Summary of highlights of scientific review of safety datalink information

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Abstract

A meeting was convened by the Centers for Disease Control and Prevention (CDC) to discuss the findings of Dr. Thomas Verstraeten relating to the positive statistical association between Thimerosal-containing vaccines and neurodevelopmental disorders. There were 51 scientists and physicians in attendance, including Dr. Howe of Smith-Kline Beecham, Dr. Guess of Merck, Dr. Blum of Wyeth, and Dr. White of North American Vaccine.

One of the concluding speakers, Dr. Clements on Page 247 concludes: "I am really concerned that we have taken off like a boat going down one arm of the mangrove swamp at high speed, when in fact there was not enough discussion really early on about which way the boat should go at all. … I know how we handle it from here is extremely problematic. The ACIP (Advisory Committee on Immunization Practices) is going to depend on comments from this group in order to move forward into policy, and I have been advised that whatever I say should not move into the policy area because that is not the point of this meeting. … But that pure science has resulted in splitting the atom or some other process which is completely beyond the power of the scientists who did the research to control it. And what we have here is people who have, for every best reason in the world, pursued a direction of research. But there is now the point at which the research results have to be handled, and even if this committee decides that there is no association and that information gets out, the work that has been done and through the freedom of information that will be taken by others, will be used in ways beyond the control of this group. And I am very concerned about that as I suspect it is already too late to do anything regardless of any professional body and what they say.…"

The transcript of this meeting was finally obtained through the Freedom of Information Act, despite the fact that each page of the transcript was stamped "DO NOT COPY OR RELEASE" and "CONFIDENTIAL."

Keywords: Thimerosal, neurodevelopmental disorders, vaccines

Attendees: 51 scientists and physicians
Of special interest:
Dr. Howe: Smith-Kline Beecham;
Dr. Guess: Merck;
Dr. Blum: Wyeth;
Dr. White: North American Vaccine.

A meeting was convened by the Centers for Disease Control and Prevention (CDC) to discuss the findings of Dr. Thomas Verstraeten relating to the positive statistical association between Thimerosal-containing vaccines and neurodevelopmental disorders.

Dr. Bernier: Page 12 "In the United States there was a growing recognition that cumulative exposure [to Thimerosal in vaccines] may exceed some of the guildlines [established by regulatory agencies including the Agency for Toxic Substances and Disease Registry (ATSDR), the FDA, and the Environmental Protection Agency]."

Dr. Johnston: Page 20 "…there is absolutely no data including animal data, about the potential for synergy, additivity or antagonism, all of which can occur in binary metal mixtures that relate and allow us to draw any conclusions from the simultaneous exposure to these two salts in vaccines."

Dr. Clarkson: Page 21: "There is an issue that pharmacokinetics might be different too. Again this is all animal work, but the animal studies suggested, for example, a suckling animal does not eliminate methylmercury until the end of the suckling period, and there is a mechanism on the study for that. So there could be an age difference in the excretion rates."

Dr. Rapin: Page 22: "I don't know if anyone has looked at the literature of old Pinks disease which was present in the twenties or thirties when mothers wore shields that contained mercury." (Editorial comment: it was a teething powder that was rubbed on the baby's gums)

Dr. Weil: Page 24: "One, up until this last discussion we have been talking about chronic exposure. I think it's clear to me anyway that we are talking about a problem that is probably more related to bolus acute exposures, and we also need to know that the migration problems and some of the other developmental problems in the central nervous system go on for quite a period after birth. But from all of the other studies of toxic substances, the earlier you work with the central nervous system, the more likely you are to run into a sensitive period for one of these effects, so that moving from one month or one day of birth to six months of birth changes enormously the potential for toxicity. There are just a host of neurodevelopmental data that would suggest that we've got a serious problem. The earlier we go, the more serious the problem.

The second point I could make is that in relationship to aluminum, being a nephrologist for a long time, the potential for aluminum and central nervous system toxicity was established by dialysis data. To think there isn't some possible problem here is unreal."

