The Committee met pursuant to adjournment in the Superior Room, The Renaissance Madison Hotel, Seattle, Washington, at 8:30 a.m., Joyce C. Lashof, Chair, presiding.

PRESENT:

JOYCE C. LASHOF Chair

MARGUERITE KNOX Member

ROLANDO RIOS Member

ALSO PRESENT:

HOLLY L. GWIN, Deputy Director/Counsel

342 RESEARCH STAFF:

JOSEPH S. CASSELLS, Senior Advisor for Medical and Clinical Affairs

KATHI E. HANNA, Senior Advisor for Policy Implementation

THOMAS C. McDANIELS, JR., Policy Analyst

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MS. LASHOF: I think we're ready to get started.

We changed the order of presentations this morning because of schedules, and so let me start with Dr. Adolfo Correa. We're very happy you could join us.

ASSESSING REPRODUCTIVE HEALTH IN SPECIAL POPULATIONS

COMMENTS BY ADOLFO CORREA

MR. CORREA: Thank you for inviting me.

This morning what I'd like to do is
present two studies of reproductive effects in relation to occupational and environmental exposures and some of the methodologic issues that these kinds of studies raise.

The first study will be -- or is about an investigation of reproductive health in semiconductor manufacturers in two manufacturing plants in the northeastern United States. The second one is a case-controlled study of cardiac defects and environmental factors conducted in the States of Maryland, northern Virginia, and Washington. D.C.

In 1988 Pastidas and colleagues reported an increased risk of spontaneous abortions among women working in a semiconductor manufacturing plant, and that led to two additional studies to elucidate those -- that association.

One study was conducted by investigators at University of California, Davis and University of Massachusetts at Lowell, and they investigated, I believe, fourteen plants across the United States.

The second study was conducted by investigators at Johns Hopkins University. And I was involved with this study, and we evaluated the reproductive health of workers at two plants.
The specific aims of the Johns Hopkins study were, one, to examine the reproductive outcomes of female workers and the couples, of male workers in relation to work areas -- specifically, semiconductor clean-room manufacturing area, other manufacturing, and non-manufacturing areas -- and also to examine the relation between reproductive outcomes and work with specific processes or chemicals in the clean-room manufacturing area.

For this study we used a retrospective cohort design, and then also a short or small prospective cohort design to try to corroborate some of the results of the historic cohort study.

For the historic cohort study we identified the active workers from employment records in 1989, we recruited workers -- that is, female workers and male workers and their wives. And we specifically excluded workers who had had surgical sterilization prior to 1980.

The unit of observation in this study was a pregnancy conceived between 1980 and 1989 during employment in these two plants. The information on pregnancies was obtained on interviews of the female workers and the wives of male workers. And the information on exposures was
obtained by interviews of the workers to elicit
details of histories, as well as from records in the
plant that indicated the processes and agents used
in different settings of the plant. And I'll spend
a few minutes on the job histories because this was
very crucial for our study.

Just a word about semiconductor
manufacturing. This is a very complex, multi-step
process that involves the working with these silicon
wafers. They're discs that resemble compact discs.
And on these discs a number of processes are carried
out, including the application of photoresistive and
photosensitive material. As shown here, this is for
the silicon wafer with photoresist on it. Then this
silicon wafer is exposed to light. That is shown
through this particular pattern that has the
semiconductor circuits, and this leads to the
imprinting of these microelectronic circuits on the
wafers. This process is then followed by a number
of other developmental -- development processes and
chemical exposures.

This slide shows a worker in one of
these plants. And the things I want to emphasize
are that this worker is wearing a cap, a mask, a
special suit to prevent the release of particles
that might contaminate the products and damage the
products.

The air in this environment is
circulated through special exhaust systems to remove
the number of particles in the air, also to prevent
damage to the circuits. So these environments are
called clean-room manufacturing rooms.

Traditionally in an occupational
study, exposure assessment is based on the job
histories that are then translated into potential
exposures that the workers may have incurred over
time. And in this study we had also employment
records for all the workers. This shows the
effective dates when a particular transition in the
worker's employment status took place, their
position title, and the department name.

We felt that this information would
not necessarily enable us to capture the variability
in processes that the two workers may have had
performing the same job title or having the same job
title, and that over time in this industry there
were a number of changes that would not be reflected
by the job titles. So we decided to combine this
with other techniques to try to obtain a more
detailed history of exposures.

We showed this employment record to
8 each worker and asked the worker to identify the
9 periods of time during which he or she performed the
10 same tasks, and that defined for us jobs.
11 Then for each one of those jobs we
12 asked the worker to tell us a little bit about that
13 job, the dates that that job was held, the building
14 in which that job was performed, and department or
15 area. And then within one -- within each one of
16 those jobs we also asked information about the
17 processes that the worker performed or worked on,
18 and the tools within each process.
19 This represents one of the memory
20 cues that we used to help the workers remember the
21 processes in the clean-room and for the particular
22 processes or tools that they may have worked in. So
351 1 we used a number of cognitive techniques to try to
2 help the workers remember the tasks they performed.
3 We also had records from the plants
4 that indicated to us what chemicals were required
5 for each one of these processes, so this allowed us
6 to construct what we called the process/chemical
7 matrix. That would enable us to tell, for any given
8 worker performing certain processes at a given point
9 in time, what chemical exposures that worker may
10 have had.
11 We were also interested in specific
12 chemicals, in particular the short-chain ethylene
glycol ethers, because of their known toxicity.
14 They're readily absorbed by inhalation or dermal
contact. They have reproductive and developmental
16 -- developmental toxicity. And in the study of
17 Pastidas where work with photolithography had been
18 identified as a risk factor, the question was
19 whether these chemicals were involved there.
20 In our study we found from the
21 records of the plants that the glycol ethers, here
22 represented by cellusolve acetate and dyline, were
3 present and photo- -- photo-applied in an area of
2 semiconductor clean-room manufacturing called
3 photo-apply. That is where photolithography takes
4 place.
5 But the concentrations were low. The
6 air concentrations were low. So we thought that if
7 there was going to be enough variation in exposure
8 between the workers, that would not be accounted by
9 inhalation, that it would have to -- it would have
10 to come from differentiations, differences in dermal
11 contact.
12 So if we wanted to conduct an
13 exposure assessment of expose- -- in relation to
14 ethylene glycol ethers, we wanted to rely, then, on
15 the time that the workers spent in photolithography
16 as an indication of the potential for exposure to
17 the ethylene glycol ethers. And for that purpose,
18 then we looked at the processes within a given job
19 and said that if the worker performed only
20 photoresist processes that require ethylene glycol
21 ethers, the potential for exposure to these
22 chemicals was high.

353 1 If the worker worked on these
2 processes as well as other processes, then the
3 potential for exposure was moderate, since that
4 meant that the worker would spend less time on the
5 photoresist ethylene glycol ether processes.
6 If the worker performed processes
7 that used other solvents, other than those involving
8 photoresist or -- we felt that the potential for
9 exposure to these chemicals was low.
10 And if the worker worked in processes
11 that really require no chemicals or solvents, we
12 felt the potential for exposure there was going to
13 be none.
14 So this information that we collected
15 retrospectively allowed us to conduct different
16 exposure classification systems, one based on area
17 such as clean-room, other manufacturing, non-
18 manufacturing, or more specific classification
19 systems, and including the one that I just
20 described, the exposure to ethylene glycol ethers in
21 photoresist.
22 So with this information, we linked
354
1 the reproductive histories that we obtained by
2 interview to the chronology of area processes that
3 the workers had been working on at the time of
4 conception. That allowed us to divide these
5 pregnancies into these three exposure groups by
6 area.
7 We also linked the processes at
8 conception with the process chemical matrix in
9 semiconductor clean-room manufacturing, to give us
10 an indication of the potential for exposure to these
11 chemicals, the ethylene glycol ethers.
12 And so we ended up with four groups
13 of pregnancies: those with a high potential for EG
14 exposure, those with medium potential for exposure,
15 those with low potential for exposure, and those
16 with no potential for exposure.
17 The analysis by -- of reproductive
18 outcomes by area showed no variation, no consistent
19 variation of spontaneous abortions, subfertility,
20 low birth weight, prematurity, or malformations, by
21 semiconductor clean-room manufacturing, and other
22 manufacturing and non-manufacturing. So I'm going
1 to present only the results of the analysis we conducted within the clean-room workers. This table shows the number of pregnancies to female clean-room employees and the number of pregnancies to the wives of male clean-room employees during the study period, and the numbers of spontaneous abortions, as well as the percents of spontaneous abortions for those pregnancies. And we have here percents or rates that are comparable to those reported in other studies that have been on interview data.

When we actually looked at the rate of spontaneous abortions in female employees by potential for exposure to these short-chain glycol ethers, we observe, however, that there was some variation in the rate of spontaneous abortions. We in fact saw an increase in the rate of spontaneous abortions with potential for exposure -- almost a threefold increase in risk in the high-exposure group, compared to the no-exposure group.

We looked also at the variation in spontaneous abortions among the wives of male employees with potential for exposure to these chemicals. And in this group we didn't observe any variation with exposure.

We also examined subfertility -- that
is, the delayed time to conception, or taking more than a year to conceive -- among the female employees in relation to these chemicals. And we increased an increase in the risk of subfertility with potential for exposure to these chemicals -- almost a fivefold increase in risk in the high-exposure group, compared to the no-exposure group.

We examined subfertility in the couples, of male workers, in relation to these chemicals, and in this case we also observed an increase in the rate of subfertility, although the rate was less dramatic here than for the female employees.

So in summary, in this study of semiconductor manufacturers we observe an increased risk of spontaneous abortion among female employees, and increased rates of subfertility among female employees, and among couples, of male employees, in relation to potential exposure to the short-chain glycol ethers or photoresist mixtures.

This study has a number of strengths.

One is that it was large enough to allow us to look at spontaneous abortions and subfertility in relation to these chemicals.

The data on spontaneous abortions
9 was validated through medical records, and we were
10 able to confirm that 94 percent of those on whom we
11 had medical records, the diagnosis was confirmed.
12 There was -- time to pregnancy had
13 relatively good consistency when we looked at some
14 of the questions, several questions that we asked
15 about this.
16 Our exposure assessment was conducted
17 independent of pregnancy outcome ascertainment.
18 And we had detailed and reliable work
19 histories.
20 Specific measures of exposure that
21 were time-dependent and allowed us to rank exposures
22 to the short-chain glycol ethers and to conduct
23 exposure response analysis.
24 Our results are consistent across
25 plants, and are consistent with the known toxicology
26 of these chemicals.
27 The limitations of this study are
28 several.
29 One is that we were really unable to
30 examine the independent effects of the short-chain
31 glycol ethers, of the effects -- possible effects of
32 the photoresist chemical mixtures that -- in which
33 they were present.
34 We didn't have a biomarker to
indicate exposure to these chemicals.

We don't know what the critical

exposure period for subfertility is.

And we didn't have a large enough

sample size of pregnancies to allow us to look at

malformations. The numbers that we found were very

small, to -- for an adequate analysis.

Okay. The second study I'd like to

turn to --

MS. LASHOF: I --

MR. CORREA: Very well.

In the second study, of congenital

malformations of the heart, we found that there were

no associations between the heart defects and many

environmental factors that we looked at when we

considered the cardiac defects as a group.

But when we examined diagnostic

groups and specific paternal exposures, we found

associations between specific diagnostic groups and

paternal exposures, such as ionizing radiation in

ejewelry-making. And there were some suggestions of
a dose-response effects and interaction with family
history -- that is, family history increased
susceptibility to these -- some of these defects.
Now, that study was an exploratory
study, so the results could be interpreted as being
due to chance. And I think additional studies are
needed to replicate those findings.
QUESTIONS
MS. LASHOF: Thank you very much.
Are there questions from the panel
first?
If not, let me ask just a couple.
Certainly the silicon -- the solvent
study, semiconductor industry study, is a very well
designed, very careful, and has many strengths; its
limitations you mentioned.
How would you evaluate our ability to
do anything as scientifically sound as that, and the
problems we're facing in looking at exposures in the
Gulf War veterans?
MR. CORREA: I don't know enough
about the Gulf War veterans, but my -- the limited
knowledge that I have tells me that it's probably a
more complicated type of exposure setting. I don't
know what the different exposures might have been,
but my impression is that there may have been
20 several. The -- but I'm not sure that it's really
21 necessarily that much more complicated, as -- than
22 this study that we did. I think that there are some
361 1 similarities there.
2 Now, the one -- one advantage, I
3 think, in the Gulf War's setting is that there was
4 limited time of exposure. I think that that -- that
5 may facilitate the exposure assessment. We had to
6 look at a nine-, ten-year period. And I think
7 that's more difficult to recall the information.
8 The -- in the Gulf War setting there
9 is a fair amount of publicity now about the possible
10 relationship between exposure and outcomes. So the
11 recall of particular jobs or tasks or potential
12 exposures there may be subject to some effect from
13 outcomes -- that is, there might be some recall bias
14 that -- but that might be addressed, I think, in
15 some -- with some looking, including some questions
16 that specifically look at that possibility of
17 recall.
18 I think that sample size is probably
19 going to be an issue.
20 MS. LASHOF: Yeah.
21 MR. CORREA: A big issue.
22 MS. LASHOF: And in the result of the
362 1 spontaneous abortions, this was among people in the
2 high exposure, during the period of their exposure.
3 Is there any aftereffect of people who've worked in
4 high exposure areas then move out? How long would
5 you expect the effects to linger?
6 MR. CORREA: We haven't actually
7 examined that, and that's actually one of the
8 questions that remains: are the effects that we
9 observed -- that we observed in this setting chronic
10 or reversible? And if they're reversible, how
11 quickly are they reversed? I couldn't tell you
12 that.
13 MS. LASHOF: So those that you did
14 report on all were being exposed at that time?
15 MR. CORREA: Yes.
16 MS. LASHOF: And you have no data,
17 then, at this point, but you are planning to follow
18 that up?
19 MR. CORREA: We have the -- we have
20 the data in this study that may enable us to look at
21 subsequent pregnancies within the time period in
22 relation to past exposures. But we haven't analyzed
23 that.
2 MS. LASHOF: Okay. Thank you very
3 much.
4 Any other questions? Marguerite?
5 MS. KNOX: Yeah, I have a question.
When you were categorizing the chemicals, what made you put the -- you categorize "other solvents" along with the ECG as a low possibility risk.

MR. CORREA: Yes.

MS. KNOX: How did you decide upon that?

MR. CORREA: Okay. We knew that the category of "other solvents" -- we had four categories: the high, the medium --

MS. KNOX: Medium.

MR. CORREA: -- that used EG and other solvents; that was medium. And then we had other solvents as the low.

We knew that at one plant that did not include the glycol ethers. At the other plant the glycol ethers had been used in a very limited manner. That was from the records at the plant. So we decided to consider that as low, rather than none or medium. Because it really -- we felt that there was really little potential for exposure, definitely in one plant, and in the other one, very low potential.

I don't know if that clarifies the question.

MS. KNOX: Well, it just makes you wonder, looking at -- say for instance, we've got
10 four veterans. We're looking at pyridostigmine bromide and DEET, and the combination of that, those two drugs together. And I just wondered if you -- if you combined the chemical that you were talking about with another solvent, would it be more potent or less potent, or did you -- you know, did you investigate that?

MR. CORREA: We didn't investigate that, but that is a very important question, because we -- it is possible that in the presence of other solvents, that these glycol ethers might be absorbed more quickly, and maybe their effect potentiated. And if -- and in fact, the glycol ethers were always present in association with the photoresist mixtures, the particular -- the specific nature of which we don't know. And so it is possible that those mixtures enhance the absorption as well as the effects, but there's no way for us to know that.

MS. LASHOF: Let me follow that up, then, a little bit. The glycol ethers you selected as the possible culprit based on pharmacology or toxicology before, and the solvents -- the other solvents you had no reason to suspect them, so that you considered them as not germane to the study, and put them with the control? Is that correct or
13 incorrect?
14 MR. CORREA: No, no; I didn't have
15 time to really go into detail here, but --
16 MS. LASHOF: Yeah, I know. We cut
17 you short, and then we ask you tough questions and
18 -- but that gives you the chance to do that, anyway.
19 MR. CORREA: Yes.
20 We actually examined about twenty-
21 eight chemicals specifically in this plant,
22 chemicals that were used in high volume that had
366 known prior reproductive toxicity, and for which
2 there was potential for exposure. And we found that
3 really, of all of those, it didn't -- it seemed like
4 only the glycol -- glycol ethers, or those chemicals
5 that were used in conjunction with the glycol
6 ethers, were suggested in association.
7 MS. LASHOF: And what kind of
8 examinations did you do with the twenty-eight? I'm
9 trying to see what we can draw out of this that will
10 be applicable to the Gulf War.
11 MR. CORREA: Yeah. We did -- you
12 know, compared rates of people exposed to the
13 particular -- each particular chemical, versus the
14 rates among those who were not exposed to that
15 particular chemical.
16 It's not -- it's difficult, because
within these reference groups you may end up with individuals who are exposed to other chemicals that may be toxic, so you may dilute some associations. If you try to use a common reference group that has no exposure to any chemicals, you may have very small numbers. We did both analyses, and in both analyses we found the same -- similar results, so --

MS. LASHOF: I see. Thank you very much.

Any further questions?

If not, thank you very much.

Oh, I'm sorry, Joe; I didn't see your hand.

MR. CASSELLS: Just to further clarify the categorization with the ethylene glycol, basically it's a categorization of time of exposure potential? Is that correct? If they did the jobs that were --

MR. CORREA: Yes.

Related strictly to the time of use of that?

MR. CORREA: At time of conception.

Yes, at the time of --

And if they did other tasks, it was a matter of time relationships?
MR. CORREA: Right.

MR. CASSELS: Thank you.

We also looked at other times: before conception, after conception.

MS. LASHOF: Thank you very much.

Appreciate it.

Betty Mekdeci. Very happy to have you with us this morning.

ASSESSING REPRODUCTIVE HEALTH IN SPECIAL POPULATIONS

COMMENTS BY BETTY MEKDECI

MS. MEKDECI: Good morning. I'd like to thank the members of the Committee for bringing me here all the way from Florida. I appreciate it very much.

The Association of Birth Defect Children, the organization that I direct, is a national non-profit organization started in 1982.

We provide information to parents all over the country about all kinds of birth defects. We do national parent-matching, connecting families of similar birth defects. And we sponsor a project called the National Birth Defect Registry.

