIX FOR ME BECAUSE I CAN MEASURE WHAT THESE ELEMENTS DO AT SPECIFIC TIME PERIODS IN DEVELOPMENT.

Q EXACTLY.

A AND THAT'S --

Q EXACTLY.

HE SAYS RIGHT HERE. "BOTH THESE ELEMENTS HAVE BEEN ASSOCIATED WITH ATTENTIONAL AND BEHAVIORAL OUTCOMES RELATIVE TO ASD."

SO LET'S GO INTO SEE WHAT HIS ACTUAL CONCLUSIONS WERE AFTER -- I MEAN, WHAT WE KNOW HERE -- AND I JUST THINK THIS IS PRETTY COOL. THEY ACTUALLY HAD A LASER GO INTO THEIR TEETH TO MEASURE THE EXACT TIMING OF EXPOSURES; IS THAT RIGHT?

A YES.

Q AND, DOCTOR, I MEAN, I THINK WHEN YOU HAVE A STUDY LIKE THIS THAT'S THIS SPECIFIC AND THIS DETAILED OF THE AMOUNT OF EXPOSURES THE PARTICIPANTS WERE EXPERIENCING AT THIS EARLY STAGE IN THEIR LIFE, DO YOU HAVE ANY CONCERNS HERE ABOUT REVERSE CAUSATION?

A ABSOLUTELY NOT.

Q WHY IS THAT?

A WELL, BECAUSE THE TOOTH, WE KNOW SO MUCH ABOUT TOOTH DEVELOPMENT AND BIOLOGY, YOU KNOW, WHAT WE KNOW FROM BIOLOGY IS REALLY HARD FACTS, HOW THE TOOTH DEVELOPS AT WHAT POINT OF TIME WHICH LAYER OF THIS TOOTH WAS ACTUALLY FORMED, AND, YEAH, WE MAY BE WRONG A FEW DAYS, BUT WE'RE NOT WRONG MONTHS OR YEARS. AND WE DEFINITELY, WITH THIS KIND OF METHOD, CAN TIME THE EXPOSURE VERY WELL.

Q NOW, DOCTOR, THE DR. ARORA HAS SET UP THIS HYPOTHESIS, HE SAYS THIS IS WHAT WE'RE GOING TO TEST, OKAY, LET'S LOOK AT SEE WHAT THE CONCLUSION OF THAT

HYPOTHESIS WAS.

HE WRITES, "TAKEN TOGETHER THIS SUPPORTS THE HYPOTHESIS THAT PRE-NATAL AND EARLY CHILDHOOD DISRUPTION, EXCESS OR DEFICIENCIES OF MULTIPLE METALS DURING CRITICAL DEVELOPMENTAL PERIODS" -- SORRY -- "DEVELOPMENTAL WINDOWS IS ASSOCIATED WITH ASD AND SUGGESTS A ROLE FOR ELEMENTAL DYSREGULATION IN THE ETIOLOGY OF ASD."

DO YOU SEE THAT?

A YES.

Q SO HE SETS THIS HYPOTHESIS. HE RUNS AN EXPERIMENT AND HE CONCLUDES THAT IT, TAKEN TOGETHER, THAT THAT HYPOTHESIS IS ESTABLISHED, THAT, IN FACT, DURING THESE EARLY DEVELOPMENTAL WINDOWS, IT APPEARS TO BE A RELEVANT TO THE ETIOLOGY OF ASD.

DO YOU SEE THAT?

A YES.

Q WHAT ROLE DOES THIS STUDY WHICH SUFFERS FROM NO ISSUES RELATED TO REVERSE CAUSATION HAVE IN YOUR ANALYSIS?

A WELL, IT WAS ONE OF THE VERY IMPORTANT STUDIES THAT I CONSIDERED AND THAT, YOU KNOW, INFORMED MY OPINION OF CAUSALITY.

Q OKAY. GREAT.

I WANT TO LOOK AT ANOTHER STUDY THAT SPECIFICALLY I MENTIONED EARLIER.

LET'S LOOK AT THE FILON STUDY. THIS IS THAT

CASE CONTROL STUDY THAT WE DISCUSSED A MINUTE AGO.

DO YOU RECALL?

A UM-HMM.

Q OKAY. SO I'M SHOWING HERE EXHIBIT 57.

AND THIS IS, YOU CAN SEE HERE A STUDY BY A DR. FILON, AN ANALYSIS OF LEAD, ARSENIC AND CALCIUM CONTENT IN THE HAIR OF CHILDREN WITH AUTISM SPECTRUM DISORDER.

DO YOU SEE THAT?

A YES.

Q OKAY.

AND THIS IS A CASE CONTROL STUDY. SO THIS IS ONE OF THOSE SITUATIONS -- WELL, EXPLAIN TO US WHAT THEY DID HERE, IF YOU RECALL.

A YEAH, SO WHAT THEY DO HERE IS THEY ASSEMBLE CHILDREN WITH AUTISM FIRST AND THEN THEY MATCH THEM TO A CONTROL POPULATION AND THEY ASK THEM TO SHARE SOME HAIR, SOME MATRIX, IN THIS CASE HAIR, AND THEY THEN APPLIED THE SAME MEASUREMENTS TO THE HAIR OF ALL THE CHILDREN, THE CASES AND CONTROLS, AND THEN COMPARE THE LEVELS IN CASES TO THE LEVELS IN CONTROLS.

Q AND SO WHEN THEY DID THAT AND THEY MEASURED IT, THEY SHOW HERE THAT THE LEAD LEVELS WERE STATISTICALLY SIGNIFICANTLY GREATER IN THE CASE, IN THE AUTISTIC KIDS, THAN IN THE CONTROL GROUP.

DO YOU SEE THAT?

A YES, UM-UM.

Q AND IT LOOKS LIKE IT'S ABOUT DOUBLE OF AMOUNT

OF HAIR LEAD.

DO YOU SEE THAT?

A YES, UM-HMM.

Q AND THEY ALSO ACTUALLY INTERESTINGLY ENOUGH FOUND A STATISTICALLY SIGNIFICANT RESULT FOR ARSENIC AS WELL.

