

Collaborative on Health and the Environment (CHE)

Environmental Contaminants and Fertility/Early Pregnancy Compromise

Infertility Disease Data and Tracking: What Do We Have?; What Do We Need? How Might We Get It?

Working Group Call # 5 Jan. 5, 2005 9:00 am. PDT (32 callers)

(Transcript marked in red font suggests material for potential follow up discussion or action by CHEfertility members and/or others who are interested in helping to promote infertility disease tracking.)

ALISON CARLSON: Welcome to the new year, and our fifth teleconference. One announcement: Because our group has quite a few new members and it would take too long to do new introductions during teleconferences as we've done before, I am instituting a new practice so you can know who your CHE-fertility colleagues are. I hope this approach will also promote ideas for useful collaboration. Within a week, you will receive via our listserv an email "call for introductions" which will propose a brief reply format for all group members to profile themselves at some point before [February 15th]. I urge you to look for this email and respond. Going forward, new members will be asked to do this email introduction within a week of joining.

[Roll call: Alison Carlson, Paul English, Germaine Buck-Louis, Linda Giudice, Shanna Swan, Mary Lou Ballweg, Susan Benoff; Myriam Laura Beaulne, Stephanie Dahl, Anna Dillingham, Edith Eddy, Mimi Johnson, Michael Lerner, Lisa Ledwidge, Kirsten Moore, Pete Myers, Lois Shapiro-Canter, Rhonda Schlangen, Robert Rebar, Sharyle Patton, Diane Clapp, Ted Schettler, Elizabeth Sword, Mary Wade, Susan Marmagas, plus 6-7 late callers who did not announce.]

About today's topic: If we really want to understand whether and how environmental agents affect our fertility or fecundity, it is important to have good baseline data on prevalence, incidence and severity of related disease conditions which could help us understand if there are trends over time or space that we should look at. For this discussion, we need to define what exactly we mean by fertility, infertility, subfertility, fecundity, subfecundity, incidence and prevalence and so on, because one of the problems looking at infertility is that it means different things to different people. Rather than use up teleconference time doing this, I circulated definitions put together by Shanna Swan. If you have not seen those, see <http://lists.cheforhealth.org/lists/info/chefertility> under filesharing, document name 1-05-05 Swan Definition of Terms for Teleconference.

I should distinguish up front that we're seeking to understand what data we have and need on *involuntary* infertility, and are not concerning ourselves today with demographic fertility rates, which is altogether a different question for which there are plenty of good data sets.

DR ROBERT REBAR: About definitions, *the World Health Organization, ESHRE and the American Society for Reproductive Medicine have all met on the issue of definitions and you may well see in the next few years a world-wide effort to arrive at common definitions*, because they are used differently in different countries and regions of the world.

ALISON CARLSON: That would be a terrific eventuality. One I hope we see quickly.

SHANNA SWAN: Is there anything written on that, that we could get a hold of?

ROBERT REBAR: Not at this time. We've had two preliminary meetings and are scheduled to have another one at the ESHRE meeting this summer in Copenhagen.

ALISON CARLSON: Thanks for that note. I came to be concerned about involuntary infertility baseline data with many of you when we began by asking whether infertility, like many human disease conditions, is on the rise or not. As a patient, I saw claims in the media that it is, so I was curious what the source data

for that was and whether they really support claims that humans may be experiencing infertility more than they used to. I heard repro med professionals say anecdotally that it seems conditions contributing to infertility - like POF, PCOS, endometriosis, fibroids, sperm count, morphology and quality problems - are more prevalent. Infertility patients hear sympathizers say they 'know more and more people struggling with infertility challenges these days.' So I've wondered if there is any really organized tracking of these things. Is there more to these perceptions than, say, just more attunement, greater diagnosis and reporting, and baby boom demographic transition?

Unlike with, say, asthma or breast cancer, it seems we're still taking some baby steps in terms of tracking and articulating infertility and subfecundity incidence rates and prevalence trends. One problem is that involuntary infertility and subfecundity are hardly discreet, fixed syndromes. Once you diagnose breast cancer, you pretty much know what it is. But with infertility, it can be male factor, female factor, couple dependent – or unexplained. There can be degrees of it, or variability depending upon the mate with whom one is trying to conceive. It can be characterized by inability to conceive, implant or carry. So it is just harder to fix and measure infertility as a disease compared to other more discreet endpoints.

