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341

UNITED STATES OF AMERICA

- - - - PRESIDENTIAL ADVISORY COMMITTEE ON GULF WAR VETERANS' ILLNESSES

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PUBLIC AND PANEL MEETING REPRODUCTIVE HEALTH OF GULF WAR VETERANS

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VOLUME II

- - - - TUESDAY, JUNE 18, 1996

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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

343 A G E N D A

PAGE

345 1 P R O C E E D I N G S

2 (8:30 a.m.)

3 MS. LASHOF: I think we're ready to

4 get started.

5 We changed the order of presentations

6 this morning because of schedules, and so let me

7 start with Dr. Adolfo Correa. We're very happy you

8 could join us.

9 ASSESSING REPRODUCTIVE HEALTH

10 IN SPECIAL POPULATIONS

11 COMMENTS BY ADOLFO CORREA

12 MR. CORREA: Thank you for inviting

13 me.

14 This morning what I'd like to do is

to 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 -- 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

each worker and asked the worker to identify the periods of time during which he or she performed the same tasks, and that defined for us jobs. Then for each one of those jobs we asked the worker to tell us a little bit about that job, the dates that that job was held, the building in which that job was performed, and department or area. And then within one -- within each one of those jobs we also asked information about the processes that the worker performed or worked on, and the tools within each process. This represents one of the memory cues that we used to help the workers remember the processes in the clean-room and for the particular processes or tools that they may have worked in. So

351

we used a number of cognitive techniques to try to help the workers remember the tasks they performed. We also had records from the plants that indicated to us what chemicals were required for each one of these processes, so this allowed us to construct what we called the process/chemical matrix. That would enable us to tell, for any given worker performing certain processes at a given point in time, what chemical exposures that worker may have had. We were also interested in specific

chemicals, in particular the short-chain ethylene glycol ethers, because of their known toxicity. They're readily absorbed by inhalation or dermal contact. They have reproductive and developmental -- developmental toxicity. And in the study of Pastidas where work with photolithography had been identified as a risk factor, the question was whether these chemicals were involved there.

In our study we found from the records of the plants that the glycol ethers, here represented by cellusolve acetate and dyline, were present and photo- -- photo-applied in an area of semiconductor clean-room manufacturing called photo-apply. That is where photolithography takes place.

But the concentrations were low. The air concentrations were low. So we thought that if there was going to be enough variation in exposure between the workers, that would not be accounted by inhalation, that it would have to -- it would have to come from differentiations, differences in dermal contact.

So if we wanted to conduct an exposure assessment of expose- -- in relation to ethylene glycol ethers, we wanted to rely, then, on the time that the workers spent in photolithography

as an indication of the potential for exposure to the ethylene glycol ethers. And for that purpose, then we looked at the processes within a given job and said that if the worker performed only photoresist processes that require ethylene glycol ethers, the potential for exposure to these chemicals was high.

If the worker worked on these processes as well as other processes, then the potential for exposure was moderate, since that meant that the worker would spend less time on the photoresist ethylene glycol ether processes. If the worker performed processes that used other solvents, other than those involving photoresist or -- we felt that the potential for exposure to these chemicals was low. And if the worker worked in processes that really require no chemicals or solvents, we felt the potential for exposure there was going to be none.

So this information that we collected retrospectively allowed us to conduct different exposure classification systems, one based on area such as clean-room, other manufacturing, non-manufacturing, or more specific classification 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

355 1 to present only the results of the analysis we
2 conducted within the clean-room workers.
3 This table shows the number of
4 pregnancies to female clean-room employees and the
5 number of pregnancies to the wives of male clean-
6 room employees during the study period, and the
7 numbers of spontaneous abortions, as well as the
8 percents of spontaneous abortions for those
9 pregnancies. And we have here percents or rates
10 that are comparable to those reported in other
11 studies that have been on interview data.
12 When we actually looked at the rate
13 of spontaneous abortions in female employees by
14 potential for exposure to these short-chain glycol
15 ethers, we observe, however, that there was some
16 variation in the rate of spontaneous abortions. We
17 in fact saw an increase in the rate of spontaneous
18 abortions with potential for exposure -- almost a
19 threefold increase in risk in the high-exposure
20 group, compared to the no-exposure group.
21 We looked also at the variation in
22 spontaneous abortions among the wives of male
356 1 employees with potential for exposure to these
2 chemicals. And in this group we didn't observe any
3 variation with exposure.
4 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 -- 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

was validated through medical records, and we were able to confirm that 94 percent of those on whom we had medical records, the diagnosis was confirmed. There was -- time to pregnancy had relatively good consistency when we looked at some of the questions, several questions that we asked about this.