Dr. Verstraeten: Page 31: " It is sort of interesting that when I first came to the CDC as a NIS officer a year ago only, I didn't really know what I wanted to do, but one of the things I knew I didn't want to do was studies that had to do with toxicology or environmental health. Because I thought it was too

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much confounding and it's very hard to prove anything in those studies. Now it turns out that other people also thought that this study was not the right thing to do, so what I will present to you is the study that nobody thought we should do."

Dr. Verstraeten: Page 40: "..we have found statistically significant relationships between the exposures and outcomes for these different exposures and outcomes. First, for two months of age, an unspecified developmental delay, which has its own specific ICD9 code. Exposure at three months of age, Tics. Exposure at six months of age, an attention deficit disorder. Exposure at one, three and six months of age, language and speech delays which are two separate ICD9 codes. Exposure at one, three and six months of age, the entire category of neurodevelopmental delays, which includes all of these plus a number of other disorders."

Dr. Verstraeten: Page 42: "But one thing that is for sure, there is certainly an under-ascertainment of all of these because some of the children are just not old enough to be diagnosed. So the crude incidence rates are probably much lower that what you would expect because the cohort is still very young."

Dr. Verstraten: Page 44: "Now for speech delays, which is the largest single disorder in this category of neurologic delays. The results are a suggestion of a trend with a small dip. The overall test for trend is highly statistically significant above one."

Dr. Verstraten: Page 45: "What this represents is the overall category of developmental delays, of which I have excluded speech delays because of the impression we had was some of the calculations were driven by this speech group, which was making up about half of this category. After excluding this speech group, the trend is also apparent in this group and the test for trend is also significant for this category excluding speech."

Dr. Weil: Page 75: "I think that what you are saying is in term of chronic exposure. I think that the alternative scenario is that this is repeated acute exposures, and like many repeated acute exposures, if you consider a dose of 25 micrograms on one day, then you are above threshold. At least we think you are, and then you do that over and over to a series of neurons where the toxic effect may be the same set of neurons or the same set of neurologic processes, it is conceivable that the more mercury you get, the more effect you are going to get."

Dr. Verstraeten: Page 76: "What I have done here, I am putting into the model instead of mercury, a number of antigens that the children received, and what do we get? Not surprisingly, we get very similar estimates as what we got for Thimerosal because every vaccine put in the equation has Thimerosal. So for speech and the other ones maybe it's not so significant, but for the overall group it is also significant….Here we have the same thing, but instead of number of antigens, number of shots. Just the number of vaccinations given to a child, which is also for nearly all of them significantly related."

Dr. Guess: Page 77: So this essentially is a 7% risk per antigen, in a vaccine like DPT you've got three antigens."

Dr. Verstraten: Page 77: "Correct."

Dr. Egan: Page 77: "Could you do this calculation for aluminum?"

Dr. Verstraeten: Page 77: "I did it for aluminum…Actually the results were almost identical to ethylmercury because the amount of aluminum goes along almost exactly with the mercury one."

Dr. Verstraeten: Page 78: "Then the last slide I wanted to show, there was a question concerning if there was any way from this data that we could estimate what would happen in the future if there is Thimerosal-free HepB and Thimerosal-free haemophilus influenza vaccine and only DTP has Thimerosal." Page 79 "The second column would be the same scenario but now at six months. Assuming they have received two additional DTPs, so between three and six months of age they have increased their ethylmercury amounts by 50 micrograms. If I do in this current cohort with all its limitations, because there is also the Hep B that exists in this cohort*, I can't really take it out. It is significant for this one disorder which is language delay and it is quite high. Together with that, speech or language delay which is a combination of these two disorders, also becomes significant." *Dr. Verstraeten could not determine which children got Hep B at birth in some cases so it was difficult to back the birth dose of Hep B out of the data.

Dr. Davis: Page 85: "Now in terms of a search for predisposing factors, this is actually going to be important in what I will talk about tomorrow, but I will mention it today and put a little seed in your mind. Which is that serious and chronic otitis media, by history being mentioned by the pediatrician or the specialist, was present 38% of the time."