In the US it appears we have only one national source of periodic data - on prevalence of impaired fecundity - called the National Survey of Family Growth, out of the CDC's National Center for Health Statistics. This appears to be the source for most of the variously translated claims about US infertility rates that I've seen, but I am not sure. [The ASRM states that 'infertility affects 6.1 million American women and their partners - which is about 10% of the reproductive age population.' On the NICHD's Repro Sciences Branch Overview of Male Reproduction, it says that there are 2.6 million infertile married couples in the US.' In 1991, a US GAO report claimed that 2M US couples are involuntarily childless, but I don't know what their source data was. I have seen written in mainstream media that '1 in 10 US couples experience infertility at some point.' I have seen a 1:6 and a 1:7 figure for the UK. Our CDC says their most recent survey shows that 15% of US women of reproductive age have sought or used infertility services. It would be good to know the source data for these kinds of figures, how they have been tracked, and how we can compare them over time or space.] So this is our first level of questioning: What data do we really have?

Then we'd want to talk about whether that is enough. Do we have what we need? Or are there other data we should try to track, especially if we want to understand environmental factors. As a part of this second level of questions, we'd have to understand what factors limit efforts to gather more/better data. i.e. How can we realistically achieve useful surveillance?

Then it is logical to ask how we might go about promoting better infertility disease surveillance. There are efforts in the US to create better tracking of various human diseases, but infertility/subfecundity parameters don't appear to be a part of those tracking initiatives...Could and should they be?

Do these questions need to be examined and resolved before we can meaningfully answer the "why" questions via epidemiological investigations into whether environmental exposures are playing a role?

To get started, we have four speakers, and after that we'll open it up for discussion on this set of three questions.

Dr Shanna Swan is, as of this month, Professor in the OB/GYN Dept at the University of Rochester School of Medicine, where she has adjunct appointments in Environmental Medicine and Community and Population Medicine. Dr Swan has a doctorate in statistics from UC Berkeley, and a masters in biostatistics from Columbia – which give her a strong methodological background for her significant epidemiological work since. While she was at the California Dept of Health Services between 1981 and 1998, she developed and became Chief of their Reproductive Epidemiology Program. She is known for her work as Principle Investigator of a multi-center pregnancy cohort study called the Study for Future Families, which

she designed to examine environmental causes of geographic variation in reproductive health endpoints such as semen quality and time to pregnancy. Dr Swan has agreed to take the next five minutes to give us an overview of baseline data we do have; how she suggests we frame this discussion, and what directions she suggests we head in.

~ **Dr. SHANNA SWAN:** Thanks, Alison, for that summary and for an overview of what we're up against, here. I have perhaps an unusual stance on these questions of trends, which is that they're probably not the most helpful way to look at questions, whether that's trends in semen quality or trends in age to puberty or fertility, because you're left with the problem of dealing with old data. And so I don't think we should spend a lot of time addressing that question, but rather how could we better answer that question in the future, starting now, what can we do. As you said correctly, the National Survey for Family Growth is really what we have available, and I think it's a very valuable resource, but it's limited in not separating out very well the differences between voluntary and involuntary fertility. When I say 'involuntary' I mean couples who try to conceive and cannot. 'Voluntary' might be choosing to delay conception until an age when it becomes very difficult, and those trends...there's an interesting paper coming out soon from Finland where the author shows that depending on trends in sociological factors, like use of contraception and pelvic inflammatory disease and voluntary delay of childbearing, you can get trends going every which way, even when nothing is going on.

So, how can we do better? I'd like to propose something for discussion, which is that **there is a CDC-maintained sample of people who are interviewed periodically, and it might be possible to include in that some very limited questions about current attempts to conceive, things like, "are you now trying;" "have you tried before (to become pregnant);" "how long have you been trying."** And if we asked those questions of people of comparable age, a couple of times a year in representative samples, I think we might actually be able to get some useful data on trends; and also we could focus on particular subgroups that might be of most interest to our study.

I'd also like to say that this question of whether there should be surveillance at all is a really difficult one. There's not even complete cancer surveillance, birth defect surveillance, fields on which there's a lot of agreement. And for infertility, I have to say that we as a scientific community are a bit schizophrenic. When I reported a decline in sperm count, a high level scientist said to me, "Why should we care? There are plenty of babies in the world." I think just **having infertility viewed as an end-point of concern, an adverse end-point and a disease – having that accepted would be a first step in getting buy-in on having a surveillance program.** I don't think we have that now, and I don't think you would get the funds to have a national surveillance program on infertility, until people accept the fact that this is a real problem. Many people think declines in fertility are great, and there is an aspect of that that I agree with, but that's not our objective today. So, I think part of our discussion would be, how do we get buy-in, and how do we encourage the health community to see this as a legitimate public health problem.