DO YOU SEE THAT?

A YES, CORRECT.

Q AND THAT'S ABOUT THREE AND A HALF TIMES MORE ARSENIC; RIGHT?

A RIGHT.

Q OKAY.

NOW, WHAT I FOUND FASCINATING ABOUT THIS IS IF YOU GO TO THE CONCLUSION -- WELL, LET'S ACTUALLY LOOK AT THE DISCUSSION FIRST.

YOU SEE DOWN HERE THERE'S A DISCUSSION ABOUT LEAD.

DO YOU SEE THAT?

A YES.

Q TALKS ABOUT LEAD BEING ONE OF THE MOST DANGEROUS METALS DUE TO ITS COMMON OCCURRENCE IN THE ENVIRONMENT.

YOU'D AGREE WITH THAT, RIGHT, DOCTOR?

A ABSOLUTELY.

Q IT'S HIGHLY TOXIC, HAS THE ABILITY TO EASILY CROSS BIOLOGICAL BARRIERS AND ACCUMULATES IN THE INTERNAL ORGANS.

YOU AGREE WITH THAT?

A OH, YES, WE HAVE IT ALL IN OUR BONES.
Q "MAY AFFECT THE FUNCTIONS OF BOTH THE CENTRAL AND PERIPHERAL NERVOUS SYSTEMS AS WELL AS THE SENSES."
DO YOU SEE THAT?
A YES. ABSOLUTELY.
Q IT SAYS THAT, "NUMEROUS STUDIES HAVE CONFIRMED THAT EXCESS EXPOSURE TO LEAD RESULTS IN AMONG OTHER THINGS CONVULSIONS, CHANGES OF BRAIN FUNCTIONS AND THEN ENCEPHALOGRAM CHANGES AS WELL ACUTE ENCEPH --
A ENCEPHALOPATHY.
Q THANK YOU.
"AND OTHER BRAIN DISORDERS."
DO YOU SEE THAT, DOCTOR?
A YES, YES.
Q AND IT GOES ON AND ON.
AND THEN ON THE NEXT PAGE IN THIS DISCUSSION IT CONTINUES.
IT SAYS, "THE NERVOUS SYSTEM OF FETUSES AND SMALL CHILDREN SHOW HIGHER SENSITIVITY TO LEAD INTOXICATION COMPARED TO ADULTS."
DO YOU SEE THAT?
A YES.
Q "THIS RESULTS FROM A GREATER SUSCEPTIBILITY OF THE BRAIN TO DISORDERS ESPECIALLY IN THE PERIOD OF FAST GROWTH."
DO YOU SEE THAT?

A YES.
Q ALL RIGHT.
AND THEN IT GOES ON, I MEAN, I'M SHOWING THIS BECAUSE I WANT TO GIVE THE COURT SOME CONTEXT OF WHAT THE CURRENT LITERATURE IS SAYING.
IT SAYS HERE, "IN OUR REACH RESEARCH MEAN ARSENIC AND LEAD CONTENT IN THE HAIR OF CHILDREN WITH ASD WAS STATISTICALLY SIGNIFICANTLY HIGHER COMPARED TO THE MEAN CONTENT OF THESE ELEMENTS IN THE HAIR OF CHILDREN FROM THE CONTROL GROUP. NUMEROUS STUDIES HAVE CONFIRMED THAT HEAVY METALS PLAY A CRUCIAL ROLE IN THE DEVELOPMENT OF AUTISM SPECTRUM DISORDERS."
DO YOU SEE THAT?
A YES.
Q AND THERE'S A BUNCH OF CITATIONS. AND THEN IT GOES ON TO DISCUSS SOME OF THEM LIKE YASUDA AND FIDO AND ASAD.
DO YOU SEE THAT?
A YES.
Q AND THEN AT THE VERY END OF THIS HAVING REVIEWED ALL THAT LITERATURE, THE BIOLOGICAL PLAUSIBILITY, THE AUTHORS OF THIS STUDY STATE:
"NOTWITHSTANDING EVIDENCE LIMITATIONS, THE STUDY SUGGESTS THAT ABNORMAL CONCENTRATIONS OF THE ANALYZED ELEMENTS MAY INDICATE A PATHOPHYSIOLOGICAL ROLE OF HEAVY METALS AND

TRACE ELEMENTS IN THE GENESIS OF SYMPTOMS OF SYMPTOMS OF AUTISM SPECTRUM DISORDER."

DO YOU SEE THAT?

A YES.

Q NOW, DOCTOR, IS IT NORMAL FOR AN EPIDEMIOLOGIST PUBLISHING A CASE CONTROL STUDY LIKE THIS TO REACH SUCH SWEEPING CONCLUSIONS IN ISOLATION?

A NO, THEY WOULDN'T DO IT IN ISOLATION AND THEY WOULDN'T DARE DOING IT UNLESS THERE WAS SO MUCH PREVIOUS EVIDENCE AND THEY WANT TO KIND OF TELL YOU THAT, WELL, NOT ONLY IS THERE SO MUCH EVIDENCE, OUR STUDY IS ACTUALLY RIGHT THERE WITH EVERYBODY ELSE.

Q BETTER WAY TO PUT IT; CONSISTENT?

A IT'S CONSISTENT, YES. AND YOU'RE ALWAYS HAPPY WHEN YOU CAN SAY MY STUDY RESULTS ARE CONSISTENT WITH PREVIOUS LITERATURE, MEANING I HAVE NOT MADE IT UP.

Q NOW, DOCTOR, THIS STUDY, WE LOOKED AT AN EARLIER ONE ON TEETH, AND WE TALKED ABOUT HOW RELIABLE THAT WAS AS A BIOMARKER.

WHAT ABOUT HAIR? IS HAIR A PRETTY RELIABLE BIOMARKER FOR MEASURING PAST EXPOSURES?