Our exposure assessment was conducted independent of pregnancy outcome ascertainment. And we had detailed and reliable work histories.

Specific measures of exposure that were time-dependent and allowed us to rank exposures to the short-chain glycol ethers and to conduct exposure response analysis.

Our results are consistent across plants, and are consistent with the known toxicology of these chemicals.

The limitations of this study are several.

One is that we were really unable to examine the independent effects of the short-chain glycol ethers, of the effects -- possible effects of the photoresist chemical mixtures that -- in which they were present.

We didn't have a biomarker to

13 indicate exposure to these chemicals.

14 We don't know what the critical

15 exposure period for subfertility is.

16 And we didn't have a large enough

17 sample size of pregnancies to allow us to look at

18 malformations. The numbers that we found were very

19 small, to -- for an adequate analysis.

20 Okay. The second study I'd like to

21 turn to --

22 MS. LASHOF: I --

359

1 MR. CORREA: Yes?

2 MS. LASHOF: I would suggest that you

3 summarize the second study very rapidly, because you

4 have about five minutes left.

5 MR. CORREA: Very well.

6 In the second study, of congenital

7 malformations of the heart, we found that there were

8 no associations between the heart defects and many

9 environmental factors that we looked at when we

10 considered the cardiac defects as a group.

11 But when we examined diagnostic

12 groups and specific paternal exposures, we found

13 associations between specific diagnostic groups and

14 paternal exposures, such as ionizing radiation in

15 jewelry-making. And there were some suggestions of

16 a dose-response effects and interaction with family
17 history -- that is, family history increased
18 susceptibility to these -- some of these defects.
19 Now, that study was an exploratory
20 study, so the results could be interpreted as being
21 due to chance. And I think additional studies are
22 needed to replicate those findings.
360 1 QUESTIONS
2 MS. LASHOF: Thank you very much.
3 Are there questions from the panel
4 first?
5 If not, let me ask just a couple.
6 Certainly the silicon -- the solvent
7 study, semiconductor industry study, is a very well
8 designed, very careful, and has many strengths; its
9 limitations you mentioned.
10 How would you evaluate our ability to
11 do anything as scientifically sound as that, and the
12 problems we're facing in looking at exposures in the
13 Gulf War veterans?
14 MR. CORREA: I don't know enough
15 about the Gulf War veterans, but my -- the limited
16 knowledge that I have tells me that it's probably a
17 more complicated type of exposure setting. I don't
18 know what the different exposures might have been,
19 but my impression is that there may have been

several. The -- but I'm not sure that it's really necessarily that much more complicated, as -- than this study that we did. I think that there are some similarities there.

Now, the one -- one advantage, I think, in the Gulf War's setting is that there was limited time of exposure. I think that that -- that may facilitate the exposure assessment. We had to look at a nine-, ten-year period. And I think that's more difficult to recall the information.

The -- in the Gulf War setting there is a fair amount of publicity now about the possible relationship between exposure and outcomes. So the recall of particular jobs or tasks or potential exposures there may be subject to some effect from outcomes -- that is, there might be some recall bias that -- but that might be addressed, I think, in some -- with some looking, including some questions that specifically look at that possibility of recall.

I think that sample size is probably going to be an issue.

MS. LASHOF: Yeah.

MR. CORREA: A big issue.

MS. LASHOF: And in the result of the spontaneous abortions, this was among people in the

high exposure, during the period of their exposure. Is there any aftereffect of people who've worked in high exposure areas then move out? How long would you expect the effects to linger?

MR. CORREA: We haven't actually examined that, and that's actually one of the questions that remains: are the effects that we observed -- that we observed in this setting chronic or reversible? And if they're reversible, how quickly are they reversed? I couldn't tell you that.

MS. LASHOF: So those that you did report on all were being exposed at that time?

MR. CORREA: Yes.