ALISON CARLSON: **Dr. Germaine Buck Louis** earned her masters and doctoral degrees in epidemiology at the University of Buffalo in New York, where she spent 13 years as a professor in the Dept of Social and Preventive Medicine in the School of Medicine. She's now Chief of the Epidemiology Branch in the Division of Epi, Statistics and Prevention at the Nat Inst of Child Health and Human Development. Dr Louis is launching a large prospective study of couples planning to conceive called the *Longitudinal Investigation of Fertility and Environment*, which she described during our last teleconference. She is also the PI for two ongoing NICHD studies: one on PCBs, Pesticides and Female Fecundity and Fertility; and another on PCBs and Risk of Endometriosis and Polycystic Ovarian Syndrome. Some of you already know her as lead author of the 2000 NY Angler's study looking at time to pregnancy in women with histories of consuming PCB contaminated fish. Dr Louis will take the next 5 minutes to speak to her and other researchers thoughts on what infertility disease measures would be most useful to track especially given our interest in environmental factors.

~ **DR GERMAINE BUCK LOUIS:** I want to say that I agree with many of Shanna's comments. I think our basic problem is to convince the world that infertility, however it's defined, is really an issue of importance. One of the ways there was buy-in for cancer surveillance was because most families were somehow affected by having a family member with cancer. If we think about fecundity-related impairment, including infertility, we could probably capture just about every household in America—those who are directly affected, and those who know someone who has been affected. But I don't think we've done a very good job communicating just how widespread the problems are. We need increased awareness about what infertility really means. I spent years trying to get funding from a number of agencies on the topic of infertility, only to be told 'it's interesting, but nobody dies from it.' In the days of limited resources there's a prioritization toward other diseases. So I think this idea where we have to think about infertility as a pathway into other chronic diseases...autoimmune diseases, for example... maybe we need to think about infertility in it's broadest sense, in terms of substantiating its relevancy for study.

I like this idea of looking at time to pregnancy, getting a sense of couples who are actively trying to get pregnant and just how long it takes for a number of reasons. I think it lends itself well to surveillance because you can do lots of different things. You can emphasize just how quickly people do conceive. We have very few data to communicate to couples about the question of how long is a reasonable length of time to try before you really need to get into care. I've certainly been very critical of the infertility definition truncating at 12 months, because there's really no biologic evidence that 12 months is the magical time. I realize it was an interval that seemed appropriate before you'd want to go into medical care, but there really is no biology behind it. In fact, the new biology that's coming out is going to say after 6 months of trying you need to go into care if you're not successful. But time to pregnancy allows us to look at conception delays, so while someone might not be labeled "infertile" they might be somebody who has some kind of fecundity impairment and just has delayed conceptions.

It's also important to think about women who experience conception delays or infertility, and look at *their* pregnancy outcomes. There are at least four papers that say that women who take more than 6, or 12 months, to conceive have two to three fold risk of having a preterm or low birth weight baby. And so somehow, just because we help people to become pregnant, we kind of lose track of the babies.

There are a number of methodological papers that have addressed the ability to do surveillance on time to pregnancy, and they've done an excellent job of looking at the biases and methodologic difficulties [see the CHEfertility listserv web page under filesharing for this call], and I think the weight of evidence suggests that it can be done. There are some ways that we could think about capturing this information. And while I agree with Shanna when I think about how we could **piggy-back onto other types of surveys**, one of the concerns that I have is that at any point in time within a population, including the US, it's very hard to find people who are actively trying to conceive. You have to talk to a lot of people. So we'd really be talking about pretty large-scale surveys to be able to do widespread geographic monitoring.

I've been thinking about this question and am wondering if we could be more ambitious. The **Census Bureau is switching to a new model, using the American Household Survey**, where they're going to be interviewing fewer households, but in more complete aspects. And I understand they are open, by a process by which you can request to have questions added to these surveys. So, of course these surveys are designed to be representative of the US population, all kinds of individuals, all walks of life, and I'm thinking that **maybe groups like us should talk to them about planning a strategy to get into their survey. Now I know there are lots of groups that are trying to get into the survey, so we would have to come with a lot of evidence to support the idea that fertility is something that needs to be included, something we don't have enough information on.**