Dr. Bernier: Page 113: "We have asked you to keep this information confidential. We do have a plan for discussing these data at the upcoming meeting of the Advisory Committee on Immunization Practices on June 21 and June 22. At that time CDC plans to make a public release of this information, so I think it would serve all of our interests best if we could continue to consider these data. The ACIP work group will be considering also. If we could consider these data in a certain protected environment. So we are asking people who have a great job protecting this information up until now, to continue to do that until the time of the ACIP meeting. So to basically consider this embargoed information. That would help all of us to use the machinery that we have in place for considering these data and for arriving at policy recommendations."

Dr. Brent: Page 130: "Dr. Jones brought up a suggestion when we were talking in the coffee break. The collaborative perinatal project had 50,000 parents. The registered them right from the beginning of pregnancy and then they followed them very closely. It was subsidized. Probably all of these children had DTP. Was mercury in the DTP in the fifties and sixties? Well, that is still on the computer and available to you. One of the things I have been taught about Epidemiology is repetition. In other words, if you could get another body of patients and demonstrate the same thing, it makes it more convincing."

Dr. Verstraeten: Page 131: "I would be the first person to try and analyze that. I have been asking all over if there is another data set I could look at and try to replicate it in a very oriented manner without doing another, analysis."

Dr. Brent: Page 131: "Well, it's on the eleventh floor of the Archives Building in Washington, D.C. and certainly any government employee would have access to that data"

Dr. Verstraeten: Page 131: "So what we want to avoid is multiple comparisons just for the specific outcomes that we are interested in. That's one and then at the same time at the U.K.,

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there is another data set of General Practitioners, where we have asked them if they can replicate our findings there. So we are waiting for those results."

Dr. Verstraeten: Page 142: "But if I can have the next slide, here instead of the proportional hazard model, we did a logistic regression model. I didn't use person time here and it's a bit tough to define exactly the control group. However, if I do it for all ages and not looking at different years, and this is for speech, the outcome is almost identical to the proportional hazard model, which suggests to me that it is not a question of bringing the diagnosis forward, but it is really the overall number that drives this estimate."

Dr. Rapin: Page 143: "I would like to make a comment. We have been focusing on all these acquired causes including mercury and prematurity, and you had a list of confounding variables that should be considered in future studies. What we know today about all of the developmental disorders is that environmental factors are in fact rather unimportant in the case of these deficits and the major cause is genetic…I find it a little difficult knowing this and putting in autism. The major cause is not environmental, it is genetic and that we are focusing just on these environmental events or adventitious events when we haven't considered, and you told us that you don't have data for example on siblings, your study does not lend itself to considering the major variable."

Dr. Johnson: Page 144: "Well, I think the assumption is that those genetic predispositions would be randomly distributed".

Dr. Rapin: Page 144: "But you don't know that."

Dr. Johnson: Page 144: "No, that's an interlining assumption".

Dr. Rapin: Page 144: "I understand that, but you don't know that".

Dr. Johnson: Page 144: "Just on principle, Dr. Rapin, it seems to me that the more we learn about genetics or the more we learn about let's say autism, the more we shift towards focusing on genetic causes, but would you rule out the possibility, and let's move away from autism, that some of these are genetic predisposition and then the second hit?"

Dr. Rapin: Page 144: "Not at all. I think that it is in fact an attractive hypothesis".

Dr. Johnson: Page 145: "Right, thank you."

Dr. Chen: Page 151: "One of the reasons that led me personally to not be so quick to dismiss the findings was that on his own Tom independently picked three different outcomes that he did not could be associated with mercury and three out of three had a different pattern across different exposure levels as compared to the ones that again on a priority basis we picked as biologically plausible to be due to mercury exposure."

Dr Brent: Page 161: "Wasn't true that if you looked at the population that had 25 micrograms you had a certain risk and when you got to 75 micrograms you had a higher risk."

Dr. Verstraeten: Page 161: "Yes, absolutely, but these are all at the same time. Measured at the same age at least."