A IT IS. IT IS A LITTLE HARDER BECAUSE HAIR CAN BE MORE EASILY CONTAMINATED AND IT DEPENDS ON WHERE ON THE SCALP YOU TAKE THE HAIR OR, YOU KNOW, HOW LONG THE HAIR IS, HOW OLD THE CHILD IS, BUT IT IS ONE OF THOSE MATRICES THAT DEFINITELY TELLS YOU A LITTLE BIT MORE ABOUT THE PAST DEPENDING ON HOW LONG THE HAIR IS, THE SAMPLE IS THAT YOU TAKE, IT TELLS YOU SOMETHING ABOUT

THE PAST EXPOSURE BECAUSE OF COURSE THE LEAD GETS IN THERE WHILE THE HAIR IS GROWING.

Q NOW, YOU SAID IT CAN EASILY GET CONTAMINATED, BUT IS THERE ANY REASON TO BELIEVE THAT THE HAIR OF AUTISTIC CHILDREN WOULD BE CONTAMINATED DIFFERENTLY THAN THE HAIR OF THE NON AUTISTIC CONTROLS?

A ABSOLUTELY NOT. BECAUSE IF THEY BOTH WOULD BE EXPOSED TO THE SAME DUST OR, YOU KNOW, CONCENTRATIONS IN THE ENVIRONMENT, UNLESS THERE IS, YOU KNOW, A -- YOU HAVE TO COME UP WITH SOME REALLY WEIRD REASON WHY THE HAIR IN AUTISTIC -- OF AUTISTIC CHILDREN WOULD BE TREATED DIFFERENTLY FROM THE NON AUTISTIC CHILDREN.

Q AND WHEN YOU DO -- WHEN YOU LOOK AT HAIR HERE AND, LET'S SAY, FOR A SECOND THAT BOTH THE AUTISTIC CHILDREN AND THE NON AUTISTIC CHILDREN HAD SIMILAR AMOUNTS OF LEAD CONTAMINATION OR ARSENIC CONTAMINATION IN THEIR HAIR, WHAT AFFECT WOULD THAT HAVE ON THE RESULTS, IF ANY?

A YOU KNOW, MEANING, IT IS ACTUALLY IN THE HAIR SAMPLE OR THE HAIR SAMPLE IS CONTAMINATED?

Q WELL, I GUESS WHAT I'M TRYING TO SAY IS IF THE HAIR IS -- IF THERE'S EQUAL AMOUNT OF ADDITIONAL LEAD OR METALS IN THE HAIR FOR BOTH THE CASES AND CONTROLS --

A OH, YES.

Q -- WHAT EFFECT DOES THAT HAVE ON THE RESULTS?

A SO IF MY EXPERIMENTER WHO TOOK THE HAIR SAMPLE WAS NOT CAREFUL AND CONTAMINATED THE HAIR, IN THE END I WOULDN'T SEE A DIFFERENCE BECAUSE IT IS A NOISE TO

SIGNAL RATIO, SO IF I CONTAMINATE EVERYTHING, I DON'T SEE THE SIGNAL ANYMORE.

Q AND THAT'S KIND OF GETTING TO WHERE I THINK IT'S REALLY IMPORTANT.

JUST BECAUSE THE RESULT IS NULL, MEANING IT'S NOT SHOWING ANY DIFFERENCE, DOES THAT MEAN THAT THERE'S NO RISK?

A NO. THAT MEANS THAT YOU HAVE TO REALLY LOOK AT HOW WAS IT MEASURED AND, YOU KNOW, WHO MEASURED IT AND IS THERE A CHANCE THAT IN THIS MATRIX THERE IS A PROBLEM LIKE IN HAIR OR URINE THERE MAY BE MORE THAN IN BLOOD, ET CETERA.

Q SO FOR EXAMPLE, WHEN WE LOOK AT THE STUDY CHART HERE, WE'VE LOOKED AT A CASE CONTROL STUDY, WE'VE LOOKED AT A RETROSPECTIVE TOOTH STUDY, WE LOOKED AT A HAIR STUDY.

THE FACT THAT YOU HAVE, FOR EXAMPLE, SOME NEGATIVE STATISTICALLY SIGNIFICANT RESULTS, DOES THAT MEAN THAT THERE'S INCONSISTENCY THAT PREVENTS YOU FROM FINDING CAUSATION?

A NO, IT DOESN'T DO THAT. IT MEANS THAT I HAVE TO LOOK AT THESE STUDIES VERY CAREFULLY AND SEE WHY THEY WOULD TELL ME THAT YOU SHOULD SPRINKLE LEAD ON YOUR CEREAL IN ORDER TO PREVENT AUTISM BECAUSE WE WOULDN'T BELIEVE THAT AS A PRIOR, YOU KNOW, THAT SEEMS KIND OF UNLIKELY.

I'M NOT SAYING THAT THESE STUDIES DID ANYTHING WRONG ON PURPOSE, BUT IT WOULD MAKE ME LOOK CLOSER AT

THEM TO AT LEAST SEE, FIND SOME EXPLANATION FOR WHY THEY SAW STATISTICALLY SIGNIFICANT NEGATIVE RESULTS.

IT COULD JUST BE RANDOM BECAUSE, YOU KNOW, RANDOM THINGS HAPPEN JUST BY CHANCE, BUT IT COULD ALSO MEAN THERE'S A BIAS, AND JUST LIKE I LOOK AT POSITIVE STUDIES CAREFULLY TO FIND A BIAS AND CONVINCE MYSELF WHETHER OR NOT THAT POSITIVE RESULT SHOULD BE TAKEN SERIOUSLY OR NOT, I DEFINITELY LOOK AT THE NEGATIVE ONES IN THE SAME WAY, BUT I DON'T USE THEM AS AN ARGUMENT FOR INCONSISTENCY. THEY IN FACT MAY MAKE THE WHOLE PICTURE MORE CONSISTENT IF I DISCOVER CERTAIN TYPES OF BIASES THAT WOULD EXPLAIN WHY I SEE WHAT I SEE.