I do differ somewhat from Shanna's perspective: I think there is some utility in looking at the NSFG data, but perhaps from a slightly different way. We have data first coming from the National Fertility Survey in 1965 through the most recent NSFG – and while some definitions have changed, I think the evidence

does strongly support that infertility has been steadily increasing, despite a number of papers in the early '90s, from NSFG, that were saying that it was flat, that it was really the aging population, greater access to care, and things of that nature. But in more recent re-analyses, that's been refuted, and it does show, I think, an increasing prevalence of infertility. Without dispute, even when it was argued that infertility was flat in this country, women aged 20-24, and black women in the US, always were at increased risk – there was steady progression of prevalence for those sub-groups. Now the **NSFG has become more inclusive**. Originally it was just married couples and didn't include Hispanics. But the last two surveys, I think, they have expanded to include that. And I'm wondering if we could, somehow, link those data with environmental data. While we wouldn't be doing individual level analyses, **we could look at geographic areas to see if fecundity impairment and infertility associate with some of the aggregate level of exposure data**. There are toxic release inventories; there are a number of environmental monitoring data sets for this country. I was thinking about seeing if we could use NSFG, somehow linked with environmental data, to begin to look at those trends and regional differences. I guess I remain a little bit concerned about how we find the evidence to champion the cause. If you don't have evidence, it's very easy to be dismissed as just being people who are particularly interested in this area.

So, the real challenge is to articulate what the [impact of the fertility] problem is, and what the descriptive epidemiology is. And on the other end, we have wonderful clinical technologies that really do work and can help, and the gap really is trying to get folks into care.

ALISON CARLSON: This is an important “charge” and we should talk further about it. On this call we have groups who I think might want to speak to and comment on your remarks. Thank you.

Most of you know **Dr Linda Giudice** is a Professor at Stanford School of Medicine; Associate Chair of the Research Department of Gynecology & Obstetrics; Chief of Stanford's REI Division; and Director of Women's Health @ Stanford and the Center for Research on Women's Health & Reproduction. She's also chair of NIH's Reproductive Medicine Network – and has been allotted the next few minutes to run down what we do and don't know about prevalence of clinical conditions that contribute to infertility; and what in an ideal world would be most useful to track if repro med doctors want to understand and advise about environmental effects on fertility related clinical conditions.

~ **DR LINDA GIUDICE:** With regard to some of the previous comments made, I just want to really stress that the quality of the data for infertility prevalence is an extremely important issue, as well as trends in infertility over the years, and one that we don't really have a very good handle on. So I was very pleased to hear our last speaker address that as a topic that needs to be highlighted. Also I think the epidemiology of infertility and on a geographic level is going to be very difficult to trace unless there are populations that don't move around, and in this country that's really quite a rarity. But I think some of Shanna's work really addresses that very nicely. So, in terms of clinical conditions, I have several issues for infertility patients. One certainly is that, as we look to conditions that are associated with infertility, like endometriosis, certainly premature ovarian failure, unexplained infertility and immune dysfunction that may be related to infertility – all of these have an unexplained, or at least a rudimentary, attachment to environmental contaminants. So these are very real causes of infertility. Also, not listed in the above are miscarriages, either undetected or documented to be repetitive, and certainly the whole process of fetal development in utero. So **on the clinical side there are a number of conditions, but the problem is that data on prevalence or incidence - or actual correlation with environmental contaminants - are actually quite scant**.

ALISON CARLSON: That was quick, and clean.

LINDA GIUDICE: You said two minutes!

ALISON CARLSON: I shouldn't have stressed time. If you have more to say [on lack of data for incidence and causations of infertility-related clinical conditions], please bring it up in discussion?

Dr Paul English is Chief of the Epidemiologic Investigations Unit of the Environmental Health Investigations Branch at California's Department of Health Services. He is the PI heading up California's Environmental Health Tracking Program, which was established with a CDC grant to develop a tracking network for environmental hazards and related diseases. Dr English will present background on CDC/California state disease tracking efforts and what some of the challenges are, especially as might pertain to infertility. And he'll outline what an expert disease tracking work group that he is a part of said in their strategy report about the availability of infertility data.

~DR PAUL ENGLISH: As you mentioned the CDC has established this program and it's goal is really to put together a national surveillance system for environmentally-related diseases, and they've gone ahead and funded 20 states and three schools of public health. Our program here in California, then, is really focusing on trying to establish on-going monitoring of these conditions, reporting and communicating these data to community stakeholders, linking the data to environmental hazards and exposures. And so far the national program and the states really haven't focused on infertility. Major focuses of the program have been on birth defects, cancer, asthma, and adverse reproductive outcomes such as preterm and low birth weight. In California in our demonstration projects we've been focusing on asthma, preterm birth, low birth weight and autism spectrum disorder. So, I think there could be some pressure placed on CDC to try to start looking at infertility. Also, **a national health tracking bill has been introduced. This is a bipartisan bill that has been introduced by Clinton and Pelosi, and also some Republican representatives,** and this would fully fund the environmental health tracking program at CDC, establish 5 regional biomonitoring laboratories throughout the country to test for human exposures to toxins, and then also developing some centers of excellence at schools of public health, establishing a scholarship program for applied epidemiology fellowships.