MS. LASHOF: And you have no data, then, at this point, but you are planning to follow that up?

MR. CORREA: We have the -- we have the data in this study that may enable us to look at subsequent pregnancies within the time period in relation to past exposures. But we haven't analyzed

363

that.

MS. LASHOF: Okay. Thank you very much.

Any other questions? Marguerite?

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

364 1 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

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 1 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.

MR. CASSELLS: Related strictly to the time of use of that?

MR. CORREA: At time of conception. Yes, at the time of --

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

21 MR. CORREA: Right.

22 MR. CASSELLS: Thank you.

368 1 MR. CORREA: At time of conception.

2 We also looked at other times: before conception,

3 after conception.

4 MS. LASHOF: Thank you very much.

5 Appreciate it.

6 Betty Mekdeci. Very happy to have

7 you with us this morning.

8 ASSESSING REPRODUCTIVE HEALTH

9 IN SPECIAL POPULATIONS

10 COMMENTS BY BETTY MEKDECI

11 MS. MEKDECI: Good morning. I'd like

12 to thank the members of the Committee for bringing

13 me here all the way from Florida. I appreciate it

14 very much.

15 The Association of Birth Defect

16 Children, the organization that I direct, is a

17 national non-profit organization started in 1982.

18 We provide information to parents all over the

19 country about all kinds of birth defects. We do

20 national parent-matching, connecting families of

21 similar birth defects. And we sponsor a project

22 called the National Birth Defect Registry.

369 1 The National Birth Defect Registry

2 was really begun because of the poor quality of data

on birth defects we have at the national level.
According to a General Accounting
report that was done for Senator John Glenn, there's
very poor quality data all around the country on
birth defects. In fact, while 2 to 3 percent of
birth defects are detectable at birth, one major
study found that continued monitoring for seven
years after birth found up to 16 percent birth
defects. That was the Columbia -- the Collaborative
Perinatal Project, which was a prospective study of
50,000 pregnancies at twelve medical centers in the
United States.
Next chart, please.
This same report surveyed a group of
experts who said that up to 60 percent of birth
defects are of unknown origin, but 74 percent of
these experts believed that 25 percent or more would
be eventually linked to environmental exposures of
one kind or another.
Although linking and finding the

total incidence rate of birth defects is a major
challenge, even a greater challenge is trying to
link particular birth defects with particular
exposures.
According to a major text on birth

defects, Congenital Defects, by Saxen and Rappala, overall incidence of birth defects may not be able to detect specific causes. And in fact, thalidomide we kind of call the great-granddaddy of teratogens, did not cause an increase in the total number of birth defects.

In fact, all the major teratogens, or most of the major teratogens that have been identified to date, have been identified by the mechanism Dr. Brent mentioned yesterday, the alert practitioner. That is, a doctor or doctors begin to see a pattern of birth defects in a group of children and begin a retrospective analysis of what might be a common factor in the background of these children. This includes, but is not exclusive to, thalidomide, rubella, fetal alcohol syndrome, fetal hydantoin syndrome, valparoic acid syndrome, methyl

371 mercury, PCBs, lithium, DES, radiation, and others.

We decided with the National Birth Defect Registry to try to adapt the process of the alert practitioner in a broad way by taking advanced computer technology and database design to look at large numbers of cases from all over the country.

We began this project in 1991 by designing an interrelational database and an original twelve-page questionnaire. Our

10 questionnaire is divided, not just by overall
11 syndrome names, but by birth defects by body system.
12 We have the ability to collect literally thousands
13 of combinations of birth defects in this way, and to
14 examine syndromes, not just by the name they've been
15 given, but by the components of those syndromes.
16 The development of the original
17 project took over a year, with multiple reviews by
18 outside experts. The American Legion gave us a
19 grant for pilot-testing of the project. And we
20 distributed 5,000 questionnaires to our entire
21 mailing list, which was at that point consisted of
22 families with children with birth defects, state and
372 1 national developmental disability programs, support
2 groups, and medical research centers and other
3 people working with birth defect populations. Of
4 this original mailing, 1,200 registry questionnaires
5 were returned for databasing.
6 One inducement to participate in this
7 project and complete our lengthy questionnaire is
8 our parent-matching component. In fact, I would say
9 that as many parents participate to be matched
10 participate because they may have some idea about
11 what caused their child's birth defects.
12 The first environmental issue that we
13 addressed with the database was the ongoing