Q NOW, DOCTOR, IF I WERE TO JUST WHITE OUT ALL OF THE NONSIGNIFICANT RESULTS AND JUST LOOK AT THE STATISTICALLY SIGNIFICANT RESULTS, WOULD THAT BE A FAIR WAY OF SAYING, WELL, LOOK HOW MANY POSITIVES STUDIES THERE ARE, CLEARLY IT'S CAUSAL?

A NO, WE -- WE DON'T -- WE DON'T ARGUE THAT WAY. I ALWAYS TELL MY STUDENTS DON'T JUST DO STUDY COUNTING. BUT IT IS KIND OF IMPRESSIVE HOW MANY STUDIES IN HOW MANY DIFFERENT PLACES ALL OVER THE WORLD SHOWED POSITIVE RESULTS.

Q AND THAT'S EXACTLY WHAT I WAS GOING TO GET AT, DOCTOR.

WHEN YOU SEE THIS LARGE NUMBER OF DIFFERENT TIME PERIODS, WE HAVE STUDIES HERE IN THE '80S, WE HAVE STUDIES HERE LAKE THE FIDO STUDY, THE FILON STUDY WE JUST LOOKED AT WAS A YEAR AND A HALF OLD.

WHAT DOES THAT TELL YOU AS A SCIENTIST INSOFAR AS -- WELL, LET ME ASK YOU THIS, LET ME ASK YOU A BETTER QUESTION.

WHEN YOU'VE CONCLUDED THAT THERE IS CONSISTENCY IN THE DATA TO SUPPORT CAUSATION, DID YOU USE ANY CONJECTURE OR LEAPS OF LOGIC TO GET THERE?

A I DON'T BELIEVE SO BECAUSE THERE'S SO MUCH EVIDENCE THAT IT'S NOT REALLY NECESSARY TO MAKE ANY CONJECTURES AND LEAPS OF FAITH HERE, I DON'T EVEN HAVE TO GO TO OTHER TYPES OF STUDIES, MECHANISM OR ANIMALS, WHEN I HAVE SO MUCH HUMAN DATA IN FRONT OF ME.

Q NOW, DOCTOR, I WANT TO ASK YOU ONE OTHER QUESTION AND I'M NOT GOING TO PULL IT OUT. I JUST WANT TO ASK YOU ABOUT IT. I WANT TO TALK ABOUT THIS KIM STUDY.

I SEE THAT IT IS A COHORT STUDY IN BLOOD; IS THAT RIGHT?

A YES.

Q AND COULD YOU JUST BRIEFLY DESCRIBE TO THE COURT WHAT THEY DID AND WHAT THEY FOUND.

A YEAH.

SO KIM IS AN INTERESTING STUDY THAT WAS DONE THIS KOREA BY SOME COLLEAGUES OF OURS WHO WENT TO SCHOOLS AND ENROLLED I THINK FROM AT LEAST TEN DIFFERENT CITIES AND EVEN MORE SCHOOLS, SCHOOL CHILDREN AT THE AGE 7 TO 8 AND THEN TOOK BLOOD MEASURES, BLOOD SAMPLES, IN WHICH THEY THEN MEASURED THE BLOOD LEAD LEVELS. AND THEY ASKED THE CHILDREN AT THE BASELINE 7 TO 8 YEARS, OR

BETTER THEIR PARENTS, WHETHER ANY OF THEIR KIDS HAVE BEEN DIAGNOSED WITH AUTISM SPECTRUM DISORDER, AND THOSE KIDS WERE EXCLUDED, SO THEY ONLY WENT WITH THE ONES THAT DID NOT HAVE A DIAGNOSIS AT AGE 7 TO 8.

AND THEY FOLLOWED THEM UP INTO THE FUTURE. THEY TOOK ANOTHER BLOOD SAMPLE WHEN THEY WERE 10 AND THEN ANOTHER BLOOD SAMPLE WHEN THEY WERE ABOUT 12, 11 OR 12.

AND AT THE TIME WHEN THEY WERE 11 OR 12, THEY ALSO ASKED THE PARENTS AGAIN TO REPORT SYMPTOMS ACCORDING TO A VALIDATED SYMPTOM QUESTIONNAIRE FOR AUTISM SPECTRUM DISORDER AND COMPARED THE BLOOD -- AND THEN ANALYZED THE BLOOD LEAD LEVELS FROM THE ORIGINAL BASELINE WHICH WAS IN FIVE, YEAH, ABOUT FIVE YEARS PRIOR TO THE ASSESSMENT BY THE PARENTS OF THE KIDS, AND THEY FOUND THAT THE BLOOD LEAD LEVEL PREDICTED THE OUTCOME ASD BEHAVIOR TYPES VERY WELL AND EVEN AT THE RELATIVELY LOW LEVEL THAT IN THIS REGULAR CHILD POPULATION IN KOREA, ALL OVER KOREA, TEN DIFFERENT CITIES, IT DESCRIBED THE CORRELATION, THE ASSOCIATION BETWEEN THOSE EARLY MEASURES AT 7 TO 8 YEARS AND THE OUTCOMES AT AGE 11/12.

Q SO THE KIM STUDY AND I'M JUST GOING TO POP IT UP REALLY QUICKLY. THIS IS EXHIBIT 87 FOR THE RECORD.

AND THIS IS THE CONCLUSION HERE, IT SAYS:

"EVEN LOW BLOOD LEVEL CONCENTRATIONS AT 7 TO 8 YEARS OLD OF AGE ARE ASSOCIATED WITH MORE AUTISTIC BEHAVIORS AT 11 TO 12 YEARS OF AGE

UNDERSCORING THE NEED FOR CONTINUING EFFORTS TO REDUCE LEAD EXPOSURES."

DO YOU SEE THAT?

A YES.

Q NOW, BECAUSE THIS IS A --

A AND BY THE WAY, THIS IS A STUDY OF THOUSANDS OF KIDS, VERY BIG.

Q SO I GUESS THE QUESTION IS, DOCTOR, I HAVE TWO QUESTIONS HERE, AND THE FIRST IS ARE YOU CONCERNED ABOUT REVERSE CAUSALITY IN THIS STUDY?

A NO.