In California we have an expert working group and their report is available on our web site, which is www.catracking.com. This report outlines some of the strategies for establishing an environmental tracking system in California. When we looked at data for infertility in California – and, again, we found a paucity of data – we knew that our **Office of Women's Health, which is part of the California Dept. of Health Services, has an annual women's health survey.** This is a random, telephone-base survey of about 4000 women that's conducted annually. Currently the question they have on this survey is “are you currently trying to become pregnant?” They don't have the follow-up question, “How long have you been trying?” which, when I've talked with Shanna we see as a very important addition to have. They also ask questions about infertility services you've received, such as: infertility testing, fertility drugs, IVF, and so on. So this **may be a resource to think about. Questions can be added if programs pay for those questions. Perhaps the tracking program could come up with funding to add some more questions on to this survey.** However, with only 4000 women statewide, you only would have enough sample size to be able to look at these trends statewide; you wouldn't be able to go down to a smaller geographic level.

When we look at some of the environmental data, it's the same issue. There was a lot of interest in the early '90s when the Endometriosis Association and colleagues came out with a report showing that monkeys exposed to dioxins in their diets were developing endometriosis. And if we wanted to do some tracking of dioxin exposures, we'd need to have some discussion on how we would look at that. About 90% of human intake of dioxins is through fat in fish and animal products. Other sources of these exposures, the major industrial source, would be looking at municipal waste incineration. There's also area sources of dioxin such as backyard trash burning. **So, it would be interesting to have some discussion on this. I know Germaine brought up this issue of trying to link some of the national data on environmental exposure sources [with infertility/fecundity data source]. It would be interesting to pursue that a bit more.**

ALISON CARLSON: All the speakers so far have brought up some interesting potentials, which I want to get more in to. Before we go to these, though, I want to note that there's a unique and accomplished model to promote state-by-state disease tracking and data collection, known as the Trust for America's

Health. Anna Dillingham is an outreach associate there. Could Anna take a moment to describe what Trust for America's Health does? We're curious if infertility has been at all on your radar screen...

ANNA DILLINGHAM: We have been a long-term advocate for a nationwide health tracking network, which is what Paul was just talking about. As he and others have mentioned, diseases like cancer, asthma, birth defects have been on the radar screen...there's a greater awareness of these publicly and there's already some tracking for these. I did want to mention one thing quickly that I think might have some significance: Paul mentioned there was authorizing **legislation for the nation-wide health tracking network. That will be re-introduced again next year in Congress. The interesting thing is that they are reworking, rewriting the legislation. It was fairly specific as to what diseases would be looked at re: environmental exposures. I understand that they're looking to make it a little bit more general so that as it goes to the CDC they have more wiggle room to work on issues that are of import. So, like Paul said, there might be a way you could work with CDC on what diseases and illnesses are included in the tracking networks.** That's all I have to say.

ALISON CARLSON: Let's open this up for comment, discussion and questions. Probably it's most important to focus on the latter two questions. But perhaps we could start with a few minutes, if there are comments about the state of the data we have – i.e. what do we have, and how good is it? I was wondering if Dr. Eric Surrey is on the call – who is head of SART, the Society for Assisted Reproductive Technology? Or, Bob Rebar? If so, what kind of interest do SART and ASRM have? I know there's been a lot of literature out of both groups on the use of ART services, which tells us something, but how strong an interest would SART have to promote gathering incidence and prevalence data?

ROBERT REBAR: I can't really speak to that issue, other than to say **if there were a definitive question that could be asked as data were collected for IVF cycles, it clearly could be added to the information now collected.** But one of the difficulties in the whole field is the fact that there is very little information internationally with proven data; and although there are good experimental models, as Linda Giudice pointed out earlier, just translating this to the human is difficult indeed. And it's difficult to know where to begin to ask those kinds of questions.

ALISON CARLSON: Are there other questions or comments related to the data we currently rely on? If not, it would be useful to move on to that second matter. What would be more useful data? All the speakers addressed this...