14 controversy regarding Agent Orange and birth
15 defects. Although 65,000 cases of adverse
16 reproductive outcome had been reported to the court
17 during the Agent Orange litigation, nobody seemed to
18 have any idea what these reports consisted of.
19 There was no tally made, no examination of the case
20 reports.
21 So under a contract from the State of
22 New Jersey and working with the New Jersey Agent
373 1 Orange Commission, we added an additional page to
2 the questionnaire, and we did send that page to all
3 5,000 of the original participants on service in
4 Vietnam.
5 In 1992 the Association and the New
6 Jersey Commission made a dual report to the National
7 Academy of Science committee appointed to review the
8 health effects of herbicides and dioxin in veterans
9 and their children. At that point we compared the
10 disabilities in 800 Vietnam veterans' children to
11 400 non-veterans' children in the database. And to
12 do this, we convert these cases into cases per
13 hundred in the database, so that we'll have some
14 comparative. We put these statistics into Harvard
15 Graphics charts. And at the first instance we do
16 some basic things, and then New Jersey did some
17 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.

22 Consistent and impressive differences

375 1 in emotional and behavioral disorders.

2 And a variety of miscellaneous

3 conditions which are very consistent with some of

4 the effects of chronic fatigue syndrome.

5 We also have increases in endocrine

6 disorders, benign tumors, and cysts, but I didn't

7 want to take up the time with too much Agent Orange

8 today.

9 The National Academy referenced our

10 report in their book Veterans And Agent Orange, and

11 they did indicate that we had found some increases.

12 They had two problems with our data collection. One

13 was the potential for recall bias, and the second

14 was for self-selection.

15 So after their report, our

16 organization brought together a team of seven

17 national experts -- they didn't know each other;

18 they came from all different disciplines in

19 different parts of the country. We brought in

20 people who had expertise in reproductive

21 epidemiology, biometrics, environmental biology,

22 genetics, endocrinology, biochemistry, obstetrics

376

1 and gynecology, and developmental biology. We

2 brought them down to Orlando. We laid the project

3 before them and said, "What do you think? We'll
4 just do what we say it can do, and are we doing it
5 the right way?" They didn't let me talk, which is
6 an achievement in itself, and they settled down to
7 work.
8 And they came up with a consensus
9 statement in support of what we were doing. And
10 that is looking for potential clusters of birth
11 defects associated with potential exposures. This
12 does not constitute proof. This simply is pointing
13 a direction to start looking.
14 They also decided that they wanted to
15 redesign the questionnaire to make some of our
16 questions less biased, to add some component for
17 medical records, to get medical records to confirm
18 diagnoses. They recommended trend testing, to
19 continue looking at things as we gathered numbers
20 and to help offset self-selection processes. And
21 they asked us to do a different type of outreach for
22 the project that would reach more families for the
377 1 parent-matching component where they didn't have a
2 biased idea of what might have caused their child's
3 birth defects.
4 So at that point we started to
5 advertise the registry's parent-matching component
6 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

378

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

379 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

heart syndrome.

Next chart, please.

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. 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.

We have an impressive difference in lung absence -- either absence or underdevelopment in these cases.

Next chart, please.

And finally, this is kind of a duke's mixture of gastrointestinal, genitourinary, and some chromosomal problems that we are seeing differences

22 in at this point in time.

382 1 If we could go back to the first

2 chart for a minute and talk a minute -- back to the

3 chart 13; I'm sorry.

4 A lot of attention has been given to

5 the Goldenhar syndrome. We have twenty-four cases

6 of children in the database now who have external

7 ear anomalies. Any external ear anomaly case

8 technically can be termed a branchial arch syndrome.

9 Branchial arch syndrome anomalies can be autosomal

10 dominant, they can be sporadic, or they can be

11 multifactorial.

12 In the case of Goldenhar syndrome,

13 which is technically a branchial arch syndrome

14 deformity, there are, historically, some familial

15 cases in the literature. But there are also cases

16 that have been linked to well known teratogens:

17 thalidomide was connected with branchial arch

18 deformities, most particularly Goldenhar;

19 primadone, which is an antiseizure medication; and

20 of course, acutane.