Dr. Brent: Page 161: "I understand that, but they are different exposures."

Dr. Verstraeten: Page 161: "Yes".

Dr. Brent: Page 161: "What is your explanation? What explanations would you give for that?"

Dr. Verstraeten: Page 161: "Personally, I have three hypotheses. My first hypotheses is it parental bias. The children that are more likely to be vaccinated are more likely to be picked up and diagnosed. Second hypothesis, I don't know. There is a bias that I have not recognized, and nobody has yet told me about it. Third hypothesis. It's true, it's Thimerosal. Those are my hypotheses."

Dr. Brent: Page 161: "If its true, which or what mechanisms would explain the finding with?"

Dr. Verstraeten: Page 162: "You are asking for biological plausibility?"

Dr. Brent: Page 162: "Well, yes"

Dr. Verstraeten: Page 162: "When I saw this, and I went back through the literature, I was actually stunned by what I saw because I thought it is plausible. First of all there is the Faeroe study, which I think people have dismissed too easily, and there is a new article in the same Journal that was presented here, the Journal of Pediatrics, where they have looked at PCB. They have looked at other contaminants in seafood and they have adjusted for that, and still mercury comes out. That is one point. Another point is that in many of the studies with animals, it turned out that there is quite a different result depending on the dose of mercury. Depending on the route of exposure and depending on the age at which the animals were exposed. Now, I don't know how much you can extrapolate that from animals to humans, but that tells me mercury at one month of age is not the same as mercury at three months, at 12 months, prenatal mercury, later mercury. There is a whole range of plausible outcomes from mercury. On top of that, I think that we cannot so easily compare the U.S. population to Faeroe or Seychelles populations. We have different mean levels of exposure. We are comparing high to high in the Seychelles, high to high in the Faeroe and low to low in the U.S., so I am not sure how easily you can transpose one finding to another one. So basically to me that leaves all the options open, and that means I can not exclude such a possible effect."

Dr. Brent: Page 191: "Finally, the thing that concerns me most, those who know me, I have been a pin stick in the litigation community because of the nonsense of our litigious society. This will be a resource to our very busy plaintiff attorneys in this country when this information becomes available. They don't want valid data. At that is my biased opinion.. They want business and this could potentially be a lot of business."

Dr. Koller: Page 192. "..As you increase the vaccination, you increase effects, but you don't know. You have modified live viruses. You have different antigens. There is a lot of things in those vaccinations other than mercury, and we don't know whether this is a vaccination effect or a mercury effect. But I am almost sure it is not a mercury effect. Positive as a matter of fact, and there are several experts particularly that have reviewed this, the methylmercury aspect who would agree with that due to dose response."

Dr. Johnson: Page 193: "Are you really comfortable with the way neurologic function was tested in the Seychelles?"

Dr. Koller: Page 193: "I have to admit that there were many other tests that could have been conducted…. We are talking about very subjective, very sensitive assays and yes, there could have been others done and there should be more done…"

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Dr. Roger Bernier: Page 198: "...the negative findings need to be pinned down and published...other less responsible parties will treat this as a signal." In other words, Dr. Bernier is suggesting that a manuscript should be written that demonstrates no association between Thimerosal-containing vaccines and nuerodevelopmental disorders.

Dr. Johnson: Page 198: "This association leads me to favor a recommendation that infants up to two years old not be immunized with Thimerosal-containing vaccines if suitable alternative preparations are available. I do not believe the diagnosis justifies compensation in the Vaccine Compensation Program at this point. I deal with causality, it seems pretty clear to be that the data are not sufficient one way or the other. My gut feeling? It worries me enough. Forgive this personal comment, but I got called out at eight o'clock for an emergency call and my daughter-in-law delivered a son by C-Section. Our first male in the line of the next generation, and I do not want that grandson to get a Thimerosal-containing vaccine until we know better what is going on. It will probably take a long time. In the meantime, and I know there are probably implications for this internationally, but in the meantime I think I want that grandson to only be given Thimerosal-free vaccines.".