Q AND THAT'S BECAUSE THEY MEASURED THEIR BLOOD ALONG THE WAY JUST LIKE YOU SAID YOU COULD DO TO SEE IN A COHORT STUDY IF THAT'S WHAT'S HAPPENING; RIGHT?

A RIGHT. AND THEY DIDN'T ONLY MEASURE IT ONCE, THEY MEASURED IT THREE DIFFERENT TIMES AND THEY FOUND THAT IT'S REALLY THESE FIVE YEARS PRIOR THAT WERE PREDICTIVE.

Q OKAY.

NOW, THERE'S TWO OTHER QUESTIONS ABOUT THOSE THAT I THINK WE'VE GOT TO MAKE SURE WE UNDERSTAND.

I MEAN, THE FIRST IS WE'RE TALKING ABOUT 7 AND 8 YEAR OLDS AND THEN FOLLOWING THEM UNTIL THEY ARE 11 AND 12. I MEAN, I THOUGHT BY THAT POINT AUTISM WAS ESTABLISHED AND SET IN STONE. HOW CAN THIS TELL US ANYTHING ABOUT THE EARLIER EXPOSURES AND THE EFFECTS THEY HAVE ON ASD?

A WELL, IT DOESN'T TELL US SOMETHING ABOUT THE

EARLIER EXPOSURES. BUT WHAT IT DOES TELL US IS AUTISM OF COURSE IS A SPECTRUM AND NONE OF THESE CHILDREN THAT AT AGE 11/12 HAD THE AUTISTIC BEHAVIORS WERE REALLY AUTISTIC CHILDREN. BUT WE KNOW, AND IT'S NOW VERY WELL ACKNOWLEDGED, THAT AUTISM IS A SPECTRUM DISORDER AND THAT CERTAIN BEHAVIORS CATEGORIZE -- NOT CATEGORIZE YOU -- THEY PUT YOU CLOSER TO THAT PHENOTYPE OF AUTISM.

SO IF LEAD AT AGE 7/8, AND THAT'S ABOUT THAT TIMING OF EXPOSURE -- AT THE LOW LEVELS THAT IT WAS IN THIS POPULATION HAS AN EFFECT ON THESE KIND OF BEHAVIORS, THAT'S ACTUALLY VERY WORRISOME BECAUSE THE BRAINS AND AS VULNERABLE ANYMORE AS THEY WOULD HAVE BEEN MUCH EARLIER IN LIFE. AND WE ARE STARTING WITH A POPULATION WHERE, YOU KNOW, NONE OF THESE KIDS WAS AUTISM SPECTRUM AT 7 OR 8 BECAUSE THE PARENTS HAD BEEN ASKED ABOUT IT, PLUS THESE ARE NORMAL SCHOOLS. AND ACTUALLY I THINK THE AUTHORS EVEN SAY THAT IN THEIR DISCUSSION THAT REAL AUTISTIC CHILDREN WOULD BE NOT IN THESE TYPES OF SCHOOLS, ENROLLED IN THESE SCHOOLS, SO THE AUTISM BEHAVIOR THEY ARE SHOWING IS HIGHLY FUNCTIONAL, THEY ARE AT THE VERY FUNCTIONAL END OF AUTISM.

BUT EVEN AT THAT AGE YOU CAN SEE LEAD EFFECTS AT THE LOW LEVELS OF LEAD AND THAT'S REALLY WORRISOME.

Q IF THEY ARE TELLING THAT LOW LEVELS OF LEAD CAN INDUCE AUTISTIC BEHAVIORS AT THIS LATER STAGE IN BRAIN DEVELOPMENT --

A RIGHT.

Q -- DOES THAT INFORM YOUR ANALYSIS OF WHAT KIND OF LEAD EXPOSURES WHEN YOU'RE SIX MONTHS YEAR OLD WOULD HAVE?

A ABSOLUTELY. I MEAN, WE KNOW THAT YOU'RE MUCH MORE VULNERABLE TO TOXINS, TO NEUROTOXINS AT AN EARLIER AGE, AND YOU KNOW, IF YOU SEE THOSE IN 7 TO 8 YEAR OLDS, THEN YOU'RE DEFINITELY WORRY MORE ABOUT THE YOUNGER KIDS AND THEIR EXPOSURES.

Q ALL RIGHT. WE'RE RUNNING OUT OF TIME QUICKLY, SO I WANT TO -- SORRY, THAT WAS THE WRONG EXHIBIT. I WANT TO GO BACK TO THE HILL FACTORS. I WANT TO TALK ABOUT TEMPORALITY VERY QUICKLY. I THINK WE'VE COVERED IT MOSTLY ALREADY, AND THEN I WANT TO FINISH UP ON ADHD WHICH SHOULDN'T TAKE TOO LONG.

SO IF WE GO BACK TO THE HILL ARTICLE AND WE GO TO THE TEMPORALITY CRITERIA, IT STARTS HERE AT THE BOTTOM.

HE WRITES, "MY FOURTH CHARACTERISTIC IS THE TEMPORAL RELATIONSHIP OF THE ASSOCIATION, WHICH IS THE CART AND WHICH IS THE HORSE? THIS IS A QUESTION WHICH MIGHT BE PARTICULARLY RELEVANT WITH DISEASES OF SLOW DEVELOPMENT, DOES A PARTICULAR DIET LEAD TO DISEASE OR TO THE EARLY STAGES OF DISEASE LEAD TO THOSE PARTICULAR DIETARY HABITS?

DOES A PARTICULAR OCCUPATION OR OCCUPATIONAL ENVIRONMENT PROMOTE INFECTION BY THE TUBERCULOBACULUS OR ARE THE MEN AND WOMEN WHO

SELECT THAT KIND OF WORK MORE LIABLE TO CONTRACT TUBERCULOSIS, WHATEVER THE ENVIRONMENT OR INDEED HAVE THEY ALREADY CONTRACTED IT? THIS TEMPORAL PROBLEM MAY NOT ARISE OFTEN, BUT IT CERTAINLY NEEDS TO BE REMEMBERED, PARTICULARLY WITH SELECTIVE FACTORS AT WORK IN INDUSTRY."