The National Birth Defect Registry was really begun because of the poor quality of data
3 on birth defects we have at the national level.
4 According to a General Accounting
5 report that was done for Senator John Glenn, there's
6 very poor quality data all around the country on
7 birth defects. In fact, while 2 to 3 percent of
8 birth defects are detectable at birth, one major
9 study found that continued monitoring for seven
10 years after birth found up to 16 percent birth
11 defects. That was the Columbia -- the Collaborative
12 Perinatal Project, which was a prospective study of
13 50,000 pregnancies at twelve medical centers in the
14 United States.
15 Next chart, please.
16 This same report surveyed a group of
17 experts who said that up to 60 percent of birth
18 defects are of unknown origin, but 74 percent of
19 these experts believed that 25 percent or more would
20 be eventually linked to environmental exposures of
21 one kind or another.
22 Although linking and finding the
370
1 total incidence rate of birth defects is a major
2 challenge, even a greater challenge is trying to
3 link particular birth defects with particular
4 exposures.
5 According to a major text on birth
6 defects, Congenital Defects, by Saxen and Rappala,
7 overall incidence of birth defects may not be able
8 to detect specific causes. And in fact, thalidomide
9 we kind of call the great-granddaddy of teratogens,
10 did not cause an increase in the total number of
11 birth defects.
12 In fact, all the major teratogens, or
13 most of the major teratogens that have been
14 identified to date, have been identified by the
15 mechanism Dr. Brent mentioned yesterday, the alert
16 practitioner. That is, a doctor or doctors begin to
17 see a pattern of birth defects in a group of
18 children and begin a retrospective analysis of what
19 might be a common factor in the background of these
20 children. This includes, but is not exclusive to,
21 thalidomide, rubella, fetal alcohol syndrome, fetal
22 hydantoin syndrome, valparoic acid syndrome, methyl
23 mercury, PCBs, lithium, DES, radiation, and others.
2 We decided with the National Birth
3 Defect Registry to try to adapt the process of the
4 alert practitioner in a broad way by taking advanced
5 computer technology and database design to look at
6 large numbers of cases from all over the country.
7 We began this project in 1991 by
8 designing an interrelational database and an
9 original twelve-page questionnaire. Our
questionnaire is divided, not just by overall syndrome names, but by birth defects by body system. We have the ability to collect literally thousands of combinations of birth defects in this way, and to examine syndromes, not just by the name they've been given, but by the components of those syndromes.
The development of the original project took over a year, with multiple reviews by outside experts. The American Legion gave us a grant for pilot-testing of the project. And we distributed 5,000 questionnaires to our entire mailing list, which was at that point consisted of families with children with birth defects, state and national developmental disability programs, support groups, and medical research centers and other people working with birth defect populations. Of this original mailing, 1,200 registry questionnaires were returned for databasing.

One inducement to participate in this project and complete our lengthy questionnaire is our parent-matching component. In fact, I would say that as many parents participate to be matched participate because they may have some idea about what caused their child's birth defects.
The first environmental issue that we addressed with the database was the ongoing
controversy regarding Agent Orange and birth defects. Although 65,000 cases of adverse reproductive outcome had been reported to the court during the Agent Orange litigation, nobody seemed to have any idea what these reports consisted of. There was no tally made, no examination of the case reports.

So under a contract from the State of New Jersey and working with the New Jersey Agent Orange Commission, we added an additional page to the questionnaire, and we did send that page to all 5,000 of the original participants on service in Vietnam.

In 1992 the Association and the New Jersey Commission made a dual report to the National Academy of Science committee appointed to review the health effects of herbicides and dioxin in veterans and their children. At that point we compared the disabilities in 800 Vietnam veterans' children to 400 non-veterans' children in the database. And to do this, we convert these cases into cases per hundred in the database, so that we'll have some comparative. We put these statistics into Harvard Graphics charts. And at the first instance we do some basic things, and then New Jersey did some statistical work.
Today the charts that I'm going to present are just the first level. You can go ahead with the next chart. And I want to emphasize that we have found this pattern of disabilities in veterans' children from the first time we analyzed 300 cases. Now we have almost 2,000 cases. And it hasn't changed. We haven't added a condition, nor have we subtracted a condition. In the first chart you'll see we have increases in a variety of childhood cancers. Next chart, please. We have consistent increases in allergic conditions of a variety of kinds. We have impressive increases in growth disorders. Persistent skin problems. And notice particularly the "acne-like rash"; this is not teenage acne. These are unusual acne-like skin manifestations in strange parts of these children's bodies. Next, please. Increases in attention deficit disorders. Increases in all areas of learning and -- learning problems.
Consistent and impressive differences in emotional and behavioral disorders. And a variety of miscellaneous conditions which are very consistent with some of the effects of chronic fatigue syndrome. We also have increases in endocrine disorders, benign tumors, and cysts, but I didn't want to take up the time with too much Agent Orange today.

The National Academy referenced our report in their book Veterans And Agent Orange, and they did indicate that we had found some increases. They had two problems with our data collection. One was the potential for recall bias, and the second was for self-selection.

So after their report, our organization brought together a team of seven national experts -- they didn't know each other; they came from all different disciplines in different parts of the country. We brought in people who had expertise in reproductive epidemiology, biometrics, environmental biology, genetics, endocrinology, biochemistry, obstetrics and gynecology, and developmental biology. We brought them down to Orlando. We laid the project
before them and said, "What do you think? We'll just do what we say it can do, and are we doing it the right way?" They didn't let me talk, which is an achievement in itself, and they settled down to work.

And they came up with a consensus statement in support of what we were doing. And that is looking for potential clusters of birth defects associated with potential exposures. This does not constitute proof. This simply is pointing a direction to start looking.

They also decided that they wanted to redesign the questionnaire to make some of our questions less biased, to add some component for medical records, to get medical records to confirm diagnoses. They recommended trend testing, to continue looking at things as we gathered numbers and to help offset self-selection processes. And they asked us to do a different type of outreach for the project that would reach more families for the parent-matching component where they didn't have a biased idea of what might have caused their child's birth defects.

So at that point we started to advertise the registry's parent-matching component in the premier national disability magazine,
Exceptional Parent. Since that time our figures for Agent Orange in our registry is -- our registry is over 3,000 cases now. Our Agent Orange cases represent over 1,600.

We have the same pattern. It has not changed. It has stated consistent all along. The pattern --

Once we've found a pattern and it is consistent as we double and redouble and redouble the data, we go out and look other forms of more highly controlled research: animal work, cell culture work, studies that were recently done in children at Times Beach. And we found support in these studies for the patterns that we were finding.

And in fact, the 2,000-page EPA's "Reassessment of Dioxin" also points out that postnatal functional alterations involving learning and developmental reproductive system are most sensitive endpoints to the prenatal dioxin exposure, as is the developing immune system and growth and skin problems. So what we found in the veterans' children is very consistent with other forms of data. Still, I wouldn't say that we have cause and effect here; that will require an actual case-controlled study or a more refined epidemiological effort.
At the same time that the committee came down to look at the project, I wrote up the question to them of the Gulf War cases that we were starting to get, because we were starting to get calls to our office of families who had served in the Gulf and were having children with birth defects. And I innocently asked the committee "Should we make a special effort to collect this data?" and they said, "Yes," so -- I wonder why. So they added a new page on that, and this -- the page on our questionnaire on Gulf War is based on information that we got from Senator Riegle, Senator Rockefeller, and other research that we did on our own.

I didn't have time to do a new set of charts for you, but I did bring the set that we did in September.

Currently we have case reports from 227 male veterans in our database, 30 veterans where both males and females served, and 13 where the mothers only served.

I would venture to say that we hear from about twice as many people as those who actually returned the questionnaire. There's a great concern in the veteran population, particularly the active-duty military, about being
too active on this issue.

Although the case reports we have are based on figures from September, I think they're representative of what we are seeing. In this instance, rather than show you all twenty-six charts I would normally show you, I have condensed those conditions that we have found increases in when we compared the two groups in our database.

If you look down, these are cranial, facial, and neurological problems. You'll see the Goldenhar syndrome that has had a lot of conversation. I'll talk about that more in a minute. External ear anomalies are impressive. The micrognathia and the bony defect of the skull often is included within the Goldenhar. Craniosynostosis, Dandy Walker cyst, microcephaly and anencephaly.

Next chart, please.

We are also seeing some impressive differences in heart defects. And I don't need to tell you that heart defects are among the more common birth defects, so you have to look at a lot of heart defects to demonstrate any linkage.

But one area that I am particularly interested is -- in, is the hypoplastic left heart syndrome, which is a rare birth defect. We also recently have gotten some cases of hypoplastic right
19 heart syndrome.
20 Next chart, please.
21 Across the board in the veterans' cases, we find a thread of immune dysfunction,
whether these are just functional birth defects or children with severe structural problems. Chronic upper respiratory infections, chronic thrush, temperature instability -- these children spike temperatures for no reason -- a frank immune deficiency in some cases, skin color changes.
7 I added the hemangiomas and the strawberry marks to this chart because part of the new treatments for hemangioma is interferon, which might suggest there is some immune basis for that. Strawberry mark is a hemangioma, but it's a small one, so most parents aren't given that technical term. So we separate those out, but those technically are all hemangiomas.
15 We have an impressive difference in lung absence -- either absence or underdevelopment in these cases.
18 Next chart, please.
19 And finally, this is kind of a duke's mixture of gastrointestinal, genitourinary, and some chromosomal problems that we are seeing differences
If we could go back to the first chart for a minute and talk a minute -- back to the chart 13; I'm sorry.

A lot of attention has been given to the Goldenhar syndrome. We have twenty-four cases of children in the database now who have external ear anomalies. Any external ear anomaly case technically can be termed a branchial arch syndrome. Branchial arch syndrome anomalies can be autosomal dominant, they can be sporadic, or they can be multifactorial.

In the case of Goldenhar syndrome, which is technically a branchial arch syndrome deformity, there are, historically, some familial cases in the literature. But there are also cases that have been linked to well known teratogens: thalidomide was connected with branchial arch deformities, most particularly Goldenhar; primadone, which is an antiseizure medication; and of course, acutane.

Yesterday Dr. Araneta discussed the problem with coming up with an accurate incidence figure for Goldenhar syndrome, and she cited various state registries, which we've looked at as well. We have also looked at the
Collaborative Perinatal Project, because it was a controlled and prospective study of a large number of pregnancies. In that study of 50,000 pregnancies they found one case in every 26,400.

Although I clearly can't say at this point that Goldenhar is linked to the Gulf, I will tell you that we can analyze every kind of exposure in this database, from aspirin to how many ultrasounds you had, to water you drank, to co-factors, smoking, drinking, recreational drug use. And we don't find this skewing with any other exposure category, with the exception of one.

There are two things. When we analyze Goldenhar, Gulf War service in the Gulf, and living within an agricultural area during pregnancy are the two things that we see increased right now.

Because we take this work very seriously and we know the decisions families make about their future reproductive life are very serious ones to them, we don't do this lightly. When we started seeing the increase in Goldenhar, we did a special outreach to various projects around the country that do parent-matching. We obtained the names of 175 cases of children with Goldenhar syndrome and sent questionnaires out. So we have 65 cases, total, of Goldenhar in our
database. And we can actually go into just that
9 birth defect category and, conversely, look at the
distribution of various exposures. So we can look
11 at it backwards and forwards.

As difficult as it is to look for
13 potential increases in certain disabilities, it's
14 even more difficult when you look at the
multiplicity of exposures in the Gulf. According to
the GAO report, there were twenty-one different
reproductive toxicants in the Gulf -- everything
from pesticides, lead, and mercury, arsenic,
cadmium, the potential of chemical warfare agents,
not to mention multiple inoculations, pyridostigmine
bromide. So teasing out one of these from all the
others will be a real challenge, not to mention the
interactions or synergism that might exist between
various things.

However, we already have some
interesting little tickling things going on with the
data. And that is, in our Goldenhar cases, four of
our cases were in parents' fathers who were called
up for service, given all the preliminary
inoculations, but didn't go. So that's an
interesting little aside at this point.

For several years our organization
has been monitoring ongoing research on
immunotoxicology. And we have been looking at the connection between immunotoxic agents and their potential to be teratogens. Many of the agents in the Gulf are toxic to immune function. And we have come to think, or at least to hypothesize that an immunotoxic agent at one level of exposure may cause a severe structural birth defect, but more commonly at lower levels may cause functional birth defects, such as learning, attention, immune, endocrine, and other problems.

Unfortunately, in the country today we really don't monitor functional birth defects at all, so we have no good handle on the statistics. I appreciate you inviting me here today, and I'd be most happy to answer any questions. And we would like permission to submit a more fully worked out report to you in written form.

QUESTIONS

MS. LASHOF: Thank you very much. That's very interesting data, and by all means we'd be anxious to receive any full report and any additional information up until November, when we have to put our report together.

MS. MEKDECI: Very well.

MS. LASHOF: After that, it may be harder to incorporate it.
16 Questions. Marguerite?

17 MS. KNOX: I just have one. You said

18 there were four fathers who received the

19 vaccinations.

20 MS. MEKDECI: Yes. Right.

21 MS. KNOX: And those are anthrax and

22 botulinum, or just the anthrax? Do you know what

387

1 they received?

2 MS. MEKDECI: Well, the fathers

3 weren't -- no one that I'm aware of was told what

4 they received. They were -- they received the

5 inoculations.

6 Now, one of the cases is interesting,

7 in that the father received the inoculations state

8 -- stateside, and worked with gear that was

9 contaminated when it came back. He now is being

10 treated for Gulf War syndrome.

11 And another father was working in an

12 occupation where he was working with a lot of

13 chemicals in the particular occupation he was in,

14 but we don't know for sure -- I mean, in some cases

15 people think they know that they were exposed to

16 this or that.

17 One -- one area that I'm concerned

18 about is the gamma globulin shot. Pretty much
everybody who went over got gamma globulin. It's made of multiple blood products. And while it's screened for AIDS, it is not screened for all the potential viruses that are out there today. And there are a number of new immune-affecting viruses that I have a particular interest in, particularly human herpes virus 6, 7, and 8, not to mention some mutations of the HIV virus. So that's a particular concern. And I knew that all of them would have gotten that.

MS. LASHOF: Let me try to better understand your control groups.

MS. MEKDECI: Okay.

MS. LASHOF: I mean, obviously you're not in a position to do the traditional case-control groups.

MS. MEKDECI: Right.

MS. LASHOF: And most retrospective studies where you find a defect thing, you look for a child that was born the same day in the same place, et cetera, and then look at exposures of parents. And you're not able to do that.

Can you tell me a little more about how you select who you're matching against? And when it says, "Non-Gulf War," does that all-include? And are they controlled in any other ways?
MS. MEKDECI: At this point in time when we say, "Non-Gulf," what we do is, we compare all the cases in a particular category to all the cases that are not in that category in the database. Now, that's a little tricky, because sometimes you may be comparing apples to apples, if you're not careful. For instance, within the Gulf exposures we have pesticides. So some of our other -- but we can take that out. We can actually get into removing those and putting those aside and looking at them. We don't have the illusion that our data does anything more than look for clustering. From that point, you can go -- you can go into a random selection within the database, once the numbers reach a certain critical mass. And in fact, the New Jersey Commission is trying to get us to do that on the Agent Orange, and we probably will. But what we really think our data can do is point a direction for case-control work that would be done in the traditional way. Because I realize that what we're doing is a little unusual, although there are several studies that have used malformed children as control groups -- in fact, the Center for Disease Control has done that type of
5 study before.
6 MS. LASHOF: Okay. Second question:
7 specific -- well, on all of them, but let's take
8 Goldenhar as one you've looked at particularly.
9 What is the relationship of the cases that you have
10 of Goldenhar to the time at birth in relation to the
11 time of service? What duration period post-service
12 are you still seeing the --
13 MS. MEKDECI: The latest case of
14 Goldenhar that we have in the database was born in
16 I would like to point out that the
17 thirteen cases -- we have thirteen cases in the
18 database -- does not represent all the cases that we
19 have heard of. We have five cases that have called
20 us, but for reasons unknown to me just simply won't
21 return their questionnaires. So we can't count
22 those. But I can tell you we've heard from them.
23 1 MS. LASHOF: So the total number of
24 Goldenhar is only thirteen? Is that --
25 MS. MEKDECI: We have thirteen in the
26 database that have been classified by a medical
27 professional as Goldenhar. Within our ear anomaly
28 cases we have another four or five that have facial
29 asymmetry, the ear anomaly, a vertebral column
30 problem, that in my mind could technically be
9 classified as Goldenhar. But I don't have the
10 expertise to put them in that category. We can just
11 tell you that we have that combination of defects.
12 MS. LASHOF: And how many Goldenhar
13 do you have in non-Gulf --
14 MS. MEKDECI: In the non-Gulf we
15 would have thirteen -- well, sixty-five minus
16 thirteen -- what would that be? Fifty-two.
17 MS. LASHOF: Okay. So percentage-
18 wise, you have thirteen Goldenhar with --
19 MS. MEKDECI: In the Gulf.
20 MS. LASHOF: In the Gulf.
21 MS. MEKDECI: Yes.
22 MS. LASHOF: And fifty-odd in the
392
1 non-Gulf.
2 MS. MEKDECI: Right.
3 MS. LASHOF: And the total congenital
4 defects in the non-Gulf are -- I mean, how big is
5 your non-Gulf sample --
6 MS. MEKDECI: Oh.
7 MS. LASHOF: -- and your Gulf sample?
8 MS. MEKDECI: Our non-Gulf sample --
9 our Gulf sample in the charts that I showed you was
10 194 cases, and the non-Gulf sample was -- I don't
11 remember the figure -- 2,100 and some-odd at that
12 time.
14 That's a very significant difference.
15 MS. MEKDECI: Yeah, different. It's
16 very -- and it's especially different because we
17 didn't just let things come into the database on
18 Goldenhar. We actually went out searching to bring
19 in cases to look at it in a thorough way.
20 Ordinarily, if we had just left it alone, we
21 wouldn't have nearly that many cases of Goldenhar in
22 our non-exposed, because they wouldn't have come in
23 like that. We actually searched them out.
24 MS. LASHOF: But what time period?
25 What age ranges were there in your non-Gulf
26 Goldenhar --
27 MS. MEKDECI: I can't tell.
28 MS. LASHOF: -- versus your --
29 MS. MEKDECI: I can't tell you that
30 today. I would have to do that.
31 MS. LASHOF: Yeah.
32 MS. MEKDECI: We were --
33 MS. LASHOF: It would be important
34 that we're not talking about completely different
35 time periods.
36 MS. MEKDECI: Oh, absolutely.
37 Absolutely. Actually, when we do a
report, we do go into all of that, and actually go
into some statistics work. But I just didn't have
time.

MS. LASHOF: Yeah; sure.

MS. MEKDECI: We were hoping to get
more of those cases that are out into the database
before we did a report for you.

MS. LASHOF: Okay. Well, we'll look
forward to receiving that.

Another question I have is: I think
your criticism that we don't have a national birth
defects registry is a very solid one. Would you be
supportive of federal legislation requiring that we
have a national birth defects registry, and require
that all birth defects be reported?

MS. MEKDECI: That would certainly
depend on who they were going to get to do it.

(Laughter.)

MS. LASHOF: CDC.

MS. MEKDECI: I have to tell you,
I've been doing this for twenty years, and I have
some -- I'm sure there are some salt-of-the-earth
people at CDC, but I've had some very unfortunate
experiences with CDC on a variety of issues.