Dr. Dick Johnson: Page 199: "This association leads me to favor a recommendation that infants up to two years old not be immunized with Thimerosal-containing vaccines if suitable alternative preparations are available."

Dr. Brent: Page 205: "I personally want to congratulate Dr. Johnson on his grandson. I have a small series of 11 children all who received the Thimerosal vaccine and they are all geniuses of course. But as Dr. Rapin points out, the genetics was probably most important."

Dr. Rapin: Page 205: "My grandchildren are geniuses too, I have two."

Dr. Weil: Page 207: "The number of dose related relationships are linear and statistically significant. You can play with this all you want. They are linear. They are statistically significant. The positive relationships are those that one might expect from the Faroe Islands studies. They are also related to those data we do have on experimental animal data and similar to the neurodevelopmental tox data on other substances, so that I think you can't accept that this is out of the ordinary. It isn't out of the ordinary."

Dr. Weil: Page 208: "The rise in the frequency of neurobehavioral disorders whether it is ascertainment or real, is not too bad. It is much too graphic. We don't see that kind of genetic change in 30 years."

Dr. Brent: Page 229: "The medical/legal findings in this study, causal or not, are horrendous and therefore, it is important that the suggested epidemiological, pharmokinetic, and animal studies be performed. If an allegation was made that a child's neurobehavioral findings were caused by Thimerosal containing vaccines, you could readily find a junk scientist who would support the claim with "a reasonable degree of certainty". But you will not find a scientist with any integrity who would say the reverse with the data that is available. And that is true. So we are in a bad position from the standpoint of defending any lawsuits if they were initiated and I am concerned."

Dr. Meyers: Page 231: "Can I go back to the core issue about the research? My own concern, and a couple of your said it, there is an association between vaccines and outcome that worries both parents and pediatricians. We don't really know what that outcome is, but it is one that worries us and there is an association with vaccines. We keep jumping back to Thimerosal, but a number of us are concerned that Thimerosal may be less likely than some of the potential associations that have been made. Some of the potential associations are number of injections, number of antigens, and other additives. We mentioned aluminum and I mentioned yesterday aluminum and mercury. Antipyretics and analgesics are better utilized when vaccines are given. And then everybody mentioned all of the ones that we can't think about in this quick time period that are a part of this association, and yet all of the questions I hear we are asking have to do with Thimerosal. My concern is we need to ask the questions about the other potential associations, because we are going to the Thimerosal-free vaccine. If many of us don't think that is a plausible association because of the levels and so on, then we are missing looking for the association that may be the important one."

Dr. Caserta: Page 234: "One of the things I learned at the Aluminum Conference in Puerto Rico that was tied into the metal lines in biology and medicine that I never really understood before, is the interactive effect of different ions and different metals when they are together in the same organism. It is not the same as when they are alone, and I think it would be foolish for us not to include aluminum as part of our thinking with this."

Dr. Clements: Page 247: "I am really concerned that we have taken off like a boat going down one arm of the mangrove swamp at high speed, when in fact there was not enough discussion really early on about which way the boat should go at all. And I really want to risk offending everyone in the room by saying that perhaps this study should not have been done at all, because the outcome of it could have, to some extent, been predicted, and we have all reached this point now where we are left hanging, even though I hear the majority of consultants say to the Board that they are not convinced there is a causality direct link between Thimerosal and various neurological outcomes. I know how we handle it from here is extremely problematic. The ACIP is going to depend on comments from this group in order to move forward into policy, and I have been advised that whatever I say should not move into the policy area because that is not the point of this meeting. But nonetheless, we know from many experiences in history that the pure scientist has done research because of pure science. But that pure science has resulted in splitting the atom or some other process which is completely beyond the power of the scientists who did the research to control it. And what we have here is people who have, for every best reason in the world, pursued a direction of research. But there is now the point at which the research results have to be handled, and even if this committee decides that there is no association and that information gets out, the work that has been done and through the freedom of information that will be taken by others, will be used in ways beyond the control of this group. And I am very concerned about that as I suspect it is already too late to do anything regardless of any professional body and what they say…."

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