SHANNA SWAN: I just wanted to mention that in Jorn Olsen's paper on tracking [Am J Epidemiol 2003; 157:94-97], which you put on the web site and people might have read for this call, one of the things he says is that he felt – and I'd like to bring this up for discussion – that there should be some kind of surveillance of how long it is taking people to conceive, and how many are trying...that kind of question...but also to track semen quality, or some biological marker, and I don't know what else it would be at this point, since the female side is almost impossible to track. So, to buttress, if you will, the self-reported data. What do people think about that?

LINDA GIUDICE: Well, isn't there some bias introduced to that?

SHANNA SWAN: Well, the first question is whether it a good idea, and then we could think about how to do it in a non-biased way. That's the problem with self-report as well. Personally I am very interested in trends in semen quality, but on the other hand, the studies to date – if you look at time to pregnancy studies in relation to semen quality – they're not very well correlated. And infertility is such a complex phenomenon that I'm not sure that just measuring semen quality, or any particular biological marker, will get enough of the picture to make it worthwhile. I just brought that up as a discussion starter.

TED SCHEITLER: I just wanted to toss in here that I think at some point it would be well worth it for this group to really put something to paper about *why* this is a matter of importance. At the beginning of this call, Shanna pointed out that there are some people who think this isn't a problem even worth looking at. It would be useful to get the laundry list of why it is, or why it isn't, and those answers might actually help us decide what kinds of data would be worth gathering. For example, maybe it would make more sense to look at a sub-group, either by age or some other criteria, rather than all people who are trying to get pregnant, because it sheds more light on the questions that come out of the issue of *why* this is a matter of importance.

ALISON CARLSON: That's a good point. Germaine Buck-Lewis has pointed out that there is some data showing racial disparities in infertility challenges, and so there are questions of environmental justice that come up as well. But, I think it's very important we put on paper the rationale for why this is a matter of importance, and I haven't heard anything yet today from the infertility patient group representatives who are on... Diane Clapp [Resolve] and Lisa Rosenthal [American Fertility Association], I think? Do you think that you guys could play a role in that?

DIANE CLAPP: I can't stress enough how important this kind of data is. I think that in order to get access to care, we have to document the degree of this problem. So, I think anything we can do to enlighten people about that is important. I don't know if there's anything Resolve can do on our web site... I mean, we get a lot of activity on our web site and these people are already actively concerned about getting pregnant or have experienced a pregnancy loss. I don't know if there's data from that that we could pull up that would be helpful... Again, it's self-reporting, but it's certainly something to think about.

EDITH EDDY: At the risk of putting you on the spot, Ted, I would be interested in what your own answer to the question would be...

TED SCHEITLER: Well, I have responses that go in both directions. I'm fascinated, for example, by this notion that time to pregnancy is somewhat predictive of low birth weight and prematurity. To the extent that really is borne out, that becomes really important, because we know that there's a lot of morbidity that's associated with low birth weight and prematurity. So, if time to pregnancy is a good marker for that, then we ought to be looking at time to pregnancy because it might lead us into some important opportunities for mitigating whatever is leading to that. So, that's using time to pregnancy as a marker. But you can also look at it from a perspective of evolutionary biology, and an ecological perspective would suggest that the world is overpopulated with people. Then, there's this economic analysis that is getting much more play in the press lately, that says that we've got an aging population, and if we don't start having more children, we're not going to have an economic base for economic growth and supporting the Social Security system that's going to support elderly people in their pension years. I've seen this surface more and more. So, this can't be viewed just through the lens of biology... It's in a very interesting social, economic and political context.

SHANNA SWAN: I'd like to second that and suggest that we get a medical economist involved in this discussion, not only from the points of view Ted mentioned, but also regarding the costs to society of increasing numbers of couples (which I think there probably are) going to infertility work-up, what this costs the public health system and also individuals. It's got to be huge. We could actually do some calculations: for every amount of X chemical that appears to increase the risk of infertility by Y amount, this costs society Z. I think people might notice that.

MARY LOU BALLWEG: I wonder if a concept that we've been using recently with endometriosis might be helpful here: we're beginning to talk about endometriosis as a kind of indicator disease for the general health of the population, because of the proven links to six cancers now, and a whole range of autoimmune diseases and other health problems, including in the families. I wonder if we can position infertility, which represents a number of different diseases itself, as something of an indicator for the

health of the population as a whole, including for those babies that are born. So that it's reframed rather than as a population issue as a health issue overall. Just a thought.