I want to add a little addendum. In
1984 I was diagnosed with chronic encephalopathy and
20 immune deficiency. I have had pretty much all the
21 symptoms that Gulf War veterans have had. And in
22 fact, I was exposed to one of the chemicals that was
395 1 on the federal list of procurement for the Gulf. I
2 know what these families are going through.
3 Unfortunately for them, they didn't
4 happen to go to the doctor that I went to. I was
5 diagnosed by a doctor who was formerly the head of
6 the American Academy of Allergy and Immunology. I
7 was diagnosed very quickly. No one ever told me I
8 was crazy. No one ever suggested that I had PTSD.
9 I had some very serious immune problems. They did
10 suggest I needed to be tested multiple times for
11 AIDS. I have had some of the most sophisticated
12 immune system testing available. I've been on
13 experimental treatment. I'm not dead. I think I am
14 reasonably coherent most of the time, although
15 things like this make me a little -- a little
16 uncomfortable.
17 I've done a lot of research on this.
18 I hope that every member of this Committee has seen
19 this book and read it. Because in your analysis,
20 not only of the Gulf War birth defects, but your
21 analysis of Gulf War syndrome, this is a very
22 valuable tool.
396 1 I believe that these veterans have
something going on. I don't know what it is; perhaps no one does at this point. But I can tell you definitively that there is treatment and there is diagnosis available. And I don't believe they're getting it, from what I'm hearing from the veterans I'm talking to. And they certainly are not getting the quality of care that I have gotten.

MS. HANNA: Can I ask a question?

MS. LASHOF: Yes, please, Kathi.

MS. HANNA: I have a question about your initial mailing group.

MS. MEKDECI: Yes.

MS. HANNA: You had mentioned you had 5,000 people.

MS. MEKDECI: Yes.

MS. HANNA: And that's where you collected your first set of data?

MS. MEKDECI: Right.

MS. HANNA: Can you just explain a little bit more who is --

MS. MEKDECI: Where that came from?

MS. HANNA: Yeah, where the -- who those --

MS. MEKDECI: Sure.

MS. HANNA: Who those recipients are?

MS. MEKDECI: Yes.
MS. HANNA: And you had mentioned
that one category is medical centers or whatever.
And they receive a questionnaire?

MS. MEKDECI: Yes. What we did is --
our mailing list grew from its infancy. We started
with eighty families working out of a utility room
many years ago. Our mailing list is now over
12,000. But at the point that we did this, we had
5,000. I'm not sure how it's grown; it's grown like
Topsy. We have federal programs, we have state
programs, we have support groups, we have libraries.

They just come. I don't know how they get us. We
have twenty-two countries, although we didn't send
the questionnaires to the twenty-two countries.

We actually had a state developmental
disability program send us all the labels for the
children they had served that year, which shocked
the heck out of me.

But the reason we sent it to medical
centers for that purpose, we actually got states
that were interested, we got professionals who were
interested. We were trying to send it out broadly
to see how it would fly. And it did very well,
considering it was --

MS. HANNA: And the questionnaire, is
9 that similar to the questionnaire that you submitted
10 to us?
11 MS. MEKDECI: It's similar, except
12 the original questionnaire that we sent out didn't
13 have the Gulf War page or the Agent Orange page.
14 Now, we have also rewritten a few of
15 the questions since that time. You think that you
16 have things perfectly designed until you've sent out
17 a bunch, and then you find out something needs to be
18 changed as far as the wording, certain little
19 things. And of course, the committee reworded a few
20 things that they thought could be better said, so --
21 MS. HANNA: But the questions on the
22 questionnaire are --
2399 1 MS. MEKDECI: Essentially the same,
24 yes.
25 3 MS. HANNA: Right. But they're
26 directed to an individual --
27 5 MS. MEKDECI: Correct.
28 6 MS. HANNA: -- concerning their
29 reproductive --
30 8 MS. MEKDECI: Correct.
31 9 MS. HANNA: So let's say a caseworker
32 or whatever the disability agents --
33 11 MS. MEKDECI: It goes to directly to
34 the family.
MS. HANNA: They then can copy it and
give it to --

MS. MEKDECI: Well, they don't copy
these are not copied. Each one of these is
coded by a number.

MS. HANNA: But they could request
additional surveys?

MS. MEKDECI: They can request
additional ones. We now have an 800 line where
anyone in the country who wants one of these can
call up day or night, twenty-four hours a day, and
we'll send out the packet to them, and then they can
send it back.

When they send it back, if they
choose, we'll do the parent-matching. They don't
have to do parent-matching, or at any point we can
cut that off if they don't want to do parent-
matching.

We don't match by exposures. Because
if we start that, we'll be accused of setting up
litigation or rabble-rousing or I don't know what.
So we just match by conditions. At this point we
can match by major condition or up to five separate
components of a condition. As the database grows,
we'll be able to go to more and more. We can --
eventually maybe we can match by twenty conditions.
But we try to give them a sufficient number of contacts.

MS. HANNA: So all of the people -- all of the individuals that return the questionnaire are returning it because they have a child --

MS. MEKDECI: That's right.

MS. HANNA: -- with a birth defect?

MS. MEKDECI: That's correct.

MS. LASHOF: On the parent-matching,

you're matching them for the conditions, putting parents in touch with each other.

MS. MEKDECI: Correct. Correct.

MS. LASHOF: And they have a choice of saying yes, they want to be matched --

MS. MEKDECI: Right.

MS. LASHOF: -- or "Please don't give my name to anybody" --

MS. MEKDECI: Absolutely.

MS. LASHOF: -- "under the sun" or whatever?

MS. MEKDECI: Absolutely. There's a question on here we have highlighted in red, and if at any point they want to change that -- let's say they've done parent-matching and they don't want to
do it any more, they can call us up and we just change that Yes to a No, and that's the end of it.

We have had a lot of good feedback on the parent-matching. The parents are very excited. If we send a match that they don't like, they send it back and have us rematch by a different condition. They're very enthusiastic. Because one of the things about having a child with a birth defect is, it's a very isolating type of challenge. And there's nothing like talking to somebody who's either been through it, going through it -- it just gives you, you know, some support system.

Unfortunately, for most categories of birth defects there are no support groups. You know, for the larger categories, yes. But most things, there are no support groups. So we try to give parents that emotional cushion, if you will.

MS. LASHOF: Let me try one more question on Goldenhar, if I may.

MS. MEKDECI: Surely.

MS. LASHOF: Have you found anything else other than Gulf War that -- and even before the Gulf War came into the picture, when you were looking at --

MS. MEKDECI: Yes. When we --
MS. LASHOF: -- branchial arch --

MS. MEKDECI: When we analyze our

total Goldenhar cases, we do find living in an

agricultural area to be impressively skewed. And

I'm not sure what the meaning of that is. My guess

would be pesticides, but that might be a little

prejudiced, so --

MS. LASHOF: Yeah. When you say,

"living in an agricultural area," have you been able

to break it down to those who were actively engaged

in agricultural --

MS. MEKDECI: We haven't done that.

MS. LASHOF: -- activities --

MS. MEKDECI: We haven't done that.

MS. LASHOF: -- versus those who just

live there?

MS. MEKDECI: We have a -- within --

I believe it's within three miles of an agricultural

area. And we haven't broken it down.

One of the things that the project

will do is, if we find something like that that

we're interested in, we can do another questionnaire

and go back. Because we have a question "Can we get

back to you for further research?" So our committee

at any point can go back to them and say, "All

right, now, let's find out: are you working in
farming? Are they farming next door?"

MS. LASHOF: Farm, yeah.

MS. MEKDECI: You know, "What's been going on?"

MS. LASHOF: "Are you using pesticides yourself?"

MS. MEKDECI: "Are you using pesticides in your home?" We do ask that question, "Are you using pesticides in your home, in your office?" -- whatever.

MS. LASHOF: Thank you very much.

Tom?

MR. McDANIELS: When your association receives queries from Gulf veterans about the incidence of birth defects in their offspring, what type of education and information do you give out on the incidence of environmentally-produced birth defects?

MS. MEKDECI: Okay.

The most difficult questions that we handle at our office are "I served in the Gulf" or "I was exposed to this" or "What's going to happen? Am I going to have a child with a birth defect?" -- a tough question for us to have to answer.

And what I tell parents routinely is this: all known teratogens -- even if we had
identified something in the Gulf, all of them only affect a minority of children. With thalidomide it was 20 percent, with dilantin it's about 5 percent, fetal alcohol syndrome is one percent of those exposures in the country. So when you're looking at environmental birth defects, fortunately, even if you took 100 women and exposed them all, only a minority would be impacted.

So I always tell them that "The chances are always greater than not that you're not going to have a problem. However, everybody is at risk in our country of having a child with a birth defect. Most of us don't ever think about it. I certainly never thought about it. And if this is a problem for you, if the child -- if your child is born with a birth defect, if that's going to be a problem for you, then you need to think about getting pregnant altogether, because none of us get a gilt-edged guarantee."

We can't tell them at this point that we have seen an increase, or an increase over the base line from exposures in the Gulf. We can tell them that we're seeing some interesting clusters; we're not sure what that means yet. But I can't tell them to not have a child because they served in the Gulf. I can tell them that everyone is at risk
14 of having a child with a birth defect.
15 MR. McDANIELS: And do they tend to
16 understand that? Does that tend to assuage their
17 fears?
18 MS. MEKDECI: They always seem --
19 yes, they do. They seem to feel better. In fact,
20 we get very nice letters, you know, that "Gee, it
21 was wonderful that you talked to us." And I can
22 talk to parents, because I have a son with a birth
407 l defect. I've been there -- going through it. He's
2 twenty-one now; we've been through all the ages and
3 stages. And I can tell them, too, that it's not the
4 worst thing in the world that ever happens to you.
5 Of course, that also depends on the type of birth
6 defect. You know, with David, he's able to go to
7 school and work and everything. So I have a
8 particular insight.
9 I don't think anyone ever calls our
10 office and comes away horrified by anything we've
11 told them. I think they feel relieved. And I think
12 if you talk to some of the families, they would
13 share that with you.
14 MS. LASHOF: Marguerite?
15 MS. KNOX: Would you give us that
16 1-800 number that you spoke of earlier?
17 MS. MEKDECI: Sure. Sorry; I'm
18 getting a little hoarse. It's 1-800 313-2232. And
19 the 1-800 number, we've recently changed that.
20 We've had some problems with funding
21 in the last year, because half of our funds come
22 from the federal campaign, and this year,
23 unfortunately, there was the federal work stoppage
24 during the campaign, so a lot of organizations, not
25 just ours, suffered from that.
26 We are now -- we offer free
27 information on the line, and we do market several
28 kits that we're trying to use to pay for the
29 information line, so that we have everything
30 supported. So if you call that line, you'll have a
31 component where you can get free information about a
32 birth defect, you can get a free questionnaire
33 packet. You can order an Agent Orange information
34 package for a $15 donation. You can order a Gulf
35 War package, an environmental birth defect package.
36 Or you can become a member over the line.
37 I think we've caught the same thing.
38 MS. LASHOF: It's contagious.
39 Okay. Thank you very much.
40 MS. MEKDECI: Thank you.
41 MS. LASHOF: We do appreciate your
42 coming.
43 MS. MEKDECI: I appreciate it.
MS. LASHOF: And we look forward to receiving further information from you.

MS. MEKDECI: Thank you.

MS. LASHOF: The next presenter is Linda Shortridge-McCauley.

**ASSESSING REPRODUCTIVE HEALTH IN SPECIAL POPULATIONS**

**COMMENTS BY LINDA A. SHORTRIDGE-MCCAULEY**

MS. McCAULEY: Betty was hoarse at the end of her talk and I'm hoarse at the beginning of mine, so bear with me.

MS. LASHOF: Well, hopefully, you'll get better by the end.

MS. McCAULEY: Good morning, Madam Chairman and members of the Committee. My name is Linda McCauley, and I'm a scientist at the Oregon Health Sciences University Center for Research on Occupational and Environmental Toxicology and lead epidemiologist of the Portland Environmental Hazards Research Center, a joint research enterprise of OHSU and the Portland Veteran Affairs Medical Center.

I've been asked to speak to you this morning on the assessment of reproductive health in special populations, specifically those having occupational or environmental exposures to chemical,
physical, or psychological factors. Knowledge of
the potential reproductive toxicity of even rather
common occupational exposures is limited, as we've
heard frequently yesterday and this morning.
Assessing the impact, the health impact of exposures
to mixtures of chemicals and other types of agents
represents an extraordinary epidemiological
challenge.
Reproductive health effects have been
documented in populations defined by particular
workplace or environmental exposures. As discussed
yesterday, some of the best known associations
between environmental exposures and these health
effects are: lead salts and spontaneous abortions
and decreased fertility; DBCP; carbon disulfide;
also reports on spontaneous abortion increases with
workers exposed to anesthetic gases; and
reproductive effects in populations exposed to anti-
neoplastic drugs. The difficulty of delineating
relationships between environmental exposures and
reproductive health problems is increased when
exposures are multifactorial -- exactly what we're
dealing with with the experience of veterans of the
Persian Gulf War.
Second overhead, please.
At the Portland Environmental Hazards
Center we've designed a study that's looking specifically at an array of different factors that were present in the Gulf, including chemical and biological exposures from petroleum products, solvents, smoke, insect repellents, pyridostigmine bromide, vaccines, vectors, diet, water. Physical and psychological exposures include sand and heat, crowded living conditions and stress, and perceptions of exposure to danger. It creates a very complex picture. And it's difficult to look at traditional reproductive epidemiological studies and try to figure out a sane way to approach this, this population.

Next overhead, please.

In an ideal situation when you're trying to look at exposure determination, there are four components that help you begin to get a true picture of what happened in relation to exposure.

But five years after the war, exposure determination presents a particularly difficult task. Real-time measures are not available: it's impossible to verify exposures to vaccines, PB, insecticides, solvents, and infection agents, for the large majority of veterans. We have no work records to verify these exposures, and self-reports are extremely problematic. We do have
data on smoke dispersion, but exposure to smoke can only be correlated to troop unit movements, and not movements of individuals in the theater of operations.

Exposures may be gleaned, in part, from an analysis of duties. But there are thousands of codes for the types of work that the troops were engaged in in the theater of operations. And another important component is that there's no details of the work outside of the usual duties recorded in any systematic manner.

Some of the chemicals of specific interest in the Persian Gulf War theater of operations are PB and vaccines and pesticides. However, none of these agents are known to induce male-mediated genetic effects. Exposure to alkylating agents associated with chemical warfare, notably mustard gas, could theoretically have the potential of causing germ cell damage. However, we do not have confirmed documentation of any airborne levels of these agents in the theater of operations.

Sparse information exists on the body burden of environmental contaminants that our veterans were exposed to in the theater, with the exception of lead exposures and some troops exposed to depleted uranium. Indeed, the problems of
15 exposure assessment seem insurmountable, at least in 16 comparison to methods routinely used in studies of 17 exposure and health effects in working populations. 18 We do, however, have an opportunity 19 to compare and contrast groups of veterans who had 20 disparate sets of potential exposures, because they 21 were deployed in the theater of operations for 22 distinct, identifiable periods.

And the Portland Environmental Hazards Research Center, as you may already know, is 3 using this approach to assess risk factors and 4 unexplained illness in deployed Persian Gulf War 5 veterans. This research program was designed and 6 funded to focus on unexplained illness in veterans, 7 specifically cognitive problems, fatigue, and 8 musculoskeletal complaints -- not reproductive 9 problems. But the exposure determination issues are 10 relevant for whatever health condition that you're 11 focusing on.

Next overhead, please.

This overhead, which some of you have 14 already seen from previous presentations by Dr. 15 Spencer, head of our -- the Center for Occupational 16 and Environmental Toxicology -- it illustrates the 17 relationship between discrete deployment periods and
unique sets of chemical, biological, physical, and psychological factors.

For example, those who were deployed during the period of December 31st, 1990 to March 1st, 1991 may have been exposed to a unique set of factors that included PB, special vaccines, munitions, stress from combat and chemical warfare alarms, and exposure to enemy prisoners of war. By contrast with this Desert Storm period, veterans who served only in the Desert Shield or desert cleanup would have experienced quite different exposures, which included the absence of PB and special vaccines. Other factors, such as smoke from the oil well fires, overlapped two deployment periods.

Although focusing on distinct deployment time periods does not address all exposures of interest in this population, it does provide an excellent mechanism to determine differences between risk of disease in relation to some of the key exposures of interest.

As I mentioned before, the Portland Environmental Hazards Research Center's mission is to look at the impact of environmental hazards encountered in military service on human health. And we look at this mission both in terms of hazards in the past, in the present, and in the future. And
our initial focus has been on unexpected
illnesses, but we are cognizant of the reproductive
problems that veterans are reporting, and are
looking at our research program to see how it might
be adapted to more specifically address these health
problems.

The next slide shows the framework
for the Portland Environmental Hazards Center, which
is a joint effort between OHSU and the Portland VA
Medical Center. There is an epidemiology core. We
coordinate with the Persian Gulf Registry. We have
a multidisciplinary team of clinicians,
edemiologists, biostatisticians, and also some
scientists who specialize in the area of biological
markers. We have a protozoa disorder study.

And then we have research projects
that are laboratory-based in the areas of
neuropsychology, neuroendocrinology,
neurotoxicology, and genetic toxicology.

The epidemiology core -- I want to
give you a little more detail on exactly the
population that we're accessing to identify the risk
factors for unexplained illness. We're focusing on
veterans from the northwest United States who were
deployed to the Persian Gulf region during the
approximate one-year period after August 1990.
We're using data provided by the U.S. Department of Defense as our sampling frame. A stratified random sample of subjects has been selected, and they are being mailed a self-completion questionnaire. Now, we grouped our population into strata according to the deployment periods that I described previously. And those deployment periods, again, are the Desert Shield only, the Desert Storm only, and the desert cleanup only, and then veterans serving in a combination of those time periods. We had to use a purposeful oversampling of those, what we call the clean deployment periods, because if you look at the total deployed veteran population, each of those clean deployment periods were less than 10 percent of -- each were less than 10 percent of the total population. We've designed a sampling strategy in which 50 percent of the veterans that we will be contacting will have served in only one of these clean specific deployment periods. And the other 50 percent of our sample includes veterans who served in a combination of time periods, with an oversampling of women and reservists. This overhead shows that at the time of deployment to the Gulf, there were approximately
24,000 veterans who listed Oregon or Washington as their home state of residence. To be able to contact these veterans and to bring them in for clinical studies, we focused on only those veterans who still remain in the Northwest, which is approximately 8,000. We're mailing the survey to a randomly selected, stratified sample of 3,000 veterans.

We're mailing the questionnaires in waves. Because we follow the responders to the questionnaires with telephone -- a random selection of responders are contacted to participate in our clinical case-control studies, so we're doing the questionnaire mailing in waves so that there's not a long time lapse between the time that they receive the questionnaire, perhaps are interested in participating in the research, and then will come in and participate in the clinical component.

Women comprise 7 percent -- approximately 50,000 of the total PGW deployed population. Of the 8,000 veterans in our Northwest cohort, 535, only 6 percent are women. We are contacting all of these women in our -- in our survey, and this will only increase our proportion to 12 percent females. While this rather low percentage hampers our efforts to explore the
relationship between risk factors and unexplained illness in veteran -- female veterans, it presents severe limitations in investigations of reproductive health effects in females.

Though the major aim of our survey is to contact this random population-based sample to study unexplained illness, we're sensitive to the concern of many veterans regarding the status of their reproductive health, and receive and answer many inquiries and questions regarding reproductive health from veterans who hear of our Center.