21 Yesterday Dr. Araneta discussed the

22 problem with coming up with an accurate incidence

383 1 figure for Goldenhar syndrome, and she cited various

2 state registries, which we've looked at as well.

3 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

384

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

8 database. And we can actually go into just that
9 birth defect category and, conversely, look at the
10 distribution of various exposures. So we can look
11 at it backwards and forwards.
12 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
15 multiplicity of exposures in the Gulf. According to
16 the GAO report, there were twenty-one different
17 reproductive toxicants in the Gulf -- everything
18 from pesticides, lead, and mercury, arsenic,
19 cadmium, the potential of chemical warfare agents,
20 not to mention multiple inoculations, pyridostigmine
21 bromide. So teasing out one of these from all the
22 others will be a real challenge, not to mention the
385 1 interactions or synergism that might exist between
2 various things.
3 However, we already have some
4 interesting little tickling things going on with the
5 data. And that is, in our Goldenhar cases, four of
6 our cases were in parents' fathers who were called
7 up for service, given all the preliminary
8 inoculations, but didn't go. So that's an
9 interesting little aside at this point.
10 For several years our organization
11 has been monitoring ongoing research on

12 immunotoxicology. And we have been looking at the
13 connection between immunotoxic agents and their
14 potential to be teratogens. Many of the agents in
15 the Gulf are toxic to immune function. And we have
16 come to think, or at least to hypothesize that an
17 immunotoxic agent at one level of exposure may cause
18 a severe structural birth defect, but more commonly
19 at lower levels may cause functional birth defects,
20 such as learning, attention, immune, endocrine, and
21 other problems.
22 Unfortunately, in the country today
386 1 we really don't monitor functional birth defects at
2 all, so we have no good handle on the statistics.
3 I appreciate you inviting me here
4 today, and I'd be most happy to answer any
5 questions. And we would like permission to submit a
6 more fully worked out report to you in written form.
7 QUESTIONS
8 MS. LASHOF: Thank you very much.
9 That's very interesting data, and by all means we'd
10 be anxious to receive any full report and any
11 additional information up until November, when we
12 have to put our report together.
13 MS. MEKDECI: Very well.
14 MS. LASHOF: After that, it may be
15 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?

389 1 MS. MEKDECI: At this point in time
2 when we say, "Non-Gulf," what we do is, we compare
3 all the cases in a particular category to all the
4 cases that are not in that category in the database.
5 Now, that's a little tricky, because sometimes you
6 may be comparing apples to apples, if you're not
7 careful.
8 For instance, within the Gulf
9 exposures we have pesticides. So some of our other
10 -- but we can take that out. We can actually get
11 into removing those and putting those aside and
12 looking at them.
13 We don't have the illusion that our
14 data does anything more than look for clustering.
15 From that point, you can go -- you can go into a
16 random selection within the database, once the
17 numbers reach a certain critical mass. And in fact,
18 the New Jersey Commission is trying to get us to do
19 that on the Agent Orange, and we probably will.
20 But what we really think our data can
21 do is point a direction for case-control work that
22 would be done in the traditional way. Because I
390 1 realize that what we're doing is a little unusual,
2 although there are several studies that have used
3 malformed children as control groups -- in fact, the
4 Center for Disease Control has done that type of

study before.

MS. LASHOF: Okay. Second question:

specific -- well, on all of them, but let's take

Goldenhar as one you've looked at particularly.

What is the relationship of the cases that you have

of Goldenhar to the time at birth in relation to the

time of service? What duration period post-service

are you still seeing the --

MS. MEKDECI: The latest case of

Goldenhar that we have in the database was born in

1994.

I would like to point out that the

thirteen cases -- we have thirteen cases in the

database -- does not represent all the cases that we

have heard of. We have five cases that have called

us, but for reasons unknown to me just simply won't

return their questionnaires. So we can't count

those. But I can tell you we've heard from them.

391 1 MS. LASHOF: So the total number of

Goldenhar is only thirteen? Is that --

MS. MEKDECI: We have thirteen in the

database that have been classified by a medical

professional as Goldenhar. Within our ear anomaly

cases we have another four or five that have facial

asymmetry, the ear anomaly, a vertebral column

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.