MICHAEL LERNER: First of all, I just think this is an excellent call, and would like to make a couple of observations. If we look at the patient groups that have succeeded in making their conditions a major concern, it is not always the groups that have the tightest, strongest science. It's breast cancer, it's autism...both of which have been very complicated to figure out. Sometimes we have good science, for example with asthma and endometriosis, as Mary Lou Ballweg just pointed out. But usually it's the groups where there is a very committed patient base that really has strong concerns. That's why I think that when we look at the sub-groups, in the broader set of infertility issues, that are most naturally advocates, it is the couples and particularly the women who have the experiences in infertility, who have gone to RESOLVE and to the clinics to try resolve it. So then the question is of bringing them into the discussion about what science we want, and not trying to do it just from an abstract point of view of all the possible science questions we could ask. It seems to me it would be enormously valuable to ask what the science questions are that the highly educated, very committed women who go to infertility treatment, and to infertility support organizations, are. And to make the linkages as Mary Lou Ballweg and Ted Schettler have pointed out, that this is an indicator condition.

I also want to add that male infertility issues should be included in this. People are obviously aware of this, but we shouldn't simply be looking at the female dimensions of this subject. The final point I'd like to make is, and I wonder if Shanna could address this: It was very effective in the development of the science on endocrine disruption to have the Wingspread Conference. The Wingspread Conference, for those of you who don't know, was a conference with a methodology that simply asked what we know, what do we not know but think is true, and what are we concerned about – something like that. It arrayed the issues in that way. And I wonder, if we were to take a focus of the concerns of women and couples seeking infertility treatment, and ask them to join with the scientists in arraying the research questions along Wingspread-type paradigm, whether that might not help us toward a focus on the issues that we could move forward in policy advocacy.

SHANNA SWAN: Michael, you addressed that to me, but I'd like to turn it to Alison, because she might want to say something about a couple of upcoming events that are relevant...

ALISON CARLSON: Some of the people on this call know that Linda Guidice and CHE, along with Shanna Swan, are hosting a small workshop that will address some of these issues [and bring together infertility patient groups with leading scientists and clinical researchers]. It sounds to me, Michael, like we have two levels of "what can we do" questions to promote tracking. I know we have to back up to that second level to try to agree on "what are we looking for," and there's a lot of steps in between. As Michael said, the groups that have been most successful don't necessarily have the best science, but know how to engage patient concerns, so that issue of "why should people care, why is it worth tracking" gets some attention. So we're wanting to look on a functional level, at what kinds of things might be realistic to suggest we pursue: the Census Bureau idea that Germaine brought up, the survey done by California State on women's health...what questions could we add there? But first there has to be sort of a ground swell, or an engagement of the patient groups, and that's pretty much why I wanted to do this call. And I'm hoping this call might inspire some thinking or further effort to discuss how ASRM, SART, professional societies, especially the ones that have environment interest groups, and RESOLVE, the American Fertility Association and INCIID could get involved in articulating the need for and then promoting tracking.

MICHAEL LERNER: Right, the professional groups obviously have an interest in developing funding mechanisms to do the research, and I imagine that some of them are well aware that in other situations the patient groups have been the key to getting the funding allocations to do the research that they want to do. Infertility patient groups bring this extraordinarily committed group of women to the table, and as

somebody else mentioned, there's the environmental justice dimension of this...there's the ethnic differences, and it's quite possible that some of these environmental justice groups might also be interested.

PETE MYERS: As the person who introduced that consensus statement process to the Wingspread Conference that Michael described, I would simply say that it was an amazingly effective means of changing the dynamic of the meeting from one where everyone was arguing about the little things they disagreed about to one where everyone focused on what we agreed on, what the factors were that all of us think are of one level of certainty or another. And combining that with a statement along the lines of what Ted was describing, perhaps using the upcoming Stanford meeting to move the process forward so that we do both...I think that would be an extraordinarily powerful contribution.

ALISON CARLSON: Pete, you've seen the program plans for the workshop and you'll be there...Do you think we've got enough leeway in there? We *are* looking for the points of agreement, both about the state of the science and the research gaps, and do you think we have room in there to foster this Wingspread type of approach?

PETE MYERS: I'd have to look at the program again in this light. It doesn't take a trivial amount of time.

ALISON CARLSON: No, it doesn't. And of course that's something that the organizers of the workshop can look at in light of this call, and there will be other opportunities to take this discussion further. We're very excited because the Compton Foundation has just awarded a grant to create a synopsis document on the points of consensus from the Stanford-CHE workshop. This might be a tool, depending on what actually happens at that workshop, for the professional societies and the patient groups to use in helping to articulate the need for better surveillance of infertility?