We have included reproductive health components on our survey questionnaire. These items are similar to those that are included in the VA National Prevalence Survey currently in progress and the CDC-Iowa study. We purposely looked at those questionnaires in our development phase so that we would have comparable measures.

Our questionnaire contains self-reported pregnancy histories and outcomes, including stillbirths and spontaneous abortions, the health of children, the inability to conceive, decreased libido, menstrual function, use of contraceptives, sexually transmitted diseases, and abnormal Pap smears. The survey instrument also includes in-
It's important to remember that our survey is not designed to compare rates of illness, including specific reproductive outcomes in deployed troops, to rates in non-deployed troops. We're specifically looking at the deployed population. The next slide, please.

We knew, going into the study, that we would not have the sample size to do reproductive effects with any success. If we achieve a 70 percent response rate to our mailed survey -- and as you may have heard from some of the other research going on in the country, achieving a 70 percent response rate is going to be a champagne day in Portland. But if we were to get 70 percent response, we expect to have approximately 400 pregnancies conceived after March 1991.
19 potentially leaked with -- linked with pregnancy
20 outcome data from other studies, our study alone, as
21 shown on this overhead, does not have the power to
22 do anything statistically to detect differences
422 1 between deployment groups.
2 We project that we may have the
3 sample size to compare rates of infertility among
4 responders in the different deployment strata, and
5 perhaps to do some analysis of spontaneous abortion
6 rates if female veterans and spouses of male
7 veterans are combined. This would be preliminary
8 analysis only; we would not have the sample size to
9 do any multifactorial types of analyses.
10 Even with obtaining these
11 reproductive data, as Dr. Correa mentioned today in
12 the very well designed semiconductor study at Johns
13 Hopkins, we will not -- to verify the spontaneous
14 abortion rates would be quite a challenge in a
15 population-based survey like this. So verification
16 would be extremely difficult.
17 And also, we have no time-
18 specificity. These are pregnancies that basically
19 occurred after the veterans returned home. We
20 really don't have pregnancies that occurred while
21 the exposures were taking place.
22 From our population-based survey
design, we've been able to obtain a sample of veterans, of whom 90 percent have not previously sought medical attention in the VA or DOD registries. This population is highly mobile, and requires intensive follow-up of non-responders to achieve representative samples.

From the responders to our survey, we're recruiting 250 subjects reporting symptoms of unexplained illness and 250 health controls who will participate in the clinical evaluation component of our study. The response rate for the clinical evaluation component has been very positive: 80 percent of the questionnaire responders have agreed to be contacted for future studies, and enrollment rates for the clinical case-control study are approximately 80 percent. That's for veterans living within fifty miles of our Center. We'll have to do satellite clinics as we move out into other areas of the Northwest. The participation rates for cases and controls are comparable, to date.

During our clinical evaluation of cases and controls we obtain samples of blood, lymphocytes, and skin to assess DNA damage and repair, in a study being conducted by Dr. Glen Kisby at OHSU. Two questions are being asked by Dr. Kisby: one, the first, is to try to determine if
there's evidence of greater DNA damage in tissues from cases versus controls, in particular DNA damage that could be linked to exposure to alkylating agents; secondly, we will attempt to ascertain if the DNA-repair capacity of cases differ from that of controls.

As was discussed yesterday, could chemicals associated with the Persian Gulf War have produced infertility or genetically altered offspring in the male veteran population? We are currently considering an extension of Dr. Kisby's DNA research into the area of germ cell cytogenetics.

DNA-repair systems are present in spermatogonia and spermatocytes. There is a need to develop and validate semen markers of genetic toxicity and induced mutations, including DNA adducts in mature sperm. Studies of DNA repair have been performed also on spermatogenic cells by measuring the unscheduled DNA synthesis required to repair an excised length of damaged DNA. While the results of these studies may indicate the presence of abnormal DNA in sperm, the origin of the damage is not thereby indicated.

CROET also has available in-house a
DNA-repair-deficient mouse model which might have utility in screening chemical agents for gonadotoxic effects. Such research endeavors could benefit, not only the veterans of the Persian Gulf War, but also future military and civilian populations and their families.

In conclusion, the Portland Environmental Hazards Research Center's primary goal is to identify risk factors associated with unexplained illness. But we recognize the concerns of veterans of the Persian Gulf War regarding their reproductive health and the health of their families and offspring. We really welcome opportunities to collaborate with other researchers, particularly in the area of achieving sample sizes needed for epidemiological investigations. And we welcome opportunities to expand our research program to include specific laboratory investigations of the cytogenetic potential of exposures encountered by veterans of the Persian Gulf War and by servicemen and women of the future.

Thank you for the opportunity to present our program.

QUESTIONS

MS. LASHOF: Thank you very much, Dr. McCauley.
Are there questions for Dr. McCauley?

Joe?

MR. CASSELLS: Yes, I have two questions to begin with.

In your earlier part of the presentation you indicated in the pre-combat, the Desert Shield environment, there was absent botulinum toxoid, absent anthrax, absent PB. My understanding is that anthrax and botulinum were, in fact, administered prior to Desert Storm during the time of Desert Shield. Is that accurate?

MS. McCauleY: Towards the end of Desert Shield, but not in the group that were deployed in the August/September/October -- the buildup period. We've not had any documentation of that.

MR. CASSELLS: Anthrax is, I think, a three -- for a full course of immunization, is a three-shot at various intervals.

MS. McCAULEY: No; the anthrax was a special pre-combat type of preparation vaccine, and not part of the routine, that vaccine series that everyone would get.

MR. CASSELLS: Right; I understand.

I'm just getting some -- trying to get some feel for at what point in time anthrax was given.
MS. McCauley: We believe it was not in the early fall period, that clearly there was some -- they began giving vaccines toward the end of the Desert Shield period for people who were going to remain in the theater. But this Desert Shield group is a very interesting group. They may have gone over two or three times for short periods of time, or were there for a specific purpose, and were in the buildup period and then were returned back to the United States before the combat. So they had the environmental exposures, but they really were not part of the combat picture.

Mr. Cassells: Okay. Considering the limitations, the considerable limitations you have put upon the information that you can get relative to reproductive effects of these exposures in the veterans population you're looking at, at best, what do you think your study can do?

Ms. McCauley: Well, I think, as pointed out yesterday, if there are male-mediated genetic effects, it's -- you should be able to see those effects in infertility rates. And some of the population studies, the Portland study and some others that are being conducted in the United States, need to look at those rates, and
particularly if we have samples of non-deployed 
troops, as a first cut, to see if there's any 
evidence. It's going to be much easier, probably,
to assess an effect on fertility than it's going to 
be in terms of an effect on birth defects.

MR. CASSELS: Specifically.

MS. McCAULEY: So I think that that 
is an area that merits attention.

In spontaneous abortion rates, again,
it's just not similar to a lot of occupational 
studies where you look specifically at pregnancies 
that are conceived while the exposure is taking 
place. It's just a very different type of 
phenomenon that we're dealing with with the Persian 
Gulf War.

MR. CASSELS: So --

MS. McCAULEY: But I think as a -- I 
think as a first cut, those are two things that we 
should look at in populations.

MR. CASSELS: So at best, you may be 
able to generate a hypothesis?

MS. McCAULEY: It'd be interesting to 
see if post-Persian Gulf War there was a difference 
in fertility rates in these deployment strata. That 
would lead to some interesting speculation about 
exposures and effects. But you don't know unless
you do that preliminary look at the data.

MS. LASHOF: All right.

MS. KNOX: What are you doing in particular to attract veterans to filling this survey out? How are you going about advertising that to veterans?

MS. McCAULEY: We don't really advertise. The sample is randomly selected, and they receive the questionnaire, follow-up post card, then a replacement questionnaire. And then we are phoning all non-responders. This is something that we did not anticipate having to do, but our -- after the three contacts our response rate was 53 percent. And so by contacting non-responders, we're trying to push that up --

MS. KNOX: A little higher.

MS. McCAULEY: -- between 60 and 70 percent. We're also giving a $10 incentive to return the questionnaire, to complete and return the questionnaire. There's a $50 incentive to come in for clinical exams.

MS. LASHOF: Any other questions?

Tom?

MR. McDANIELS: In terms of branch of service, is your -- this population representative
5 of the Desert Storm and Desert Shield population?

6 MS. McCAULEY: Yes. Our data are

7 comparable to the general frequency distributions in

8 the DOD database.

9 MR. McDANIELS: Okay. I was just

10 concerned that with the Northwest population you

11 might have an overrepresentation of Navy personnel

12 and different exposures for them.

13 MS. McCAULEY: It doesn't appear to

14 be, no. I think this -- the Northwest cohort

15 included people who were stationed all over the

16 United States, but listed Oregon and Washington as

17 their home state of record at the time of

18 deployment, so it's not just people who were just

19 stationed here. So we're not seeing any distinct

20 differences in the branch of service.

21 MS. GWIN: Thanks very much, Dr.

22 McCauley.

432 1 MS. McCAULEY: Thank you.

2 MS. GWIN: We'll start our next panel

3 now on diagnosis, defining syndromes, determining

4 prevalence, and surveillance.

5 DIAGNOSIS, DEFINING SYNDROMES,

6 DETERMINING PREVALENCE, AND SURVEILLANCE

7 COMMENTS BY LEWIS HOLMES

8 MR. HOLMES: Shall we start?
MS. GWIN: Dr. Holmes, thank you.

MR. HOLMES: Thank you. I appreciate the opportunity to make my presentation. I'm here as a geneticist and teratologist. I spend my time trying to learn how to identify environmental causes of birth defects, and I spend time trying to identify specific malformations, either hereditary or environmentally-induced. So my role is that of the clinician, who presumably would -- could, in any proposed assessment of Gulf War veterans' children, assess whether there is a distinctive phenotype or not.

As you know from the presentations already been made, that the exposures known to be human teratogens have been recognized as producing a distinctive pattern of abnormalities, and this would be the role of the clinician.

In the slides I have in the carousel, I want to present four things:

The definition that I think could be used for major malformations, as opposed to minor anomalies;

The prevalence, as we've seen it in our own studies, of major birth defects;

Some observations about how one identifies a syndrome and the problems in that
And then I'd like to make the final pitch about the fact that major birth defects are now being shown to have many etiologies, and that heterogeneity of the phenotype is the rule rather than the exception.

All of these are points arguing against any cursory, long-distance analysis of large data sets that can't consider these points. So let's go through this, these slides.

Operationally, everyone struggles with the definition of a major malformation. And I'm showing you data that comes from hospital data, a hospital-based active malformation surveillance program. One of the things I would make a pitch to consider, if you're proposing large birth defect surveillance, you need -- you're going to need a subset of folks who are able to look closely at the affected children themselves.

We've used this cumbersome definition -- it works. It's structural. It has -- it has surgical, medical, or cosmetic importance. And you have to distinguish it from the much more numerous minor anomalies and normal variations. I submitted a handout that I'll use to follow -- I'll follow along that handout in my comments. But this will be
one of the points I'd like to illustrate, that the structural major abnormalities are the key that we're talking about.

Frequency. We carried out at Brigham and Women's Hospital in Boston an analysis of the birth defects identified in children through ten years of our active hospital surveillance. You'll see that in this ten-year period 69,000 infants were born, and the overall prevalence rate was just a little over 2 percent.

We carried out something that hadn't been done before we did this, which is, break it down by recognized cause. You can see -- everyone always talks about the unknowns. Clearly, there's still a large group that's unknown. The different categories of recognized causes are listed. There clearly is a group of about 25 percent that's in the strictly genetic category. And another large group -- we only put in this category conditions where the data available from large studies were consistent with the understanding of multifactorial inheritance.

Now, you'll notice the parentheses. One of the advantages of a hospital-based surveillance program is that you can identify elective terminations for structural abnormalities,
a problem that all the data sets that have been discussed so far have had to struggle with.

We're finding at this hospital about a third now of all the children with major birth defects, the abnormalities have been identified in utero. And so there's a steady increase in the number of elective terminations. If you're dealing with a data set that doesn't include elective terminations, you obviously have an enormous problem of "What am I missing?"

This data analysis was completed in '85. So if you look for the data for, say 1995, the numbers in parentheses will be much higher. This table comes from -- this paper is in the materials I submitted to the panel.

Race makes a difference. You can see here, not data from us, but from CDC, showing the obvious variation between two large racial groups that are available to them in the greater metropolitan area where they carry out their active surveillance program.

Another thing that makes a big difference is excluding minor anomalies and normal variations. These are some that, if written into the hospital medical record, would be very common.
A Sidney line is one of the creases on the palm of your hand; you're probably more familiar with the simian crease. But the point is, when you're doing studies like this, you know birthmarks and minor anomalies are very common, and you're pointedly excluding those from your tabulation.

Now some comments about the clinician's role and the specificity of the phenotype. These things make a difference. Noting not just that there's syndactyly, but that it's webbing between the third and fourth fingers in the hand and the same in the feet -- this is a specific genetic phenotype. And if you had a generic syndactyly group, it would miss that specificity: the mother had the same thing.

Here's another child. You can see how when you take pictures of infants and children, you end up with larger magnification of the holder's hand than you do of the poor child, who's not too interested in the photograph being taken. The fourth and fifth finger here are webbed together.

1 And the point is, this is obviously distinctively different from the one I showed before.

And then here's a third variation.

Here the child has -- you'd probably say, "Well, gee, that arm is a bit turned" -- that's because
there's underdevelopment of the radius -- and the
webbing is between the first and second fingers.
This is a totally different disorder. This is a
child who actually had the Holt-Oram syndrome where
the father and several siblings had shortening of
the radius to various degrees, and this one happened
to have syndactyly of the first and second fingers.
So the specificity is important for
the major problems. And it's equally important to
exclude things that are usually categorized as minor
anomalies of no great significance.
One of the things that bedevils
surveillance programs is that webbing between the
second and third toes, which is extremely common,
gets listed with the same weight as the things I
just showed you. And it's clearly a trivial finding
with low predictive value of any associated major
birth defect.
Polydactyly. We heard yesterday the
comment that race makes a big difference. This kind
of polydactyly is much more -- ten times more common
in blacks than in whites. It has no great medical
significance, but shows up on all the birth
certificates in passive medical systems.
In terms of recognizing a syndrome,
that kind of polydactyly is very different from this
one, which doesn't show, which is -- there's a thumb here with an extra bone, which I think will show up better in the X-ray. This is called preaxial polydactyly, on the other side of the hand, where there is an extra bone in the thumb. So in terms of recognizing syndromes, those that have postaxial polydactyly over here, like in the previous child, picture of the little infant, there's some entities that have postaxial polydactyly. This is showing you preaxial. So the record has to be specific enough to note where the polydactyly is and the nature of the polydactyly, or else you'll miss the whole point.

Now, here is an example of -- I'm going to show you a few syndromes with some of the problems that would bedevil the listing of these in medical records.

This woman has a condition that's associated with normal intelligence and lifespan, but some terrible birth defects -- shortening of the forearm, with shortening particularly of the radius, missing the thumb, sometimes index finger. This individual would be recognized easily from a medical record because of the severity of the problem. By contrast, other members of the family who have the gene will simply have these very
14 prominent thumbs. And this would be the part of the
15 phenotype that would be easily missed. So here's an
16 example of a genetic condition. If you were
17 considering, as Dr. Brent pointed out, that the
18 exposure might be mutagenic, this would be the kind
19 of thing that you'd need to be able to address in
20 your surveillance system.
21 Here's another genetic disorder that
22 would be a candidate for being increased among
441 individuals exposed to a potential mutagen. You can
2 see here it's a young child whose external ear is
3 deformed in a way that would be considered mild to
4 moderate, but is -- this kind of severity is often
5 associated with significant hearing loss.
6 For the surveillance issue, would it
7 be recognized that she had a pit here in her neck?
8 You can see the tape from the surgery that she's
9 had, already had on the other side, where these
10 branchial cleft cysts were being removed. The
11 association with the external ear malformation and
12 the cyst makes this a specific entity. So there has
13 to be enough ability to spot this.
14 And here's her mother. And even
15 though it's obvious to us, sitting here today, she's
16 got the less cosmetic scar from the removal of her
17 cysts, and the very obvious abnormality of her ears.
She didn't realize that what this is is a genetic condition until her children were found to be affected. That's -- this is the disorder. It's now pretty well recognized by clinical geneticists. A lot of the care providers aren't familiar with it, but it's a fairly well-delineated condition.

Another example, a child is born with an imperforate anus. That's obviously a serious malformation from many standpoints. If it's associated with this kind of ear deformity -- this is the kind of ear deformity associated with imperforate anus, and hands like this that Drs. Townes and Brocks reported many years ago. It's now recognized as a specific entity. Here again you have the polydactyly, where the thumb simply has an extra bone in here, shown on the radiograph. So that would be the kind of phenotype you'd be wanting to rule out if you were looking at a record of a child with imperforate anus.

Well, we've talked a lot about Goldenhar syndrome. And I just wanted to show visually the issue of variation in phenotype, with some commonality of the components: the asymmetric lower face with a hypoplastic mandible; the ear deformities can be quite variable, often as severe
21 as a very poorly developed external ear; varying
degrees of pits and tags in front of the ears; an
asymmetric mouth; some lesions on the eye that are
called epibulbar dermoid; and occasionally a variety
of other malformations such as vertebral anomalies
or heart defects.

So if you were trying to pick this
up, you'd be looking for a variety of outcomes, and
you'd certainly need to have the benefit of somebody
examining the child who was familiar with things
like this.

So this will show you what microtia
looks like, severe end of the spectrum; sometimes
the ears are not nearly so malformed. Here's
obviously a much more normally formed ear, but in
association with these dramatic tags in front of the
ear. You probably wouldn't be sure of it, but the
side of the mouth here is extending around further
than it should. That's what macrostomia means. And
here's a newborn who's got the microtia on one side,
and you can see -- while asleep, you can see the
macrostomia very easily.

The key is that the person who's
writing the material on the form is sensitive to
these findings. The problem with this kind of work
is that busy pediatricians -- and with discharge
earlier and earlier, you can imagine it’s harder for
everyone to get the thorough exam that might be
needed to settle the presence or absence of some of
these findings.
Dr. Olney yesterday was commenting
that the key to recognizing the Goldenhars in the
cases they surveyed was that someone took the time
to do the consultation exam that really was the key
to settling that it was, indeed, Goldenhars.
The epibulbar dermoid doesn’t cause
any pain or any problems, but it creeps out in a way
that scares you that it’s going to impede the pupil
of the eye. But fortunately, that usually does not
cause problems. I wasn’t sure how well that would
project, and I put in another slide from an older
boy showing the same thing.
Okay, so that shows you a lot of
specific examples.
When we went through our data set, we
identified in these years, through about 160,000
births, six infants with the Goldenhars phenotype.
And I think you can appreciate the issue of
variability as you look at the pluses across the
table here. Yes, microtia occurred frequently, but
not in all infants. The tags were also common, but
not in all, and so forth. The smallness of the
mandible is the key finding -- occasional cleft lip
or palate, occasional vertebral anomalies, and a
variety of other malformations.

You might not have noticed when you
quickly scanned this the point I'm making here about
transfer status. When you work at a tertiary
d hospital, you have to exclude the women who hadn't
planned to deliver there, because that's a bias of
being at a tertiary center.