DO YOU SEE THAT, DOCTOR?

A YES.

Q AND HERE IN YOUR REPORT YOU STATE, AND I'LL JUST PULL IT UP SINCE WE CAN KEEP IT -- KEEP THE RECORD CLEAR.

YOU WRITE: "TEMPORALITY. THAT DISEASE OCCURRED AFTER EXPOSURE AND THAT THERE'S AN EXPECTED DELAY BETWEEN THE CAUSAL FACT HAS ALSO BEEN REPORTED, I.E., EXPOSURES WERE ASSESSED AND RECORDED FOR EARLY INFANCY IN BABY TEETH."

THAT'S THE ARORA STUDY; RIGHT?

A RIGHT.

Q AND THE KOREAN CHILD COHORT STUDY AND THE NORWEIGIAN MOBA COHORT.

DO YOU SEE THAT?

A YES.

Q BECAUSE YOU'VE SEEN STUDIES THAT SHOW TEMPORALITY AND WHEN YOU COMBINE THAT WITH THIS VERY LARGE DATA OF OTHER STUDIES, DO YOU BELIEVE AS AN EPIDEMIOLOGIST THAT THE TEMPORALITY REQUIREMENT IS SATISFIED?

A YES. AND THAT'S WHY I SAID IT IN THIS WAY. IF I HAD ONLY HAD THE CASE CONTROL STUDIES, I WOULD PROBABLY NOT HAVE BEEN CONVINCED. BUT GIVEN THE CASE STUDIES, GIVEN THE COHORT STUDIES, I THINK WE HAVE A VERY CLEAR AND VERY CONSISTENT PICTURE ON TEMPORALITY.

Q NOW, WE DISCUSSED PICA ALREADY.

I WANT TO SHOW YOU A STUDY.

THIS IS EXHIBIT 15. THE ADAMS STUDY FROM 2006.

DO YOU SEE THAT, DOCTOR?

A YES.

Q AND IF WE GO DOWN HERE THEY ACTUALLY MEASURED THE HAIR OF CHILDREN WITH AUTISM VERSUS CONTROL.

DO YOU SEE THAT?

A YES.

Q AND THEY DID A PICA SUB GROUP ANALYSIS.

DO YOU SEE THAT?

A YES. BEAUTIFUL.

Q AND RIGHT HERE WE HAVE LEAD. THAT'S PB; RIGHT?

A RIGHT.

Q AND THEY COMPARED THE AVERAGE AMOUNT OF LEAD FOUND IN CHILDREN WITH -- AUTISTIC CHILDREN WITH PICA VERSUS AUTISTIC CHILDREN WITHOUT PICA TO SEE HOW MUCH LEAD WAS IN THEIR SYSTEMS.

DO YOU SEE THAT?

A YES.

Q AND HERE IT SHOWS A VERY SLIGHT DIFFERENCE BETWEEN THEM.

DO YOU SEE THAT?

A YES.

Q THEY ARE DEFINITELY NOT STATISTICALLY SIGNIFICANT; RIGHT?

A NO. AND IF IT WERE STATISTICALLY SIGNIFICANT, THEY WOULD HAVE TOLD YOU BECAUSE THEY DID A T TEST FOR PICA VERSUS CONTROLLED.

Q RIGHT.

A YEAH. AND THEY SAW THAT FOR ARSENIC AND URANIUM BUT NOT FOR LEAD.

Q YEAH. IN FACT, FOR ARSENIC CHILDREN WITH PICA HAD STATISTICALLY SIGNIFICANT LESS ARSENIC IN THEIR SYSTEM THAN THE NON PICA KIDS.

DO YOU SEE THAT?

A YES.

Q AND THIS DATA IS OBVIOUSLY JUST ONE STUDY, BUT DOES THIS STUDY ADD TO THE WEIGHT OF EVIDENCE WE'VE ALREADY DISCUSSED REGARDING WHETHER OR NOT PICA IS EXPLAINING ALL OF THIS DATA?

A YES. ABSOLUTELY.

I MEAN, THIS IS A BRILLIANT APPROACH THAT THESE AUTHORS TOOK BY, YOU KNOW, ASKING ABOUT PICA AND THEN DOING EXACTLY THE KIND OF COMPARISON THAT YOU WOULD CALL A SENSITIVITY ANALYSIS TO SEE WHETHER IT IS REALLY PICA THAT INCREASES THE LEVEL OF LEAD VERSUS HAVING NOTHING TO DO WITH THE LEAD LEVELS.

Q DO YOU THINK IT'S APPROPRIATE, DOCTOR, TO SPECULATE ABOUT POTENTIAL REVERSE CAUSATIONS THAT DON'T HAVE ANY SUPPORT IN THE EVIDENCE?

A WELL, YOU CAN ALWAYS SPECULATE AND YOU CAN ALWAYS QUESTION. AND, YOU KNOW, AS EPIDEMIOLOGISTS WE ALWAYS QUESTION. THAT'S NOT A -- THAT'S NOT A SIN. IT'S ACTUALLY A VIRTUE. BUT YOU THEN USE YOUR DATA TO FIND AN ANSWER.

AND THAT'S WHAT THESE AUTHORS HAVE ACTUALLY DONE. THEY CONSIDERED THE QUESTION OF PICA. THEY DID THIS SUB ANALYSIS OF PICA CHILDREN VERSUS NON PICA AND THEY GOT THEIR ANSWER AND I REALLY APPLAUD THEM FOR THAT.

Q ALL RIGHT. DOCTOR, I REALLY APPRECIATE GOING THROUGH ALL OF THAT. WE'VE COVERED YOUR METHODOLOGY. WE'VE COVERED LEAD AND ASD. I DO WANT TO DO A FINAL QUESTION ON THAT AT THE END OF YOUR TESTIMONY.

I WANT TO QUICKLY COVER LEAD AND ADHD IN THE LAST FEW MINUTES THAT WE HAVE HERE, AND THEN I'LL PROBABLY HAVE YOU COME BACK TOMORROW MORNING AND WE'LL WRAP YOU UP; OKAY?