MICHAEL LERNER: Well, first of all let me ask Linda to comment. Since you are heading the workshop, Linda, I wonder what your thoughts are on what is essentially an emerging proposal to see whether a Wingspread-type methodology could be used as a guiding perspective in preparing the agenda for the workshop, and see then if the synopsis document could move at least toward a first approximation of a Wingspread-type survey of the field?

LINDA GIUDICE: Sure. I think this would be an extremely important outcome of the workshop, and the support by the Compton Foundation is really quite a godsend, so Edith [Eddy, Compton Foundation Executive Director], thank you. I think as we go through the program it's important that we keep this goal in mind, so we eventually have essentially at least the outline of the type of structure we want to promote. I think and hope this is just the beginning in a bigger move forward.

ALISON CARLSON: Shanna Swan, since you are co-chair of this workshop, do you have a sense that what we have planned will service the discussion of infertility data tracking?

SHANNA SWAN: I'm not sure. But I think that the current question about this Wingspread-type consensus document is a little bit different. It's more of an over-arching question, and I think that would be a really good way to focus our further planning discussions, maybe even including Pete in that aspect of it. I've said that we should have a few specific questions, such as "Do we agree that fertility has declined?"We could put those out there at sessions and come to some consensus statements in the document that will be produced from the workshop.

ALISON CARLSON: That would be a good step. Shanna was mentioning further planning meetings by the way because we hope that between Shanna at University of Rochester and Linda at Stanford, with other collaborators, we may be able to establish a rotating (every two year) "Summit on Reproduction and the Environment." So that's what Shanna was referring to earlier.

I have one other general question: Do we know how US fertility and sub-fecundity data compare with other countries?

SHANNA SWAN: I don't think that we can really make meaningful comparisons. I don't know how Germaine feels about that, but I don't know that any one has tried to do that. There are of course figures on what the average number of children per couple of reproductive age, but that's not what we're talking about here.

ALISON CARLSON: I'm just wondering if there are other countries that have figured out how to do this tracking thing better than the US has.

SHANNA SWAN: Well, there is going to be a large workshop, as some on the call may know, in Europe in a couple of weeks, and some of us will be there. That's one of the things we're going to definitely keep an eye out for, to see if anyone knows how to do it better.

ALISON CARLSON: I want to now thank all the speakers, who've all brought up interesting ideas. I wish we had about 10 more hours. It's clear that we need to work on the ground-laying level of articulating why this is important, and that there's a big role for the professional societies, repro med societies, and the patient groups in helping to do that. Then working on having important discussions about what's feasible to track. It sounds way more complicated than I had anticipated. We have to keep in mind that patients have pretty simple questions, and they are a driver here, and we do need to survey and understand them, so Michael's suggestion of really putting patient groups together with researchers is right on. We have a lot of explaining to do before we can get to the questions of what specifically we can promote for tracking. I hope that this call will inspire some other form of discussion. I wonder if anyone has comments on how we might go about that, beyond the workshop? Are there patient groups that would like to sponsor some sort of disease tracking discussion, for instance?

DIANE CLAPP: Again, I don't mean to be a broken record, but our web site gets about 2500 unique visitors every month, and they stay on the site for a while. When we did a Harris-supported poll on embryo donation, Harris said they had never gotten such a fast response. We met the number that we needed within two days. So this is a population that is really willing to answer surveys and questionnaires. We could e-blast our members as well and ask them to visit a particular web site to provide information. They're ready and willing and certainly anxious to have this illuminated as a major health problem.

ALISON CARLSON: I'd like to mention that for the Stanford-CHE small retreat/workshop, we'd like to have been able to invite hundreds of people – but for budget and other strategic reasons kept it quite small and focused. The patient groups will be there and I hope that this preliminary conversation today will inform discussions during the workshop. We again we'll have a white paper coming from that, so perhaps from there we can make some decisions about how to move this along.

BOB REBAR: I want to remind you that I encourage you to [submit this to *Fertility & Sterility* from the standpoint that that is a forum which might lead to further interest.](#)

LINDA GIUDICE: That is a great suggestion.

ALISON CARLSON: That's a wonderful suggestion. The white paper, Bob, is specifically geared toward lay use and...

ROBERT REBAR: I understand, but it certainly should be possible to develop something for *Fertility & Sterility*, and I know that the editor, Dr. DeCherney, certainly would entertain it.

ALISON CARLSON: I appreciated your email to that effect. At this point we've run out of time. I just

wanted to quickly close, again thanking the speakers, and point to the reference materials we posted on the CHEfertility listserv webpage. We want to schedule our **next teleconference** – I don't know the topic yet – for **April, shooting for the 13th or the 20th**. I do a survey to determine date, etc. Thank you everybody for joining us today.