One of the mothers had had prenatal
screening that picked up that the child was
stillborn, and came simply for termination of
pregnancy after fetal demise. The other had
hydrocephalus diagnosed, had planned to deliver at
another hospital. So if you're establishing
prevalence rates, you've got to be able to do that,
you'd exclude these two cases from your
estimates of prevalence, and come out with roughly
four in 160,000.

MS. LASHOF: That's a lower incidence
than many others we've heard so far, isn't it?

MR. HOLMES: Well, statistically I
don't know whether most -- the larger data sets that
have similar quality in the data will come in at one
in 25,000. And we haven't done a calculation of
whether our one in 40,000, out of 106,000, is
11 significantly different from one in 25,000, out of,
12 say, 950,000 births, so -- but I think it
13 illustrates the impact of prenatal detection of,
14 obviously, the stillbirth.
15 So you come back to this group. What
16 you'd expect to see -- I'd like to make the next
17 point about phenotypic heterogeneity, which
18 obviously pushes a child around in the apparent
19 etiology, depending on how you put the things
20 together.
21 The first point I would make concerns
22 the well-known disorder of spina bifida, shown here
447
1 on the right. We've looked at the data over many
2 years. This is an old slide, but it make the point.
3 Everyone is very familiar with anencephaly and
4 encephaloceles and spina bifida. Most of these
5 conditions are now being diagnosed prenatally. The
6 pregnancies typically do not get to term, so they
7 would be missed if you were not including elective
8 terminations for birth defects.
9 Down at the bottom is a key point:
10 out of the children being surveyed here, 10 percent
11 had, in association with a neural tube defect,
12 either a chromosome abnormality or were part of a
13 specific syndrome, many of which are hereditary.
14 And so if you were looking at neural tube defects, heart defects, any group you want to name, being able to separate out the chromosome abnormalities, separate out the autosomal recessive disorders, is very crucial before you allege an environmental exposure.

20 Just another example. We're just starting a sample of the apparent association of limb deficiencies and the prenatal procedure of chorionic villus sampling. Here is a visual illustration of what a mixed group of infants' limb deficiencies are.

4 My colleagues in epidemiology always like to lump these children together. And our concern is that it's a very heterogeneous group. So if you had in your study limb deficiencies as a single outcome, look at what a mixture you'd have: disorders due to dominant or recessive genes, chromosome abnormalities, specific syndromes, then the much smaller group that would be relevant to your alleged environmental exposure.

13 So just to complete the point about etiologic heterogeneity, let's go back to the entity that I mentioned earlier, the microtia, which is a feature of Goldenhars. And this child actually is one of that group of children.
If we looked at the 160,000 births and said, "Okay, let's just focus on microtia," would that lead us to the Goldenhars? I think you can see here very vividly that it's quite a mixed group of infants. There are -- there were, out of the 160,000 births, fourteen with just isolated microtia, eleven who had microtia as part of multiple malformations. You can see that there were dominant and recessive genes accounting for one subgroup; chromosome abnormalities is another group; specific syndromes, which included Goldenhars. The impact of twinning, which is a major issue for some birth defects is shown here. And then there are a lot of unknown etiology. So if you -- if you used microtia as if it were Goldenhars, you can see how you'd misrepresent the data. You'd have twenty-five infants listed, only four of whom really had this disorder. Finally, the impact of minor anomalies, which bedevils surveillance programs, because the people extracting medical records have difficulty excluding minor features from major ones. And the minor features are much more common. Here's an infant who on one side of his face has big preauricular tags, on the other
side has very small preauricular tags. When we did a study of the prevalence of minor features, you can see how very common these are, whether it's the tags in front of the ear, on the ear lobe, or in other regions.

So in summary, what I've done is make a pitch for the need for folks involved in looking at the birth defects, who are sensitive to the many etiologies of common birth defects and would be able to exclude the much more common and less significant minor physical features.

If out of this, these hearings, there is a proposal made to examine Gulf War-exposed children, or fathers who were exposed in the Gulf War, or mothers, I would stress the fact that we've learned the hard way from other studies of exposures that simply coming up with an exam protocol doesn't solve the problem. Because folks, well-meaning, who've got the same definition in front of them, we've shown in other studies they don't find the same frequency, because that internal definition overrides whatever is written on the paper. And you'd need to be sure you had a small number of examiners, and they'd need to be given the opportunity to see whether there really is anything distinctive about the phenotype or not.
Thank you.

QUESTIONS

MS. LASHOF: Thank you very much.

Questions? Kathi?

MS. HANNA: Dr. Holmes, in your studies and when you're trying to determine etiologies, you obviously have to go back and collect extensive family histories sometimes --

MR. HOLMES: Sure.

MS. HANNA: -- pregnancy histories.

Can you give us any idea of the amount of time that has to be spent? And once you have a diagnosis and you're trying to collect data to try to determine if etiology can be determined, how much time does it take per case, very roughly? And what kind of people are needed to collect that kind of data and those histories?

MR. HOLMES: Well, if you look at the way this is done, there is the exhaustive "spend an hour getting the pedigree" approach, versus focusing on the immediate family. If you look in the reprint I enclosed with this, there's a list of the frequency with which the child, even with genetic disorders, is a total surprise to healthy parents, and there is no family history. And there are X-linked causes of malformations, but most are
8 dominant and recessives. And the immediate family
9 is the key.
10 And so what I would -- what I do when
11 I do this kind of work is have an individual
12 designated who will do the pregnancy history review
13 with the mother, do the pedigree, confirm it with
14 both parents, pursue anything in the close members
15 of the family that seems worth pursuing, but not go
16 into exhaustive detail on distant relatives, because
17 that really doesn't help you very much.
18 And that individual can be trained to
19 do this work. A college graduate who is motivated,
20 interested, and organized is a starting point.
21 Obviously, the more experienced the person, the more
22 help they would be. But you don't have to have
453
1 someone who is coming at this with a lot of
2 postgraduate training.
3 MS. LASHOF: To confirm the diagnosis
4 of Goldenhar, how extensive would the exam --
5 MR. HOLMES: How many features have
6 to be there?
7 MS. LASHOF: Who would we need?
8 Would we have to bring every case to you, or send
9 you to each one to examine them to confirm? It
10 strikes me that if indeed Betty Mekdeci's group has
nineteen Goldenhars in Gulf War veterans,
considering how many births there have been, if these were all Goldenhar, it would probably be significant. But how are we going to find out whether they would meet the criteria to compare to these incidence figures?

MR. HOLMES: Well, whether the prevalence rate is increased would be a separate issue. But this -- there are lots of clinicians who do this. The key is that the person who examines the child has the knowledge up front of what they're looking for. You know, there's a sensitization issue that goes on when you learn how to do this.

And so if you pick people who are experienced clinicians, all of whom are aware of -- have participated in developing whatever protocol they're going to use, there are lots of people who could do it.

I think the key, as I would suggest, is that the examiner be unaware of who was who, and that if there is a group of children who are -- whose fathers served in the Gulf War, with birth defects, that there be a comparable group who have similar malformations, whose fathers didn't serve, and that some consideration go into trying to decide how to match them, so that there wouldn't be an
obvious difference in severity or something like that in the group. And then let the experienced individuals do the exam.

Because if you look at what we've learned from other environmental causes of birth defects, there should be some specificity to the phenotype. And if there isn't, that's helpful. And you know, they'd examine the children blindly, figuratively speaking, and then --

(Laughter.)

-- the data would be pulled together and you'd be able to speak to that point.

I think geographic constraints are an issue. You'd want to -- if you have a group of folks that are in the Pacific Northwest, there are lots of people who are well-trained clinicians, could do this in the Pacific Northwest.

The thing I'd want to caution you about, which I mentioned earlier, is, we tried in other studies to have everyone agree on an exam protocol, and that doesn't solve the problems of variations from examiner to examiner. That's just a real fact of life in this work. I doubt that it would be a fact of life for the outcomes I showed for Goldenhars. Saying whether an epibulbar dermoid was there or not is probably going to have a high
reproducibility level. I think subtleties like "Is the bridge of the nose depressed?" "Are the fingernails small?" -- that kind of subjectivity is where you get in trouble with these protocols.

MS. LASHOF: Thank you very much.

MR. HOLMES: You're welcome.

MS. LASHOF: Very interesting.

Any other -- Joe?

MR. HOLMES: I was supposed to share this, share the microphone with Larry Edmonds, who's here, CDC.

MS. LASHOF: Yeah. Right. That's what I --

MR. HOLMES: Which is going to get all the money that comes out of this.

MS. LASHOF: I'll ask Larry to come forward now.

DIAGNOSIS, DEFINING SYNDROMES, DETERMINING PREVALENCE, AND SURVEILLANCE

COMMENTS BY LARRY EDMONDS

MR. EDMONDS: Good morning. Thank you very much for the invitation to address the Committee.

My name is Larry Edmonds. I'm an epidemiologist at the CDC in the Birth Defects Branch. I've worked at CDC for a number of years,
and a majority of that time has been managing surveillance activities in our branch. And in the last few years I've been working with state health departments on developing and implementing a surveillance program.

I was asked by the staff to talk about surveillance methodologies for birth defects and talk about what we do at CDC and what's going on in surveillance in the United States with state health departments and other programs. You've seen some of these slides before, but I think it's important to talk about why we're interested at CDC in birth defects and prevention, in that you know that birth defects are the leading cause of infant mortality.

I think it's important to point out that -- how many children are affected each year with a major birth defect. We talk about 3 or 4 percent, but that's a large number of infants that are affected each year. So depending on how you define a birth defect, 120- to 160,000 babies a year.

Thirty percent of these infants are admitted to a pediatric hospital. And the medical cost associated with this is phenomenal. A recently
4 published article estimates that $8 billion lifetime costs are associated with eight major -- eighteen major malformations. So a baby born in 1992 -- that will be with those eighteen malformations, the lifetime cost will be that $8 billion.

And more importantly, I think now, is that we're finding some prevention for birth defects, most notably the recent discovery that folic acid could prevent a large portion of spina bifida and anencephalics. So I think that's the positive note that we need to start with.

A definition, I think, is important for "surveillance," and this is, I think, a definition that CDC uses for a lot of their work: it's the ongoing collection, analysis, and interpretation of birth defect data essential for the planning, implementation, and evaluation of public health practice.

You asked me to address what we do at CDC. This is kind of a flow diagram that points out some of -- the building block is surveillance, collecting good quality data, and then going to epidemiologic studies, which you've heard a number of. But let me back up to the surveillance systems.

In CDC we started in this activity back in the late '60s, as a lot of countries in
Europe did, because of the thalidomide episode and the knowledge that environmental agents can cause birth defects. So we started a program, which I'll go back to in a few minutes, in 1967. And so the primary objective of most of these programs then was to look for environmental influences. And it's evolved in the last few years, especially in state programs, that states are very interested in identifying children that need services, early intervention programs, and now we're getting into trying to make sure we deliver and evaluate prevention programs. So the objectives have changed over time, although we're still very interested in looking at the environmental influences.

At CDC we do a lot of case-control studies, and you're aware of a number of those: the Vietnam veterans study, which was done a number of years back. I don't want to go into all the studies we've done. But the surveillance database is the building block for doing these studies. And more recently, the CDC is getting into the prevention activities, as we're discovering more and more things we can do. Folic acid is -- again, as I mentioned, one of our big focuses right now in our branch, and fetal alcohol syndrome also,
I want to go over basic -- some basic building blocks for what makes a good surveillance system, some of the characteristics of a good surveillance system.

Most importantly is that you identify all the data sources you can to identify children with birth defects, and as Lew, I think, has talked about very, very well, that you need an accurate and precise diagnosis. This is most critical -- not just a birth defect, but all the birth defects -- and it's described very well.

And you need a classification system that is meaningful. Major birth defects is one way, all birth defects -- but more specifically getting down to the specific birth defects or birth defects that might be associated together.

A large database, that's important for getting the numbers. I mean, you raised questions about powers. So building a large database is important.

It's very important that data be timely and that it can be used and addressed in a timely fashion, if you have a concern that you're not looking at it two, three years down the line -- kind of the situation we're doing with the Gulf War
You need to disseminate the data and get it out to the public in a timely manner, that people can use it and look at it. Probably one of the most important things about a good surveillance system is, you have to have personal identifiers to do follow-up. And this always causes a lot of concern, but you have to have this to link to other data, to link records among babies, among visits, and so on. And because you have personal identifiers, you need to develop a very well-developed confidentiality system to protect the patients' privacy.

What are the limitations of surveillance? Well, the quality of the data, the data we get, depends on the resources we expend. And I'll show you a couple of different approaches that we use at CDC. So the harder you work at it, the better the data is going to be. The case identification in a surveillance system is dependent upon the quality of the medical record. And Dr. Holmes has address that, too. If we don't get down -- written down on the medical record an accurate and precise diagnosis, we can't collect that data.
20 And I think, you know, we need to
21 realize that we're not going to identify all cases.
22 Our goal is to try to get to 100 percent, and in
463 l most cases we don't reach that goal. But we do very
2 well at it in some cases.
3 Talk about a case definition. And
4 this varies greatly among some of the states, as
5 I'll talk about later. But this is very important.
6 And Lew just went over this again: you need to
7 define what you consider a major malformation in
8 your surveillance program, what you're going to
9 include in the program. You need to define what a
10 minor malformation is, and whether you're going to
11 include it or not. There are certain conditions
12 that aren't included, as Dr. Holmes talked about:
13 the hemangiomas, polydactyly, and things like that.
14 If that's the only defect, a lot of times we exclude
15 those from our surveillance systems.
16 Other surveillance in special
17 settings may include other birth defects that aren't
18 in. At CDC we do major birth defects. Some states
19 require all malformations, because they're
20 interested in delivering services to children. A
21 number of state programs include biochemical and
22 genetic diseases that are mandated by law.
The age of the infant to be included is important. I'll talk a little bit about surveillance systems in newborn infants. And then at CDC we have a surveillance system of infants up to one year of age. So that can vary between programs too, so -- but you need to define what you're going to do: newborn one year, five year.

The gestational age. What are you going to include? What's to meet your case definition? Is it any product of conception? Which becomes very difficult to do. I don't know if I want to do all the ramifications of doing surveillance like that. But most surveillance programs in the U.S. now have a cutoff, something like generally around twenty weeks of gestation, or maybe a birth weight criteria, 500 grams or more. So that needs to be spelled out in your surveillance system: what will you count?

And again, as Lew talked about, now prenatal diagnosis is very important. We know that a number of states, 30 to 40 percent of neural tube defects are now identified prenatally. And we published that recently.

Where can you get data for surveillance? Just -- I've given some more detail in my written testimony about this, but just to
quickly review this.

The one obvious place is vital records; every baby gets a birth certificate, and all infants who die get a death certificate. This is one source. It has a lot of problems, and the sensitivity of this type of data is not very good. It's probably 14 percent of the true population are identified correctly on birth certificates.

Hospital records. This is becoming one of the predominant ways that we identify children. There are medical records, you got discharge summaries, you got physical examinations within hospital records. There may be consults with a geneticist within the medical record. It could be test results, be lab results, the karyotypes. So these are all the things we look at in a medical record.

There are many special data sources that you can go to for surveillance. You can go to the genetics clinics and identify children, go to the perinatal centers to identify prenatally diagnosed cases. And you can go to specialty clinics. In Atlanta we have a very nice heart center that sees the majority of children in the metropolitan area.

You can also go to existing data
9 sources. In this country now most states have a
10 statewide hospital discharge database that will
11 identify all hospital discharges, and you can look
12 at newborns in that database.
13 There's Medicaid data that you can
14 look at.
15 And now more and more the insurance
16 and HMO systems are building databases, and they're
17 interested in trying to look at this, especially for
18 prevention activities.
19 Trying to address some of the
20 different kinds of surveillance methods that are --
21 that are going on now or that have gone on in the
22 past. And one that was alluded to earlier and a lot
23 of you know about was the Collaborative Perinatal
24 Project. This was an ideal project. This would be
25 an ideal surveillance system, if we could do it.
26 You have a standard protocol: you go examine every
27 baby. This program followed 50,000 pregnancies, and
28 I'll come back to this and talk about the rates that
29 came out of that program.
30 You can review -- and this is
31 probably one of the most comprehensive surveillance
32 systems now, is to review medical records of
33 potential cases. And this can include records from
34 nurseries, NICUs, the specialty clinics that I
talked about, laboratories, and then all kinds of screening programs. And I will come back and talk about this with the Metropolitan Atlanta Program.

You can use hospital discharge summaries and disease indexes to identify records. Some states use that kind of approach. You can use existing hospital discharge data.

The National Birth Defect Monitoring Program, I'll talk about was a program like that. And the uniform billing data is something that exists currently.

Other approaches to ascertaining birth defect data is, a number of states now are developing legislative mandates. Probably the vast majority of the programs have a law that mandates birth defect reporting, and it requires hospitals and physicians to report. In most of these states that do that type of approach, they use some supplemental interaction with the hospitals to increase reporting.

And then you have states that link data sources. They may have the hospital discharge data, they may have the Medicaid data. Vital records is one. So they link all these data sets. And then, as I said earlier, we've got vital statistics.
17 And then, a number of states are
devolving specialized surveillance programs for
selected conditions. And that's looking at neural
tube defects; they're focusing on just one or two
malformations.

22 What kind of -- the data can vary
greatly with the intensity of surveillance effort.

2 And I wouldn't focus so much on the absolute numbers
on this slide, but the great variation of rates
depending on how much effort you put forward.

5 If you examine "Infant," you can get
a rate. The Collaborative Perinatal Project had a
rate of about 8 percent for major defects, had a
rate of around 15 percent for all defects. So lots
of minor malformations were identified.

10 Comprehensive hospital surveillance,
something like we do in Atlanta and they do in
California, the rate will be -- around 3 to 4
percent of babies will have a major defect. And
then you can start seeing the hospital reporting
systems. The rate, depending upon their methods --
some were 2 and a half to 3 percent.

17 And then as I alluded to earlier,
birth certificates don't do very well; they only
identify about one percent of the babies with a
So it can vary greatly, and so you really need to know how the data was collected.

In metropolitan Atlanta, as I said earlier, we started in the late '60s. And Atlanta served as a prototype for a lot of other surveillance systems now that are operating in the U.S.

We monitor all births in metropolitan Atlanta, around 40,000 births a year, and we look at all live and stillborn infants who are diagnosed. And we really focus on major malformations that are diagnosed up to first year of life. And we use a very intensive type of case-finding where we go to multiple sources to find the cases in the hospitals and specialty clinics. And we've used this database over the years for doing a lot of epidemiologic studies.

Another system that I think ought to be looked at, especially when you come to my kind of recommendation at the end there, is the Birth Defect Monitoring Program might be an example of what the DOD might look at for hospital discharge data. This is a program that we had operational from 1974 to '94, and it was a large database. It
monitored, in the early '80s, about 35 percent of
the births in the country, and the total time
period, about 20 percent. But this gave us good
national estimates of birth defects in the country,
and trends, and we used this for a number of
studies.
The company that provided this is now
out of business, and we're exploring new
alternatives to this, especially the uniform billing
data, as a possible surveillance system to replace
it.
This is what is going on in the U.S.
in state health departments. And I think this has
changed dramatically since the late '70s. In the
late '70s there were three states that had programs.
Currently there are well over thirty that have a
program or are trying to implement a program.
You see these blue states? They're
the states that have hospital or mandated reporting.
And then you see the intensive kinds cases they're
finding. There are about seven or eight of those
blue states that -- Atlanta and California and so
on. There's a lot -- I mean, I can't tell you how
much is going on. It's amazing in the last five
years how many states are interested in getting into
of this, not only for the epi' purposes, but for
prevention activities, intervention activities.