13 MS. LASHOF: Yeah. Yeah. Okay.

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

393 1 like that. We actually searched them out.

2 MS. LASHOF: But what time period?

3 What age ranges were there in your non-Gulf

4 Goldenhar --

5 MS. MEKDECI: I can't tell.

6 MS. LASHOF: -- versus your --

7 MS. MEKDECI: I can't tell you that

8 today. I would have to do that.

9 MS. LASHOF: Yeah.

10 MS. MEKDECI: We were --

11 MS. LASHOF: It would be important

12 that we're not talking about completely different

13 time periods.

14 MS. MEKDECI: Oh, absolutely.

15 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

that similar to the questionnaire that you submitted to us?

MS. MEKDECI: It's similar, except the original questionnaire that we sent out didn't have the Gulf War page or the Agent Orange page. Now, we have also rewritten a few of the questions since that time. You think that you have things perfectly designed until you've sent out a bunch, and then you find out something needs to be changed as far as the wording, certain little things. And of course, the committee reworded a few things that they thought could be better said, so --

MS. HANNA: But the questions on the questionnaire are --

399

MS. MEKDECI: Essentially the same, yes.

MS. HANNA: Right. But they're directed to an individual --

MS. MEKDECI: Correct.

MS. HANNA: -- concerning their reproductive --

MS. MEKDECI: Correct.

MS. HANNA: So let's say a caseworker or whatever the disability agents --

MS. MEKDECI: It goes to directly to the family.

MS. HANNA: They then can copy it and give it to --

MS. MEKDECI: Well, they don't copy it; 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.

17 But we try to give them a sufficient number of

18 contacts.

19 MS. HANNA: So all of the people --

20 all of the individuals that return the questionnaire

21 are returning it because they have a child --

22 MS. MEKDECI: That's right.

401 1 MS. HANNA: -- with a birth defect?

2 MS. MEKDECI: That's correct.

3 MS. HANNA: Okay.

4 MS. MEKDECI: That's correct, yes.

5 MS. LASHOF: On the parent-matching,

6 you're matching them for the conditions, putting

7 parents in touch with each other.

8 MS. MEKDECI: Correct. Correct.

9 MS. LASHOF: And they have a choice

10 of saying yes, they want to be matched --

11 MS. MEKDECI: Right.

12 MS. LASHOF: -- or "Please don't give

13 my name to anybody" --

14 MS. MEKDECI: Absolutely.

15 MS. LASHOF: -- "under the sun" or

16 whatever?

17 MS. MEKDECI: Absolutely. There's a

18 question on here we have highlighted in red, and if

19 at any point they want to change that -- let's say

20 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 --

403

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

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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

405

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

of having a child with a birth defect.

MR. McDANIELS: And do they tend to understand that? Does that tend to assuage their fears?

MS. MEKDECI: They always seem -- yes, they do. They seem to feel better. In fact, we get very nice letters, you know, that "Gee, it was wonderful that you talked to us." And I can talk to parents, because I have a son with a birth defect. I've been there -- going through it. He's twenty-one now; we've been through all the ages and stages. And I can tell them, too, that it's not the worst thing in the world that ever happens to you. Of course, that also depends on the type of birth defect. You know, with David, he's able to go to school and work and everything. So I have a particular insight.

I don't think anyone ever calls our office and comes away horrified by anything we've told them. I think they feel relieved. And I think if you talk to some of the families, they would share that with you.

MS. LASHOF: Marguerite?

MS. KNOX: Would you give us that 1-800 number that you spoke of earlier?

MS. MEKDECI: Sure. Sorry; I'm

getting a little hoarse. It's 1-800 313-2232. And the 1-800 number, we've recently changed that. We've had some problems with funding in the last year, because half of our funds come from the federal campaign, and this year, unfortunately, there was the federal work stoppage during the campaign, so a lot of organizations, not just ours, suffered from that. We are now -- we offer free information on the line, and we do market several kits that we're trying to use to pay for the information line, so that we have everything supported. So if you call that line, you'll have a component where you can get free information about a birth defect, you can get a free questionnaire packet. You can order an Agent Orange information package for a $15 donation. You can order a Gulf War package, an environmental birth defect package. Or you can become a member over the line. I think we've caught the same thing.