A OKAY.

Q ALL RIGHT. SO HERE'S THE CHART FOR LEAD AND ADHD THAT WE PUT TOGETHER.

DO YOU SEE THAT, DOCTOR?

A YES.

Q WHAT IS THE FIRST THING THAT YOU OBSERVED ON THIS CHART?

A WELL, WE HAVE LOTS OF BLOOD STUDIES AND LOTS OF POSITIVE AND STATISTICALLY SIGNIFICANT RESULTS AND NONE THAT ARE IN THE NEGATIVE STATISTICALLY SIGNIFICANT

COLUMN.

AND FROM WHAT I SEE A LOT OF THESE STUDIES ARE FROM GOOD OLD COLLEAGUES OF MINE.

Q I SEE HERE THERE'S ALSO QUITE A FEW COHORT STUDIES.

DO YOU SEE THAT?

A YES. ABSOLUTELY. UM-HMM.

Q YOU HAVE KANDOR MOLLY, THE HAUS STUDY, THE G STUDY, PROBABLY THE KANDOR MOLLY, THE HAU, THE G STUDY.

DO YOU HAVE ANY CONCERNS AS IT RELATED TO LEAD AND ADHD OF TEMPORALITY?

A ABSOLUTELY NOT BECAUSE THERE WERE MULTIPLE COHORT STUDIES THAT CLEARLY ESTABLISHED TEMPORALITY FOR ADHD. HAVING BLOOD STAMPS SAMPLES FROM EARLY LIFE, DOING MULTIPLE BLOOD SAMPLES ACROSS DIFFERENT PERIODS OF EARLY LIFE AND THEN ASSESSING THE OUTCOME LATER IN LIFE.

Q WHAT ABOUT CONSISTENCY HERE? DO YOU SEE ANY ISSUES WITH CONSISTENCY HERE?

A NO, THIS IS ONE OF THE MOST CONSISTENT CHAPTERS OF RESEARCH THAT YOU CAN IMAGINE.

Q WHY DO YOU SAY THAT?

A BECAUSE THERE'S SO MANY STUDIES ALL, YOU KNOW, DIFFERENT DESIGN TYPES, DIFFERENT TIME PERIODS, DIFFERENT COUNTRIES, DIFFERENT TYPES OF LEAD EXPOSURE FROM A SMELTER COMMUNITY IN AUSTRALIA TO KOREA TO NORTH AMERICA TO EUROPE.

YOU COULDN'T WISH FOR MORE CONSISTENCY IN THE RESULTS.

Q NOW, DOCTOR, I WANT TO ASK YOU ABOUT A CONCEPT IN EPIDEMIOLOGY.

NOW, YOU UNDERSTAND THAT ADHD IS A DISORDER, A DISEASE OR DISORDER THAT IS VERY HIGHLY ALSO ASSOCIATED WITH ASD; RIGHT?

A IN FACT, THERE'S A SUB TYPE OF ASD THAT HAS ADHD FEATURES, YES. IT'S WELL KNOWN.

Q AND WHEN YOU, FROM AN EPIDEMIOLOGICAL STANDPOINT, WHEN YOU START NARROWING AND SPECIFYING AND CHARACTERIZING THE DISEASE OUTCOME, AUTISM SPECTRUM DISORDER IS A PRETTY WIDE SPECTRUM, BUT WHEN YOU START NARROWING ON A SPECIFIC TYPE OF SUBTYPE, WHAT TYPICALLY HAPPENS IF THERE IS IN FACT A RISK THERE? WHAT DO YOU SEE IN THE DATA?

A WELL, IT'S EVEN MORE CONSISTENT BECAUSE IT TELLS YOU THAT THE SAME BRAIN STRUCTURES THAT, YOU KNOW, AFFECT AUTISM AND POSSIBLY THE ADHD SUB TYPE OF AUTISM ALSO AFFECTS THE DISEASE ALONE ADHD BECAUSE IT'S THE SAME BRAIN STRUCTURES, RIGHT. SO YOU WOULD EXPECT LEAD TO AFFECT THESE BRAIN STRUCTURES WHETHER THE CHILD ALSO HAS AUTISTIC FEATURES OR ONLY HAS ADHD.

Q WELL, WHEN DR. HILL TALKED ABOUT DIFFERENT PERSONS, DIFFERENT PLACES, DIFFERENT CIRCUMSTANCES AND DIFFERENT TIMES, YOU ALSO HAVE IT HERE IN RELATED DISEASES, DON'T YOU?

A ABSOLUTELY. SO IF I KNOW THAT CERTAIN BRAIN STRUCTURES CONTRIBUTE TO DIFFERENT TYPES OF DISEASES, THEN I WOULD EXPECT TO FIND THE EXPOSURE OR TO SEE THAT

THE EXPOSURE ACTUALLY AFFECTS THESE DIFFERENT TYPES OF DISEASES IN SAME WAY.

THE EASIEST EXAMPLE IS CANCER AND SMOKING. WE ALL KNOW THAT CANCER CAUSES -- THAT CANCER OF THE LUNG IS CAUSED BY SMOKING, BUT WE ALSO KNOW THAT IT'S CAUSING CERVICAL CANCER AND BLADDER CANCER, AND SO -- AND, YOU KNOW, MOUTH AND THROAT CANCER AND IT'S THE SAME KIND OF PROCESS OF CARCINOGENICITY THAT IS CAUSED BY THE AGENTS AND SMOKING THAT I SEE IN DIFFERENT PARTS OF THE BODY CAUSING THESE DIFFERENT TYPES OF CANCERS, IT'S THE SAME IN THE BRAIN.

IF LEAD AFFECTS CERTAIN TYPES OF STRUCTURES IN THE BRAIN, MAYBE AT DIFFERENT DEVELOPMENTAL PERIODS OR AT A DIFFERENT LEVEL OR ACCORDING TO DIFFERENT GENETIC SUSCEPTIBILITIES OF THESE INDIVIDUALS, I MAY SEE ONE PHENOTYPE OVER THE OTHER, BUT I WOULD EXPECT TO SEE IT ACROSS DIFFERENT PHENOTYPES THAT ARE ALL AFFECTED BY THIS BRAIN STRUCTURE'S WORKINGS.