We're currently funding eleven states to develop programs in this area.

Some of the other activities I think you ought to be aware of that were at CDC is that we're trying to build a national collaboration of these state programs. We hope to have within the next six months the first annual report of these surveillance programs. We currently have data from twenty of those states that we will include in this first report. So I think we're trying to build this national collaboration, and between the states.

We've done a number of studies with them. Chorionic villus sampling was one of example recently.

Another thing that we're involved in right now is risk factor surveillance. And we have an ongoing case-control study in three states, including Atlanta, to interview parents with major birth defects on a number of risk factors. And we hope to expand this very soon. We put out an RFA, in fact, last week to hopefully fund three states to develop a center of excellence and to do birth defect research.

So I think this last bullet -- this came out of legislation out of Congress that mandated CDC to expand their efforts in trying to
10 develop a national collaboration and fund
11 surveillance activities and do research. So things
12 are improving. The resources are tight, but we are
13 able to get into new areas.
14 The last thing I'd like to talk about
15 is that -- our collaborations with the Navy and the
16 studies we're assisting them with is, I think -- it
17 brought it mind that it's time to kind of think
18 about in DOD starting to collect data in a more
19 uniform and standard manner and in a little more
20 proactive phase. And I think collecting a good
21 reproductive and fertility history on all active-
22 duty personnel would be a nice thing to have
474 1 available to you.
2 And I think another opportunity
3 exists, especially with TRICARE being implemented,
4 is -- this is the time to think about an ongoing
5 surveillance system of military personnel. You
6 heard us talk about looking at the Goldenhar with
7 the DOD data. But the civilian data, we haven't
8 looked at yet. And I think with TRICARE, it might
9 be the opportunity to think about this and see if it
10 is a reasonable thing to develop an ongoing
11 surveillance system.
12 Thank you.
13 QUESTIONS
MS. LASHOF: Thank you very much.

Let me ask you a question just directly related to that approach.

So far, the efforts of trying to identify whether there's increased birth defects among Gulf War veterans are starting with the Gulf War veterans and then looking at births and looking at birth defects. What is the feasibility in your collaborative birth defect registries to start with birth defects --

MR. EDMONDS: Right.

MS. LASHOF: -- and look at what percentage of those have fathers or mothers that served in the Gulf War, and whether that's out of proportion or not?

MR. EDMONDS: That could be done.

And Happy Araneta is trying to look at that by going to a number of surveillance systems.

But another way we could do it too is to try with this risk factor assessment. You know, we'll be looking at occupational and things like -- including service. But the number's going to -- I mean, the exposures, or the people who served in the Gulf, are going to be pretty small in that population. We've thought of -- tried to start
thinking about that. I mean, it's really a
difficult thing to try to do. I don't know whether
it's better to try to continue with what the Navy
has started and go on to the civilian populations,
or think about going to some of these states and try
to --

MS. LASHOF: Yeah. I mean, even with
what Dr. Araneta is trying to do, she's going to the
three states, three states with birth defect registries,
but she's looking at all --

MR. EDMONDS: At all birth defects,
right.

MS. LASHOF: She's looking at all
birth defects and then trying to determine how many
came from the Gulf War --

MR. EDMONDS: Yes.

MS. LASHOF: -- or is she looking at
the Gulf War --

MR. EDMONDS: Yeah, they're linking
the manpower tapes to vital records in a number of
these states -- and Hawaii was the first example --
and then look at the registries and see how many of
them were -- had birth defects, and then look at
Gulf status versus non-deployment status.

MS. LASHOF: Yeah; but she's going --
she's going with non-deployed versus deployed, and
then to birth defects? Or she's starting with birth defects?

MR. EDMONDS: Well --

MS. LASHOF: I'm confused.

MR. EDMONDS: She's starting with being a veteran --

MS. LASHOF: Yes.

MR. EDMONDS: -- irrespective of deployment, and then linking to vital records, then identifying the children born to those children --

MS. LASHOF: Right.

MR. EDMONDS: -- then linking to the registries.

MS. LASHOF: And then linking.

MR. EDMONDS: And then evaluating --

MS. LASHOF: I'm suggesting going the other way. I'm asking whether it's -- whether one would be able to detect a significant increase if it were occurring in Gulf War veterans, if you started at the other end. That is --

MR. EDMONDS: Well, that's kind --

MS. LASHOF: Started at the registry and --

MR. EDMONDS: Right.

MS. LASHOF: -- said, "Okay, let's look at every Goldenhar that's been reported last
3 year in the country," and determine how many of
4 those Goldenhar syndromes --
5 MR. EDMONDS: Served in --
6 MS. LASHOF: -- served in the Gulf.
7 MR. EDMONDS: I think that's -- I
8 don't know what the power calculation is on that --
9 probably not real great. But you could. You could
10 go --
11 MS. LASHOF: I would think the power
12 would be greater than the other way around.
13 MR. EDMONDS: It probably would be.
14 MS. LASHOF: That's my thought. And
15 that's why I raise it.
16 MR. EDMONDS: You could go to all
17 these states and ask them to identify the Goldenhar
18 cases. The problem is, you're going to run into
19 some of the things we did with the DOD database,
20 that only a few of those at this point have the
21 ability to really pull out the specific diagnosis,
22 'cause Goldenhar is buried in kind of a catchall
23 category. So in about seven or eight of those
24 states you could do that approach. I don't know
25 what the numbers would be. We could probably try to
26 figure that out. But then you could go to those, do
27 a case-control study with them.
28 MS. LASHOF: Yeah.
MR. EDMONDS: I don't know what the power of that, off the top of my head, would be.

MS. LASHOF: No.

MR. EDMONDS: But the exposure is probably not going to be that great, you know, the serving in the Gulf. But I think those are the kinds of things that we need to talk to the Navy about, what --

MS. LASHOF: Yeah.

MR. EDMONDS: What's the next step, and the most reasonable?

MS. LASHOF: I would think that's worth -- appreciate it.

MR. EDMONDS: But we've offered the Navy that we'll continue to assist them.

MR. HOLMES: I think one of the things he hasn't specified, but CDC has expanded the ICD coding system to try to allow you to have more specificity in the ICD number that's used. And a lot of the states are wedded to the old ICD numbering codes, which lump. And that's where the problems arise.

Would the seven states you're citing use the expanded ICD codes?

MR. EDMONDS: Yes. And they would --
they represent somewhere around 25 percent of the births in the country, somewhere between 20 and 25 percent. So it's a large sample. Yeah.

MS. LASHOF: Now, these states with birth defect registries, are they then transmitting that information to CDC?

MR. EDMONDS: Yes; this --

MS. LASHOF: Do you have in this collaborative effort --

MR. EDMONDS: Yeah, we've just started that.

MS. LASHOF: -- the results from all the -- so you've just started that?

MR. EDMONDS: Right.

MS. LASHOF: And then what -- are there any routine studies that you're doing on a selected group of birth defects?

MR. EDMONDS: Right. That goes --

MS. LASHOF: Or how do you then follow up, and what additional information do you get from the parents for exposures, et cetera?

MR. EDMONDS: Well, the risk factors surveillance study -- we're funding two of the states, California and Iowa, and then in Atlanta, where we're interviewing the parents of a number of selected major malformations. And this in-depth
14 interview takes about an hour, looking at a lot of
15 the risk factors we currently know about, plus some
16 other ones that are -- that are suspect.
17 That database started about three
18 years ago, and we're -- the analysis of that has not
19 started. We hope to build up a large database for
20 analysis. The new centers we're going to fund that
21 will be -- one of the requirements of that is, they
22 also, whoever gets those awards, will contribute
482 1 cases-controls to that ongoing study. So that
2 hopefully we will have a good database to start
3 addressing concerns about risk factors for birth
4 defects.
5 MS. LASHOF: Could you comment about
6 any risk factors that you've identified since the
7 system is underway? Folic acid was one.
8 MR. EDMONDS: Folic acid, diabetes,
9 cocaine, smoking -- a number of studies like that
10 that -- we a number of years back funded a number of
11 states to look at toxic waste sites. They ended up
12 being predominantly drinking water studies. And
13 there were a number of things that came out of that,
14 that raised suspicions about exposures in public
15 drinking water of volatile organics and so on, and
16 byproducts of disinfection of water. There's a lot
17 of interest in our Center about trying to further
18 those studies.
19 MS. LASHOF: So that at this point
20 you can say that having this surveillance system in
effect has enabled you to identify specific risk
22 factors that we can do something about?
483 1 MR. EDMONDS: Yes. I think -- yeah,
2 the Vietnam study.
3 MS. LASHOF: We don't have that many
4 success stories.
5 MR. EDMONDS: No, we don't.
6 MS. LASHOF: To get them out --
7 MR. EDMONDS: I think the folic acid
8 study is one that came out of that.
9 MS. LASHOF: Pardon? Which one?
10 MR. EDMONDS: Folic acid --
11 MS. LASHOF: Uh-huh; yeah.
12 MR. EDMONDS: -- I think, came
13 directly out of that. Our study was one of many
14 that pinpointed that folic acid was effective in
15 preventing neural tube. So that's one of the
16 success stories.
17 MS. LASHOF: What percentage of
18 neural tube defects do we now believe are due to
19 folic acid deficiency?
20 MR. EDMONDS: Fifty percent.
21 MS. LASHOF: Fifty?
MR. EDMONDS: Or greater, that we
might be able to prevent that much.

MS. LASHOF: Uh-huh. Good. Thank
you.

Questions? Marguerite? Tom? Joe?

MR. CASSELS: I just have one.

Given what you have both said this
morning and what we heard yesterday about the
difficulty of making the diagnosis in many instances
here of a major malformation, going back to the
Collaborative Perinatal Project where every infant
is examined, how many examiners are involved in
that?

Dr. Holmes, you indicated that there
were people out there who could do this.

MR. HOLMES: The problem with a
national -- the National Collaborative Perinatal
Project was, there were thirteen centers and lots of
examiners at each center. And this is back in the
early '60s, and I know I made extra money at the
time when I was an intern: they'd hand me the form,
I'd go do the exam. And that represented the
problems they got into, and the lack of consistency
in what everyone understood they were supposed to be
finding.

What I was suggesting was, you have
4 folks that are trained as -- they usually call
5 themselves dysmorphologists, meaning they focused on
6 understanding the causes of birth defects, and
7 they're sensitive to the outcomes we're talking
8 about. Those folks are all over the United States,
9 and you could just identify individuals
10 geographically that might be interested in
11 participating in this kind of work. I would
12 recommend that over the system used in the NCPP,
13 where people like me were given the form to do for
14 $10 or something like that.
15 MS. LASHOF: Started you off on a
16 whole new career, though, didn't it?
17 MR. HOLMES: Yes.
18 MR. CASSELLS: But is that -- is that
19 data at all useful, given those caveats?
20 MR. HOLMES: For minor features, no.
21 We've looked back -- when we did our tabulation of
22 the 70,000 births in terms of the frequency of the
23 various major malformations and the etiologies we
24 recognized, we wanted to know whether other data
25 sets had seen similar abnormalities.
26 And it was impressive to see that
27 between '65, when the NCPP ended, and when we were
28 doing this in '85, the number of entities we could
diagnose, which are on table 2 in that reprint you have, has grown tremendously. And Dr. Brent referred yesterday to the Mendelian inheritance in man, this catalogue that has over -- since the mid-'60s has shown this incredible growth in the number of phenotypes identified. So the problem with the NCPP is, its folks didn't know these entities existed. So their descriptions might be all right, but you're not sure.

MS. LASHOF: Okay. Thank you very much.

We are running a little behind time, as usual. We will resume at ten after and try to make up at least five minutes. So ten after the hour.

(Recess at 10:55 a.m. to 11:12 a.m.)

MS. LASHOF: I think we'll try to resume our hearings now.

And I'm very pleased to welcome Dr. Thomas Garthwaite, Deputy Undersecretary of Health from the Veterans Affairs Agency.

GENETIC SERVICES, REFERRAL, AND OUTREACH:

DEPARTMENT OF VETERANS AFFAIRS

COMMENTS BY THOMAS L. GARTHWAITE

MR. GARTHWAITE: Thank you, Dr.

Lashof, members of the committee, others interested
in Persian Gulf War illness. It is a pleasure to meet with you today to provide you with information on the Department of Veterans Affairs policies, programs, and practices related to reproductive health in veterans.

First, I'd like to assure you that we're a system that welcomes inquiry from veterans. We know the concerns about the effects of military service on reproductive health are very significant for veterans who served in the Persian Gulf, as well as those who served in Vietnam, and those who were exposed to ionizing radiation during World War II and the ensuing cold war.

The training of our Persian Gulf coordinators and registry physicians includes the information available from research on reproductive outcomes. A recent satellite video teleconference included discussion of the only two scientifically rigorous studies available at that time, and as was discussed here yesterday, we recognize that those studies also have limitations.

The first study was an investigation of children born to Persian Gulf veterans of two Mississippi Nation Guard units as published in Military Medicine.

The second study is that, as
discussed yesterday by Dr. Cowan, the principal investigator, who appeared on our satellite broadcast and conference. He discussed his findings from his survey of children born in military hospitals to military parents who differed by whether or not they were deployed to the Persian Gulf or not. We all saw his most recent data during yesterday's hearing.

It is our intention that physicians make all credible information available to patients in counseling them. We have some limitations. VA statutory authority to deliver reproductive health services to female veterans is limited to specific services under the Women Veterans Health Care Act of 1992, Public Law 102-588. This Act excludes services for infertility, abortion, or pregnancy, including prenatal care and delivery, unless the risks of complications of pregnancy are increased by the veteran's service-connected disability.

The only authority we have to provide any evaluation to non-veterans, i.e., the spouse of a Persian Gulf War veteran, was included in Public Law 103-446, which expires September 30th, 1996. Under this authority we are going to study 1,000 family members of Persian Gulf veterans as part of
the large VA Persian Gulf study described in one of
your previous meetings.
In addition, VA is providing free
health examinations to any individual who is the
spouse or child of a Persian Gulf veteran if the
veteran is listed in the Persian Gulf registry and
has an illness which cannot be dissociated from the
veteran's service in the Gulf, and who has granted
permission for the examination data to be included
in the Persian Gulf registry. These examinations
are being provided by university-affiliated
physicians contracted through thirty-two VA medical
centers. Individuals may register through the
Persian Gulf help line, and I remind all veterans
that it's 1-800 PGW -- Persian Gulf War -- VETS,
V-E-T-S. That's 749-8387.
It is estimated that 4,500 spouses
and children can be provided examinations within the
statutory spending limits. As of May 30th, 1996,
479 family members have registered for the
examination program. The examination program --
excuse me; the examinations are done using
standardized protocols. The adult examinations
include a CBC standard chem-20 panel on the
urinalyses. Information for physicians has been
sent out in a physicians' reference guide which has
been made available to members of your staff. A follow-up letter is sent by the examining physician. However, the law includes no provision for treatment of any abnormalities detected during this examination, which would have to be referred to the individual's own physician. The results of the examinations are entered into a scannable code sheet for inclusion in the registry and analysis by VA's Environmental Epidemiology and Environmental Agent Services.

We've made multiple attempts to outreach to Persian Gulf veterans. These are done through articles in The Persian Gulf Review, which is currently sent to every veteran in our registry; through national -- regional; I'm sorry -- regional and local media; through veterans service organizations; the Persian Gulf help line, the number I just gave; through VA Online, a Web page that's one of the top five Web pages in terms of access of all pages on the Web; and through registry Gulf coordinators and physicians at local medical centers.

In your letter of invitation you specifically asked me to discuss the legislation for spina bifida in the offspring of Vietnam veterans
which VA will be seeking. As you know, the National Academy of Science in its second report, "Veterans and Agent Orange, Update 1996," found there is limited or suggestive evidence of an association with exposure to Agent Orange and other herbicides used in Vietnam with spina bifida in the offspring of veterans who served in that conflict. On May 28th the President announced that the Department of Veterans Affairs will be proposing legislation that would provide an appropriate remedy for children of Vietnam veterans with spina bifida.

The details of that legislation are still being developed, and I will gladly provide a copy to the Committee when it's available. Some of the reasons that we can't provide it now are, there are significant issues needing to be addressed in that legislation including how to provide health care to the offspring -- for example, should it be through CHAMPVA, private insurance plans, contracted care, Medicare, Medicaid, or others -- and what kind of benefits would be provided, which may include things such as monetary payments, vocational rehabilitation, adaptive housing allowances, and education. How to provide those effectively and well requires a significant amount of background research and work with veteran organizations as
Finally, I think it is generally agreed that more research into reproductive outcomes, particularly male-mediated ones, is needed. Therefore, the Department of Veterans Affairs has announced plans to establish the fourth environmental hazards research center. This one will concentrate on birth defects and reproductive health. The request for proposals was issued in May of 1996, and we anticipate selecting the site before the end of the fiscal year.

This ends my prepared remarks. I'd be happy to answer any questions.

MS. LASHOF: Thank you very much.

Questions from the Committee members?

MR. McDANIELS: All the outreach efforts that I've seen from VA as far as reproductive issues have simply been a listing of research efforts underway. Is there anything else that VA could tell Gulf War veterans? Understanding that the evidence of increased birth defects is inconclusive, is there anything else that you could transmit to them in addition to just a listing of research efforts about this matter?

MR. GARTHWAITE: Well, you know, I
came to this meeting Sunday night and sat through all the testimony yesterday and today, and feel that I've probably learned a fair amount, as I think everyone here has. I'm not sure I could conclude a lot, not being a geneticist, or someone really expert in that, but someone with a background in internal medicine and endocrinology. I'm not sure what clear and helpful piece of information I could give them other than that there are still significant issues to be resolved and that there are significant -- that there are considerable attempts being made to try to resolve those; perhaps put into perspective those good studies that show that there's not a -- that the risk of a birth defect is real in everyone who has a child, but at least so far is not demonstrably that much greater in studies, although I think you still have to put those limitations on the studies that are done.

I think it's common in science to have to have imprecise science, and try to help people make real-life "now" decisions. And I don't know what we can do to help clarify the issue. I mean, I come away from this with the sense that there's not yet clarity, and --

MS. LASHOF: I think that's very
true. And the question, I think, to follow up on Tom's question on that, is: how much information is being given to the veterans to explain how much unclarity there is, how frequent this is in the general population, what the real risks are in the general population, and how much greater the risk would have to be for us to discover it, so that they aren't looking for quick, easy answers.

MR. GARTHWAITE: Right.

MS. LASHOF: And the question is: is that included in the kind of information you're giving out, and how does it reach the veterans in general, not just those who have signed up in a registry who have a birth defect, but those who are out there wondering what to do?

MR. GARTHWAITE: Well, I think legitimate attempts have been made to do that, but I think that we need to continue to reassess whether they're being effective or not. And I think we'll go back and we'll reassess that once again to see if there are other things that we can think of in light of what's been presented here that may be more effective than the things that I listed already in our outreach efforts.

MS. LASHOF: And your satellite teleconference call, who -- video conference -- who
MR. GARTHWAITE: It was to all the Persian Gulf coordinators and all the specially-trained registry physicians. In each medical center a physician has been designated as a registry physician, and they get additional education and sensitization to the issues surrounding the Persian Gulf War.

MS. LASHOF: Okay. So it was to the professionals. It wasn't --

MR. GARTHWAITE: Correct.

MS. LASHOF: -- an effort to get a video or media out to the veterans themselves.

MR. GARTHWAITE: Right.

MS. LASHOF: Because I will admit that one of my concerns is that the media -- and I hesitate to say this in front of the TV cameras -- do tend to sensationalize these issues, and not always present the fairest picture, and I think that does a disservice to the veterans. And so I think it is important that they understand how complex this is, how much work is going on, and will go on, and that we won't be satisfied until we get the best answer possible. But those answer may not all be forthcoming very quickly.
MR. GARTHWAITE: Sure. Before I left as Chief of Staff in Milwaukee VA, we had a traveling show throughout the State of Wisconsin where we brought in the best experts we could, and held open forum meetings advertised in every media that would listen. And we got pretty good attendance, and I think, you know, some reasonable interchange between the best experts we could find on the subject and Persian Gulf veterans. I think we have to continue all those kinds of efforts because no one way is good. We have a large number of people who sign on to our Web site, but that's no good for a whole bunch of people without computers. Television advertisements aren't good for people that don't watch a lot of TV. And I it's just we have to use multiple media to try to reach as many as possible.

MS. LASHOF: Did you have other questions about the outreach, Tom?

MR. Mc DANIELS: No.

MS. LASHOF: I didn't mean to interrupt you.

Marguerite?

MS. KNOX: Yeah, I just wanted to ask your opinion, Dr. Garthwaite. Yesterday you said you stayed and you listened to testimony. What were
5 your feelings on that, knowing some of the comments
6 made about the VA system?
7 MR. GARTHWAITE: You mean with regard
8 to the patients who testified early in the morning?
9 MS. KNOX: Yeah. Early in the
10 morning. Were you surprised?
11 MR. GARTHWAITE: Well, for someone
12 who has been in the VA for twenty-two years, and who
13 has treated hundreds of veterans, and whose office
14 was down the hall from the patient representative, I
15 wasn't surprised. But I would also say that, you
16 know, any time that a veteran comes to the VA and is
17 less than 100 percent satisfied with their visit, I
18 feel badly. We see -- we have probably 25 million
19 outpatient contacts, visits, a year.
20 MS. KNOX: Uh-huh.
21 MR. GARTHWAITE: It's not going to be
22 possible to make all those visits perfect, but we
23 have to strive to do that. In listening to the
24 various comments, I think -- I was struck by the
25 fact that we need to try to help the individuals who
26 made those comments in any way possible. They all,
27 too me, seemed to have real issues and real
28 problems. The hard part is to know which of those
29 real issues and real problems are a direct result of
30 service in the Persian Gulf or not. But clearly
they all have very real legitimate problems, and
need to be addressed.
Not every time a physician or someone
who evaluates a patient, and they come up with a
conclusion, is that conclusion going to be what the
patient wants to hear. One of the most flagrant
cases in my own personal experience is when I
suggested to someone that a lot of his problems were
related to his smoking. And he didn't -- you know,
he got very indignant, and said, "I came here for
help, not to be told that I was smoking." But
legitimately, I was trying to be very kind. I was
not being difficult. But I think that sometimes the
answer isn't what we want to hear. It doesn't make
it necessarily wrong. So I think we have to be
careful.
And at the same time, we have to look
at our own system and make sure that the accuracy of
the diagnoses we give are correct, so that if you're
getting an answer you don't want to hear, we want to
make sure that it's as accurate an answer as
possible. And that has to do with professional
recruitment and training, and quality assurance, and
those sort of things, which we're aggressively
pursuing throughout the VA system. I'm sure you
know.
13 MS. KNOX: Yeah. It's disturbing at
14 times.
15 MS. LASHOF: Let me ask you a
16 question about the Agent Orange legislation that
17 you're struggling with. And I can imagine that
18 there are a lot of issues that have to be addressed.
19 And the decision to go ahead and reimburse for -- or
20 consider it related to service, was made on the
21 basis of the IOM report which suggested a limited --
22 a limited or suggestive category, and further
23 research will go on. I'm not familiar enough with
24 all of the research going on. It's hard to keep on
25 top of all of this, but to keep on top of all of the
26 Agent Orange research -- but are there further
27 studies going on to try to determine whether that
28 category will move from limited/suggestive to
29 definite, or move from limited/suggestive to
30 negative, unrelated, and -- well, that would be the
31 first question. Are such studies going on to try to
32 refine that category?
33 MR. GARTHWAITE: I understand there
34 are, but I would -- you know, I would really need to
35 ask someone specifically the nature of those studies
36 to be able to provide that information to you. But
37 it's my understanding --
MS. LASHOF: Well, the more important -- not the more important, but the logical follow-up to that become the question of how you will deal in the legislation with the issue that if there are further studies and those further studies show no relationship, how do you make the decision about what you do about further treatment, compensation, whatever, under those circumstances?

MR. GARTHWAITE: I think that gets into the very difficult issue of legislation, legislative intent and interpretation, and where we can go from there. You know, a lot of times we're left to try to carry out legislation and direction that we're given, whether or not it's all based on what would be true scientific facts. It really is based on what the best information in decision-making is available to the legislators at the time that they make those decisions. So there clearly appear to be some times when legislative decision-making and the scientific evidence are not totally coincident.

MS. LASHOF: You know, I was just curious as to whether you were going to try to make any effort, or whether it's probably unnecessary to try to make the effort within the legislation to look ahead and deal with that, or whether the
20 legislation will say, "Based on this, we're going to
21 go ahead, and if something else happens later, we'll
22 face that later and figure out what to do about it
504 1 then, or decide we'll ignore it." I mean, you know,
2 there are policy issues that are separate from
3 science.
4 MR. GARTHWAITE: Yes.
5 MS. LASHOF: You've been around both
6 government and science long enough to be well aware
7 of that, and it's always a dilemma how you deal with
8 it. And I was just wondering whether, in your
9 consideration in writing the legislation, you're
10 going to try to deal with it in this legislation, or
11 not deal with it.
12 MR. GARTHWAITE: Right. My limited
13 experience is that this is a complex effort that
14 involves a lot of people and a lot of different
15 considerations. And the administration will propose
16 legislation, and then -- and it certainly is subject
17 to additional modification later. And so my own
18 personal opinion would be that it might be wise to
19 anticipate that, because of the difficulty in
20 getting legislation through the Congress, and the
21 time lag, and so forth, and considerations. So
22 dealing with any anticipated changes, and dealing
505 1 with it once, and bringing everybody that needs to
2 vote on the legislation up to speed, has some
3 appeal. I appreciate those comments.
4 MS. LASHOF: Good luck.
5 MS. GWIN: Well, my questions lie
6 sort of along the same lines. You stated at the
7 beginning of your testimony that you're prohibited
8 by law from offering services to families of
9 veterans. So we have a situation that, even if we
10 did determine a link between Gulf War service and
11 families' illnesses, your hands are tied until
12 there's an act of Congress. Is that correct?
13 MR. GARTHWAITE: At the current time
14 that's my understanding of the interpretation of the
15 statutes.
16 MS. GWIN: So when you were
17 considering this spina bifida legislation did you
18 give any consideration to going more generic with
19 your request to Congress so that you would be more
20 empowered to help families if there turned out to be
21 a need to?
22 MR. GARTHWAITE: We've been pushing
506 1 for -- just for veterans, been pushing for an
2 improvement in the eligibility legislation which is,
3 today, very complex and convoluted, very difficult
4 to explain either to employees or to veterans, and
5 have been having a great deal of difficulty because
it has been scored as costing money to the

government, and there's hesitancy in worsening the

federal deficit. And so we've not been able, so

far, to get eligibility for them through, in that

we've not approached the issue of providing care in

VA medical centers to veterans' -- and there seems

to be no compelling interest so far in Congress to

providing additional benefits to families of

veterans.

The ability for us to provide care in

VA hospitals to non-veterans has been a politically

controversial issue for many years. There was a

pilot study a few years ago in which, in rural areas

that were having trouble supporting either a VA in

terms of workload, or a non-VA medical center,

whether we could combine patient and, together,

would have a viable institution to provide that

service. And at that time, that was not politically

doable, and so we were unable to get that pilot --

those pilots done.

So I guess what I'm getting around to

is saying that although I think there's evolution of

the thinking in terms of the politics of getting

non-veterans into VA hospitals, there still would be

a fair amount of work to do to do that. If you step

back and you say, "If legislation is there to pay
10 for case in a non-VA setting, could we do that,"

11 then I think that would be a different matter, and

12 that would be a more -- would be an easier

13 legislative initiative because it doesn't imply any

14 displacement of veterans from VA hospitals. And so

15 that would just be a, "Does the United States have

16 an obligation to provide for care for non-veterans

17 in those circumstances?"

18 And I think where we had the science

19 to back it up, we're going forward. I mean, you

20 know, here I think it's right now a more difficult

21 issue in terms of, "Do we have the science to push

22 that agenda?"

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1 MS. LASHOF: Joe?

2 MR. CASSELLS: I understand the

3 problems with providing care to family members under

4 the current legislation, but male veterans have

5 reproductive concerns also. What kind of capability

6 within the VA system is there for dealing with

7 those?

8 MR. GARTHWAITE: I think we do a

9 fairly reasonable job there, simply because much of

10 that care is provided by urologists, and because we

11 have a significant number of well-trained urologists

12 within the system. We also have affiliations with
13 109 medical schools, so that we have
14 highly-qualified urologists coming into our medical
15 centers to provide consultation. So I think overall
16 our ability to provide at least some care to male
17 veterans is a bit better in terms of potential
18 fertility issues.
19 MR. CASSELLS: How about genetic
20 counseling?
21 MR. GARTHWAITE: I would say that my
22 sense is, with genetic counseling, that's a
23 relatively variable piece of the health spectrum for
24 the United States as a whole, and I would suspect at
25 the VA it's also somewhat variable. I mean, I think
26 you could find some urologists who are good at that,
27 but I suspect that also the predominant reservoir of
28 knowledge in genetic counseling probably revolves
29 around very active obstetric practices and
30 infertility clinics, and around neonatal intensive
31 care units, and less around urologists who
32 concentrate more in prostatic disease, and kidney
33 stones, and a variety of other things.
34 So I'm just saying I think that it's
35 not a -- not everyone -- as has been previously
36 testified, not everyone comes to the table with the
37 same amount of knowledge. You can hire someone to
38 examine newborns for genetic abnormalities; it
doesn't imply that they have the kind of knowledge that you need. So what I'm kind of getting around to is saying that my suspicion is that this is a very specialized area, and that to provide that kind of specialized care requires some effort. To my knowledge, we've not probably made enough efforts in making sure that's available, although I'm going to have to go back and ask that question. So --

MR. CASSELLS: I was thinking about the university affiliations --

MR. GARTHWAITE: Yeah.

MR. CASSELLS: -- that perhaps it could be available to --

MR. GARTHWAITE: Right. I think there's a lot we can do with that, but the question is, if someone comes in and asks the Persian Gulf registered veteran, have we made it easy for them to then get the counseling by the individuals who actually have that knowledge? And it's one thing to provide a small amount of knowledge to a lot of people, the generalist, but who needs the specialized knowledge, and how is that handled?

From other testimony I was impressed that experts in the field don't think that that always happens as well as it might throughout the health care spectrum. So I think we'll take a look at that. I
appreciate your question.

MS. LASHOF: Tom?

MR. McDANIELS: Just one more outreach follow-up question about genetic counseling. Is that something that -- in future outreach, is that something you would feel comfortable in placing in the outreach as a recommendation to get genetic counseling, even if VA couldn't provide those services to spouses?

MR. GARTHWAITE: This all gets relatively complex because of some of the prohibitions in law about what we can and cannot get involved in. So I think we're going to have to take a -- you know, I don't want to sound bureaucratic, but I think the reality is, there are some issues that need to be addressed. But clearly, I think what we need to do is have a clear, and reasonable, and fairly straight-forward approach that's clear from the veteran's standpoint. Yes. "If you have a concern about having children, here's how you get help." I think that needs to be simple and clear.

MS. LASHOF: Thank you very much, Dr. Garthwaite. We appreciate your coming.

Next is Diana Tabler. I guess we have a panel coming up: Diana Tabler, Captain Donald Johnson, and Colonel Robert Jarrett. And
some of the questions we've just asked will really
be addressed by this panel, who are going to talk
about genetic services, referral, and outreach.
And Diana Tabler, are you kicking it
off?
MS. TABLER: I'll begin. Thank you
very much.
MS. LASHOF: All right. Thank you.
GENETIC SERVICES, REFERRAL, AND OUTREACH:
DEPARTMENT OF DEFENSE
COMMENTS BY DIANA TABLER
MS. TABLER: Thank you. I'm here
today at the Committee's request specifically to
discuss health care benefits available for the
Military Health Services System beneficiaries who
experience reproductive problems including birth
defects and decreased fertility, and who seek care
under the Civilian Health and Medical Program of the
Uniformed Services, which is, in fact, my specific
area of responsibility.
To date, investigations by state and
national health agencies as well as the DOD have
not, as you know, identified elevated or unusual
patterns of problems, including birth defects, among
Persian Gulf War veterans. The Department of
Defense clearly understands the importance of these issues to family members, and is working with other agencies to continue to search for any undiscovered correlations.

The benefits I'll describe today are part of DOD's comprehensive care for our families and our children with special needs. They are based on eligibility for DOD-sponsored care and provided without regard to the possible cause of those needs.

The heart of the military health care system is the direct care system of about 116 hospitals and more than 500 clinics throughout the world in which we provide a comprehensive range of acute care services from primary to tertiary care to our eligible beneficiaries, depending, of course, on the size of the facility. Active duty members receive virtually all of their care from our 1 military hospitals, and nearly two-thirds of all the care delivered by DOD to our beneficiaries is provided in our system of direct care military hospitals.

When that direct care system is short on space or staff, then family members of active duty personnel, and retirees and their family members who are under the age of sixty-five, may seek care under the Civilian Health and Medical
Program of the Uniformed Services, known as CHAMPUS. TRICARE, the Department's comprehensive managed care initiative, is now replacing CHAMPUS to more effectively integrate our military and civilian health care resources, establish uniform benefits, and introduce managed care improvements throughout the system.

TRICARE provides cost sharing for medically-necessary health care purchase from civilian sources when MTF care or military treatment facility care is not available. Coverage is provided without regard to pre-existing conditions.

A key facet of TRICARE is the beneficiaries' voluntary enrollment, selection of a primary care manager who either provides or arranges for a family's health care. Because of the relative youth of our active duty population, family planning and reproductive health are important components of the care we provide.

Beneficiaries who experience fertility problems can use their TRICARE benefit to obtain a variety of reproductive health services including infertility testing and treatment. Covered services include diagnostic testing, surgical intervention, hormone therapy, and other procedures performed to correct or monitor progress.
14 in overcoming the causes of infertility. Chromosome
15 analysis in cases of habitual spontaneous abortion
16 is also a covered benefit. Like many other health
17 care plans, TRICARE does not cover non-coital
18 reproductive technologies such as artificial
19 insemination and in vitro fertilization, but some of
20 these fertility programs are offered to a limited
21 extent in certain military hospitals, primarily
22 tertiary teaching hospitals.
516 1 When an eligible beneficiary becomes
2 pregnant a primary care manager or obstetrician
3 oversees the course of her antenatal postpartum
4 care. If a patient has questions or concerns about
5 the health of the fetus, genetic counseling and
6 testing such as amniocentesis, chorionic villus
7 sampling may be covered. High-risk pregnancies are
8 managed in accordance with accepted practice
9 guidelines. Under the Civilian Health Care Program,
10 ultrasound testing is a covered benefit in a
11 high-risk pregnancy situation.
12 For fetal testing, the general
13 guidelines for sharing the costs of care purchase
14 from civilian sources, if a pregnant woman is
15 thirty-five years or older, if the parents of the
16 fetus have had a previous child or personal or
17 family history with a congenital abnormality, if the
18 pregnant woman contacted rubella during the first
19 trimester of the pregnancy, or if medically
20 necessary for any other reason. The determination
21 of medical necessity is made on a case-by-case
22 basis. The obstetrician fully evaluates each
23 patient in determining the appropriateness of
24 providing the test. If these tests detect a fetal
25 abnormality, then the obstetrician will provide
26 genetic counseling, or refer the beneficiary to an
27 authorized provider for genetic counseling.
28 The Department of Defense is
29 Congressionally prohibited by Title 10 U.S. Code,
30 Section 1093, from providing payment for abortions
31 in either the direct care system or for care
32 purchased from civilian sources in all cases, except
33 where the life of the mother would be endangered if
34 the fetus were carried to term.
35 Once born, a child with special
36 health care needs will receive a full range of
37 medical and related health care benefits from the
38 Department of Defense to the full extent of his or
39 her eligibility. In addition, the child with a
40 disability and incapable of self-support remains
41 eligible for care in the medical health services
42 systems as a family member of an active duty member
43 or retiree even after the child reaches the age of
The TRICARE program is the child's primary source for medical care. Based on two recent studies, both of which I've provided to the Committee, we believe TRICARE has had a positive impact on access to pediatric health for all of our beneficiaries. In addition to the coverage of medical needs under TRICARE, the Department also provides or arranges for special services in other ways. For example, the Exceptional Family Member Program provides for the screening of children with potential special health care needs and the coordination of duty assignments for the active duty sponsor to insure that all services of the exceptional family member can be met at the gaining duty station. This program is designed so that the active duty member who moves an average of once every three years will locate to a duty assignment that has the appropriate medical and non-medical support structure available. For children with special health care needs, this means access to care either in the direct system, such as to a base or medical center, or in the civilian community with civilian medical care costs shared through the TRICARE program.
Case workers also work with the families of children with birth defects to coordinate the delivery of services which are provided under TRICARE. When a child with special health care needs requires care, equipment, or services that are not covered for any reason, case managers will look to the next available source of care. If available locally, they are generally available through state-administered Title 5 programs, federal grants to states, programs for child and maternal health, including comprehensive health and rehabilitation.

For those who are eligible for DOD care, our case management program will permit waivers to our current TRICARE benefit for services, supplies, and care in lieu of hospitalization where it's clinically appropriate and cost effective.

Case managers will be able to authorize on a case-by-case basis supplies or services that would not otherwise be covered.

The DOD Program for Persons with Disabilities is a safety net, another program, for children of active duty families to insure that all their health care needs are met, and to protect those excluded from state programs due to residency laws. After considering the availability of other
resources, the program allows for moderately or severely disabled persons to receive cash payments or benefit payments for special institutionalized care, training, rehabilitation, and equipment not otherwise covered. It provides up to $1,000 a month to families for financial assistance, the families making a copayment based on a sliding scale according to rank and income from 25 to $250 per month.