Q WELL, THANK YOU VERY MUCH, DOCTOR. I HAVE A FEW THINGS LEFT THAT I WANT TO COVER. IT SHOULDN'T TAKE MORE THAN FIVE TO TEN MINUTES, BUT I'VE BEEN GOING THROUGH MY NOTES, YOUR HONOR, AND SPECIFYING IT AND WILL STREAMLINE IT, SO I THINK THIS WOULD BE A GOOD TIME TO BREAK FOR THE DAY.

THE COURT: BUT LET'S TALK ABOUT TOMORROW BECAUSE I HAVE US ON IN THE AFTERNOON ONLY.

MR. WISNER: THAT'S CORRECT.

THE COURT: OKAY. YOU SAID TOMORROW MORNING

WHEN YOU WERE TALKING EARLIER.

MR. WISNER: OH, I'M SORRY.

THE COURT: OKAY. I JUST WANT TO MAKE SURE THAT WE'RE ALL --

MR. WISNER: WE'RE ALL BLENDING TOGETHER, YES, AT 1:30 TOMORROW, YES.

THE COURT: SO I HAVE IT AT 1:30.

IS THERE ANY OTHER HOUSEKEEPING OR OTHER BUSINESS WE NEED TO TAKE UP TODAY?

MR. IMBROSCIO: JUST ONE FOR ME, YOUR HONOR. THIS IS MR. PETROSINELLI.

MR. WISNER: SHOULD WE EXCUSE THE WITNESS OR DOES IT MATTER?

MR. IMBROSCIO: IT DOESN'T MATTER TO ME.

MR. WISNER: OKAY.

MR. IMBROSCIO: WHATEVER YOU WANT.

MR. WISNER: ALL RIGHT.

MR. IMBROSCIO: TWO QUESTIONS, YOUR HONOR.

ONE IS NORMALLY IF WE WERE THERE IN PERSON WE WOULD HAVE HANDED YOU, BOTH SIDES, WOULD HAVE HANDED YOU SLIDE DECS OF OUR OPENINGS. WOULD YOU LIKE TO US SEND YOU THE OPENING SLIDES?

THE COURT: SURE.

MR. IMBROSCIO: AND THE SECOND QUESTION IS THE DEMONSTRATIVES THAT WERE USED JUST NOW WITH DR. RITZ, AGAIN, IF WE WERE IN COURT TOGETHER, I WOULD HAVE BEEN HANDED A COPY OF THOSE. I DON'T HAVE A COPY OF THOSE AND I WONDER WHETHER PLAINTIFF'S COUNSEL COULD SEND

THOSE TO ME AFTER WE BREAK FOR THE DAY.

MR. WISNER: YES.

THE COURT: YEAH, I THINK EVERYTHING THE COURT HAS SEEN NEEDS TO GO INTO THE COURT FILE AND NOT JUST CASE ANYWHERE OR AN INFORMAL SUBMISSION, WE NEED TO BE TRANSPARENT IN ALL WAYS.

MR. IMBROSCIO: THANK YOU, YOUR HONOR.

MR. WISNER: SO, YOUR HONOR, I THINK THE PLAN IS --

THE COURT: YES.

MR. WISNER: AND YOU CAN TELL US HOW YOU PREFER THIS.

SO OUR PROPOSAL WAS WE'RE GOING TO GO THROUGH THIS HEARING WITH ALL THE EXHIBITS, WE'RE GOING TO KEEP STUDIOUS NOTES AND AGREEMENTS ON WHAT WAS USED AND WHAT WASN'T, AND THEN WE'RE GOING TO AT THE END OF IT PUT IT ALL TOGETHER BECAUSE THERE'S HUNDREDS OF EXHIBITS, WE'RE NOT GOING TO USE THEM ALL, WHAT'S ACTUALLY USED AND THEN SUBMIT IT TO THE COURT AND FILE IT UNDER THE RECORD. I THINK THAT'S THE PLAN. IF YOU WANTED TO SEE THEM SOONER, WE COULD HAVE THEM DELIVERED TO YOU IN THE MORNING AT THE END OF EACH DAY IF YOU PREFER. IT'S UP TO YOU.

THE COURT: I DON'T THINK NECESSARY. FROM YOUR EARLIER SUBMISSIONS, I SEE THAT I HAVE MANY OF THE STUDIES.

MR. WISNER: RIGHT.

THE COURT: AND I COULD FIND IT IF I WERE

LOOKING FOR IT AND I DID SKIM THROUGH SOME OF THEM YESTERDAY. THAT SOUNDS FINE TO ME.

MR. WISNER: ON THE OTHER ISSUE OF SHARING DEMONSTRATIVES, I THINK PROVIDED WE ALL AGREE TO SHARE, I THINK WE'RE IN GOOD SHAPE, MR. PETROSINELLI. I'LL SHARE MY POWERPOINT AND SEND THEM OVER TO YOU, THAT WOULD BE GREAT.

MR. IMBROSCIO: YES, THANK YOU.

THE COURT: OKAY.

MR. WISNER: SURE.

THE COURT: WELL, I APPRECIATE THE WORK THAT WENT INTO THIS AND THE HIGH LEVEL OF ADVOCACY. AND I'LL LOOK FORWARD TO TOMORROW TO SEE YOU AT 1:30.

MR. WISNER: THANK YOU, YOUR HONOR. THANK YOU FOR YOUR TIME.

THE WITNESS: THANK YOU.

MR. IMBROSCIO: THANK YOU, YOUR HONOR.

THE COURT: THANKS, EVERYBODY.

{TIME NOTED: 4:33 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 3RD DAY OF FEBRUARY, 2022.

JEANESE JOHNSON, CSR NO. 11635, CLR
CERTIFIED STENOGRAPHIC REALTIME REPORTER
OFFICIAL REPORTER PRO TEMPORE

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