Men and women who leave active duty have some provisions for health care coverage as they transition to civilian life. The first is the right to transitional health care in our direct care and TRICARE systems of either 30, 60, or 120 days, depending on their length of service.

We've also established a continued health care benefit program of temporary continued health benefits for all who no longer have the entitlement to military health care following separation from active service. This program is premium-based. Former active duty members and their families may purchase coverage for a total of eighteen months. It generally provides the same coverage as available under TRICARE, and coverage is available regardless of the existence of any pre-existing conditions.
The Department of Defense is engaged in a variety of outreach programs which have detailed in great detail to you and outlined in your interim report, including, of course, the two hotline numbers, the Web site, and other print and broadcast outreach programs.

In response to the Committee's concern about civilian health care provided to our beneficiaries, I recently directed that information on the DOD incident reporting line, and the evaluation program, and the Internet access for the Web site devoted to Gulf War issues be disseminated to health benefit advisors and TRICARE participating physicians throughout the world to encourage them to call when they believe they have -- they or their patients have information, medical information, about the causes of health problems suffered by Gulf War veterans. And our guidance includes a specific reference to reproductive health problems.

Individuals and families eligible for DOD health care can obtain medically-necessary reproductive health benefits through the direct care system and TRICARE. The Department has also accepted responsibility to coordinate various available local, state, and federal programs. And when these programs cannot provide the needed care,
we have a backup program called the Program for Persons with Disabilities.

We are acutely aware of the concerns expressed by Persian Gulf veterans and their families regarding potential reproductive health risks, and recognize the profound impact it has on a family. No connection has been demonstrated, but we are keeping the book open with continued research.

We'll continue to provide the highest quality care and support possible to eligible service members and their families. Thank you.

MS. LASHOF: Thank you very much. I think we'll hear from the whole panel, and then we'll have questions at the end.

You're next, Dr. Johnson.

GENETIC SERVICES, REFERRAL, AND OUTREACH:

DEPARTMENT OF DEFENSE

COMMENTS BY DONALD JOHNSON

MR. JOHNSON: Good morning. I understand that I am the second Don Johnson to speak to your committee. I can assure you I do not act. I have been asked to brief your Committee concerning the U.S. Navy's policy regarding evaluation and care of high-risk pregnancy, prenatal diagnosis, and neonatal and follow-up care for children born with congenital
19 anomalies. This briefing will consist of two
20 parts. The first part will be a discussion of
21 normal procedures for high-risk pregnancy or infants
22 with congenital anomalies, and the second will be
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1 specific to Gulf War veterans.
2 With a high-risk pregnancy, each
3 woman at her first prenatal visit will receive a
4 packet of questionnaires that deal with a variety of
5 issues including general information about the
6 patient, past medical history, past obstetrical
7 history, nutritional assessment, social history,
8 genetic and infectious screens, as well as
9 occupational health screens. Physical examinations,
10 standard laboratory screening, and ultrasonic
11 examinations are done.
12 All assessments, laboratory tests,
13 and ultrasonic examinations fall within the
14 guidelines set by the American College of
15 Obstetricians and Gynecologists.
16 If, based on these screens and/or
17 physical examination, the pregnancy is felt to be
18 high-risk, the patient will be followed by -- in a
19 complicated OB clinic at the local medical treatment
20 facility, or referred to a perinatology group in or
21 outside the local medical treatment facility. If,
During ongoing prenatal checks, the mother's or fetus's condition changes, referral of the pregnant woman to the appropriate complicated OB clinic or perinatology group will be made. Perinatology groups consist of a perinatologist, geneticist, morphologist, nutritionist, and various social support personnel. All known dysmorphic fetuses are referred to the perinatology groups. After delivery, if the neonate is found to have dysmorphic features or congenital anomalies and require immediate medical intervention, that neonate will be referred to a neonatal intensive care unit. If the neonate is medically stable, the infant will be referred to a geneticist, dysmorphologist, for outpatient evaluation. Infants and children outside of the neonatal period who have congenital anomalies are referred to a dysmorphologist and/or developmental pediatrician for ongoing subspecialty care. General pediatric care is provided by the patient's primary care provider. Gulf War veterans. Gulf War veterans represent a special subpopulation of potential occupational health risk. The Department of Defense
4 has developed a specific program, the Comprehensive
5 Clinical Evaluation Program, to evaluate and treat
6 medical problems that may have arisen from exposure
7 in the Gulf War. This program is well delineated,
8 starting with initial screening at the local medical
9 treatment facility, and referral to a regional
10 medical center when appropriate. Entry into this
11 program is voluntary and may be determined -- excuse
12 me -- may be terminated by the veteran at any time.
13 If a pregnant woman who is a Gulf War
14 veteran, or whose partner is a Gulf War veteran,
15 expresses concern that their health or the health of
16 their fetus may be adversely affected because of the
17 Gulf War, the appropriate person or persons will be
18 referred to the local medical treatment facility
19 administrative head for the CCEP program for
20 enrollment. If a patient has a concern that their
21 child is suffering from a condition that was caused
22 by the parents' exposure in the Gulf War, this
23 family will also be enrolled.
24 Evaluation, or Phase 1, will consist
25 of answering a standardized questionnaire assessing
26 health risk, occupational exposure, and reproductive
27 history. An in-depth medical system-directed
28 evaluation and complete physical exam will be done
29 by an internist or family practitioner. Basic
8 screening laboratory tests are drawn. If no
9 unexplainable findings are found, then Phase 1
10 evaluation is complete.
11 However, if the physician feels that
12 subspecialty evaluation is indicated, then the
13 patient is referred to the regional medical center
14 for entry into Phase 2. In the case of a pediatric
15 patient, evaluation of that patient would be done by
16 a pediatrician or a family practice physician.
17 I hope that this brief review has
18 clarified the U.S. Navy's policies on children with
19 congenital anomalies. Thank you for this
20 opportunity to meet with your committee.
21 MS. LASHOF: Thank you very much.
22 The last speaker is Colonel Jarrett.

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2 DEPARTMENT OF DEFENSE
3 COMMENTS BY ROBERT JARRETT
4 MR. JARRETT: My comments in large
5 part will reiterate much of what has already been
6 said, and I think that is due to the nature of the
7 -- the integrated nature of military medicine. It
8 has become much more of a tri-service effort. Our
9 community hospitals and regional referral centers
10 are often intermixed. For example, Captain
11 Johnson's hospital at Bremerton is a community
hospital, and Madigan Army Medical Center, from whence I come, is a referral medical center, and we collaborate frequently on patients. And then, of course, the CHAMPUS and TRICARE system is an extension of both of our systems.

The U.S. Army provides a full spectrum of obstetrical, neonatal, and pediatric services to active duty members, their dependents, and dependents of retired active duty personnel. The organization of these services is very similar to civilian practice. Obstetricians, pediatricians, and family practitioners provide routine evaluation and treatment of uncomplicated patients in community hospitals. These community hospitals are located on U.S. Army installations throughout the United States, in Korea, and in Europe. Examples of those installations would be Fort Hood in Texas, Fort Benning, and Fort Bragg on the East Coast, Fort Riley in Kansas, and Fort Knox in Kentucky.

Complicated patients are referred to tertiary care military regional medical centers staffed with perinatologists, neonatologists, and a broad spectrum of pediatric subspecialists. Subspecialist physicians who staff these hospitals are trained in graduate medical education, residency, and fellowship programs in both the
military and the civilian sector. And these
physicians are either board-eligible or
board-certified in their area of expertise, and are
subject to the same certification requirements as
their civilian counterparts.

When appropriate subspecialty referral care is not available in the military medical center, patients are referred to appropriate civilian tertiary care facilities, often university medical centers.

Women with uncomplicated pregnancies are followed by family practitioners and obstetricians. The care they receive follows ACOG guidelines for health assessment screening, diagnosis, and treatment. When obstetrical history, laboratory, physical finding, or imaging criteria -- for example, ultrasound -- identify a high-risk pregnancy, patients are referred to subspecialists in perinatology. Those consultations may also include consultation with neonatologists, geneticists, pediatric dysmorphologists, pediatric surgeons, or other subspecialists, depending on the problems identified in that pregnancy.

For example, if a prenatal ultrasound identifies a fetus to have an abnormal heart rhythm,
a pediatric cardiologist will assist the perinatologist in evaluation of the fetus prior to delivery. If an ultrasound would show an abdominal wall defect, a pediatric surgeon would be consulted.

When prenatal evaluation detects a fetus that will need specialized neonatal care, the mother is transferred to a Level 3 regional medical facility with a newborn intensive care unit prior to delivery. When the Army community hospital is located proximate to a regional military medical center, the mother is transferred to the military center, providing the expertise is present in that center. If not, the mother is transferred to the closest civilian facility with the appropriate expertise. Infants with congenital anomalies that are not identified prenatally are transferred to regional medical centers after birth, using the same logic.

Military regional medical center newborn intensive care units are staffed by fellowship-trained board-eligible or certified neonatologists. They are assisted by a full range of pediatric and surgical subspecialists in the evaluation of therapy of infants with congenital anomalies. Chromosome analysis, dysmorphology evaluation, and genetics counseling are utilized as
medically indicated for these infants. When in-house resources are not available, patients are referred to civilian experts, usually at university medical centers. Infants with no clearly identifiable syndrome are presented as case reports and discussions at national meetings.

Many children with congenital anomalies continue to have special health care needs beyond the neonatal period. When these children's needs are identified, the Army's Exceptional Family Member Program coordinates the assignment of soldiers to locations where their children's medical needs can be addressed.

Thank you.

MS. LASHOF: Thank you very much.

Questions? Marguerite?

QUESTIONS

MS. KNOX: Yeah. I just have one.

Are you collecting any data on the number of abnormalities, and maybe what they are, that you've seen?

MR. JARRETT: The Army, as such, has no unified approach to the collection of data on children with birth defects. All of our newborns, whether they're routine newborn or are in a newborn intensive care unit, they all have charts, and the
5 charts have discharge diagnoses which go into a
6 central database. But that's a database that's not
7 -- that's a database that looks at all diagnoses
8 across the board, and it's not subject to easy
9 queries. So in answer to your question, at the
10 present time we don't have a unified system for
11 looking at birth defects.
12 MS. LASHOF: Tom?
13 MR. McDANIELS: For the panel: for
14 active duty personnel who have reproductive concerns
15 because of Gulf War service, what could the medical
16 corps do? What type of information could be
17 disseminated, general information about birth
18 defects, to counteract, I guess, the negative spin,
19 or maybe some of the misinformation that's out there
20 about the incidence of birth defects to offspring of
21 Gulf War veterans?
22 MR. JOHNSON: I think the answer to
23 that is that you give them the best available
24 information, which is usually research-driven
25 information, as we do with any risk assessment, be
26 it immunizations, or otherwise. And you try to
27 educate them accordingly.
28 MR. McDANIELS: And that would be,
29 like, specifically through message traffic, through
30 liaisons with the commanding officers? How,
specifically, would that information be disseminated to the troops? Do you have any recommendations?

MR. JOHNSON: It may come as message traffic from the appropriate surgeon generals on down. It may come from civilian literature, The American Academy of Pediatrics, the American College of Obstetrics and Gynecology, and their civilian counterparts.

MR. Mc DANIELS: And do you think that type of an outreach campaign would be effective, or do you think it's necessary?

MR. JARRETT: I'll stick my neck out on that one. I think the concern of the Gulf War veterans illness and the publicity that it's received has created a lot of concern, as we all know. Otherwise, we wouldn't be here today. I think, to allay people's anxieties with at least the initial information that is present that if there is a risk, it's probably a low risk of congenital malformations, it's probably going to have to come from the same type of public information.

Individual centers to get that type of information out, I think would be very, very difficult. And I say that because of other initiatives that we try to get local information out about our practices, and
the success that we receive on that. I think we're talking a big problem. So I really think the Committee's findings, when those are made public, when the results of ongoing studies are made public, that's going to be how we get to the people.

MS. LASHOF: Joe?

MR. CASSELS: Ms. Tabler, I have two questions for you. First, do you have any idea -- I'm sure you do -- how much of the CHAMPUS budget is devoted to reproductive problems and disabilities?

MS. TABLER: Well, actually we didn't do a specific study on that. I can give you a few numbers. And one reason -- current FY, I guess '95, we spent about $900,000 on fetal testing in that particular year. And again, it's hard to kind of tease this out, but I think we could if we were to do a special study on particular codes.

The Program for Persons with Disabilities which I've described, we spend about $8 million a year. OB care, in general, is about 218 million a year, and then neonatal care is somewhat -- about 47 million a year.

So those are very broad numbers. I think it would be possible to dissect that further with specific codes, but other than the program for the disabilities, and neonatal, and fetal testing --
MR. CASSELS: Okay. And one other question. I commend your providing the information about the Gulflink Web site, and the DOD incident reporting line to your benefit advisors and the TRICARE participating physicians. You said the guidance includes a specific reference to reproductive health problems. What's the nature of that reference?

MS. TABLER: The nature is simply a concern that it may be a concern among beneficiaries seeking care or having questions. And actually I'd be happy to provide to the Committee the actual wording of our -- of our message to our contractors. And I should also note that in every TRICARE region --

MR. CASSELS: We'd appreciate that.

MS. TABLER: Okay. I'll be happy to do so. In every TRICARE region, 800 numbers for help in TRICARE are being established, so I hope that will build even more bridges between eligible beneficiaries and the opportunity to have their questions answered and evaluated.

MR. CASSELS: Thank you.

MS. LASHOF: Granted that we're knowledgeable that you cannot fund abortions, if
there are -- but you do do ultrasound and chorionic villus sampling. And if the parent decides that she wishes an abortion because of a severe congenital defect, how available is it to them if they're overseas, and do you have any data on the number who will seek private abortions?

MS. TABLER: Let's see -- I do not have that data available. I believe that the restriction is very strict, and applies throughout the world. It's not my specific area of responsibility, but I'll be happy to provide that information to you.

MS. LASHOF: Kathi?

MS. HANNA: This is a question I guess directed to the panel, but perhaps, Diana, you can take the first crack at it.

I'm sure you're all aware that a family with a child with a disability of some type faces extraordinary problems when it comes to health -- having their health care paid for, whether they're in the civilian sector or the military sector. And in the military sector, I think sometimes people stay in their job if they have coverage for their child, just as they do in the civilian sector.

What happens to the family who is
active duty, and has a child who's getting care through the military hospital, when they separate from the military? What happens -- you described a transition period. You described a system where possibly there's an extension of benefits for a period of time. Can you describe what the options are for that family before they're forced into a civilian health insurance plan?

MS. TABLER: Well, during the period of transition, which I said can be up to 120 days, I think, depending on the amount of active service, or longer if the family elects to pay premiums in what is called the Continued Health Care Benefit Program. Any medically-necessary health care related to birth defects or congenital abnormalities, any of those things, are still available as part of their basic benefit. And included in that would be the services under our Program for Case Management. And the purpose of that program is really to find the best array of family-centered services for that person.

And it is my belief that as a -- anyway, that as a family approaches the transition, the point at which they will no longer be among -- be eligible for care in our system, that our case managers will be working with them. For example, they will have established, presumably, a state of
permanent residence, and that's where I think the
case managers can be very helpful in identifying
possible sources of care in the community following
that separation.

The next issue, about the subsequent
employment or alternative insurance is really an
issue that each family faces. No question.

Anyone else like to --

MR. JOHNSON: Each family that has a
severely handicapped child does a lot of
soul-searching before they decide to leave the
military, if they have that option. And as a
primary care pediatrician, we certainly would advise
them to think very seriously about leaving the
military and the economic impact that has on them.

Be that as it may, some people choose, and the
military chooses, sometimes, to separate these
families.

And I think I'd like to second that
most of these families actually are pretty savvy,
and have already looked at various state and local
types of programs where they're going to relocate
themselves. And a lot of these children do fall
under crippled children's or some other type of
benefit.
MS. LASHOF: I'd like to follow that -- just one more item in that regard. As you indicated, they are very cautious about leaving the military because of those benefits. And retirees continue to have benefits.

MS. TABLER: That's correct.

MS. LASHOF: Where does the category of the medically discharged -- when the military chooses to discharge someone because of medical inability to continue to serve, do they fall under the category of a retiree, or does it depend on how long in the service, or are they entitled to further benefits, or not?

MS. TABLER: I'm not sure.

MR. JARRETT: I'm sorry; as a pediatrician, I don't know the answer to that.

MR. JOHNSON: As I understand it, if they're medically retired, depending on their disability, their family may be eligible for continued care. It depends on the system, and I -- also as a pediatrician, I really don't know.

MR. CASSELS: It's based on the percent of disability --

MS. LASHOF: The percent of disability --

MR. CASSELS: -- and the family --
13 MS. LASHOF: -- determines whether
14 the family gets care?
15 MR. CASSELS: The family continues
16 to get care.
17 MS. LASHOF: Okay. It's complicated.
18 MR. JOHNSON: And there are also some
19 other categories: designees of the Secretary of
20 Navy, Air Force, Army that could get care, even
21 though they're not now on active duty.
22 MS. TABLER: Dr. Lashof, if I may
543 I make sure -- I didn't answer 'cause I wasn't sure,
2 but if a person is medically retired from the
3 service, then they remain eligible for CHAMPUS as a
4 retiree. I believe that's correct.
5 MS. LASHOF: Okay. Thank you. I
6 gather we're going to have a separate briefing on
7 compensation --
8 MR. CASSELS: We are.
9 MS. LASHOF: -- so maybe we won't
10 push you any more.
11 MS. TABLER: Okay.
12 MR. CASSELS: But I do want to
13 follow up on that eligibility question. What about
14 the instance of administrative separations, either
15 for disciplinary action or other reasons? Are those
16 transition --
17 MS. TABLER: I don't know the answer.
18 MR. CASSELLS: And those transition programs are available to the families?
19 MS. TABLER: I believe so. Yes.
20 MR. CASSELLS: In most instances, in those circumstances --
21 MS. LASHOF: Yes, they are.
22 MR. CASSELLS: -- everything is lost.
23 MS. TABLER: Voluntary -- I believe the transitional benefits are available to voluntary
24 and involuntarily separated persons. I'll confirm that and get it back to you.
25 MR. CASSELLS: Thank you.
26 MS. GWIN: No.
27 MS. LASHOF: Okay. Any other questions? If not, thank you very much.
28 That completes our formal testimony,
29 and it's a question whether the Committee has any other issues that they want to bring up to discuss before we adjourn.
30 Do you have any, Holly?
31 MS. GWIN: No.
32 MS. LASHOF: No. I'll remind you that our next meeting is July 8th and 9th in Chicago, and the subject is --
33 MS. GWIN: We're going to get different briefings, and then we'll also go over
21 staff memos on risk factors.

22 MS. LASHOF: Okay. So we'll see you all then. And if there are no other questions --

Robyn, any last-minute words of wisdom?

3 MS. NISHIMI: No.

4 MS. LASHOF: No? Okay. Thank you all very much. Thank you, all of our participants.

5 And the meeting stands adjourned.

6 (Whereupon, at 12:15 p.m. the meeting was adjourned.)