MS. LASHOF: It's contagious. Okay. Thank you very much.

MS. MEKDECI: Thank you.

MS. LASHOF: We do appreciate your coming.

MS. MEKDECI: I appreciate it.

22 MS. LASHOF: And we look forward to

409

1 receiving further information from you.

2 MS. MEKDECI: Thank you.

3 MS. LASHOF: The next presenter is

4 Linda Shortridge-McCauley.

5 ASSESSING REPRODUCTIVE HEALTH

6 IN SPECIAL POPULATIONS

7 COMMENTS BY LINDA A. SHORTRIDGE-McCAULEY

8 MS. McCAULEY: Betty was hoarse at

9 the end of her talk and I'm hoarse at the beginning

10 of mine, so bear with me.

11 MS. LASHOF: Well, hopefully, you'll

12 get better by the end.

13 MS. McCAULEY: Good morning, Madam

14 Chairman and members of the Committee. My name is

15 Linda McCauley, and I'm a scientist at the Oregon

16 Health Sciences University Center for Research on

17 Occupational and Environmental Toxicology and lead

18 epidemiologist of the Portland Environmental Hazards

19 Research Center, a joint research enterprise of OHSU

20 and the Portland Veteran Affairs Medical Center.

21 I've been asked to speak to you this

22 morning on the assessment of reproductive health in

410 1 special populations, specifically those having

2 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

7 Center we've designed a study that's looking
8 specifically at an array of different factors that
9 were present in the Gulf, including chemical and
10 biological exposures from petroleum products,
11 solvents, smoke, insect repellents, pyridostigmine
12 bromide, vaccines, vectors, diet, water. Physical
13 and psychological exposures include sand and heat,
14 and crowded living conditions and stress, and
15 perceptions of exposure to danger. It creates a
16 very complex picture. And it's difficult to look at
17 traditional reproductive epidemiological studies and
18 try to figure out a sane way to approach this, this
19 population.
20 Next overhead, please.
21 In an ideal situation when you're
22 trying to look at exposure determination, there are
412 1 four components that help you begin to get a true
2 picture of what happened in relation to exposure.
3 But five years after the war,
4 exposure determination presents a particularly
5 difficult task. Real-time measures are not
6 available: it's impossible to verify exposures to
7 vaccines, PB, insecticides, solvents, and infection
8 agents, for the large majority of veterans. We have
9 no work records to verify these exposures, and
10 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

413

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

exposure assessment seem insurmountable, at least in comparison to methods routinely used in studies of exposure and health effects in working populations. We do, however, have an opportunity to compare and contrast groups of veterans who had disparate sets of potential exposures, because they were deployed in the theater of operations for distinct, identifiable periods.

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

Next overhead, please.

This overhead, which some of you have already seen from previous presentations by Dr. Spencer, head of our -- the Center for Occupational and Environmental Toxicology -- it illustrates the relationship between discrete deployment periods and

18 unique sets of chemical, biological, physical, and
19 psychological factors.
20 For example, those who were deployed
21 during the period of December 31st, 1990 to March
22 1st, 1991 may have been exposed to a unique set of
415 1 factors that included PB, special vaccines,
2 munitions, stress from combat and chemical warfare
3 alarms, and exposure to enemy prisoners of war. By
4 contrast with this Desert Storm period, veterans who
5 served only in the Desert Shield or desert cleanup
6 would have experienced quite different exposures,
7 which included the absence of PB and special
8 vaccines. Other factors, such as smoke from the oil
9 well fires, overlapped two deployment periods.
10 Although focusing on distinct
11 deployment time periods does not address all
12 exposures of interest in this population, it does
13 provide an excellent mechanism to determine
14 differences between risk of disease in relation to
15 some of the key exposures of interest.
16 As I mentioned before, the Portland
17 Environmental Hazards Research Center's mission is
18 to look at the impact of environmental hazards
19 encountered in military service on human health.
20 And we look at this mission both in terms of hazards
21 in the past, in the present, and in the future. And

22 our initial focus has been on unexpected

416 1 illnesses,but we are cognizant of the reproductive

2 problems that veterans are reporting, and are

3 looking at our research program to see how it might

4 be adapted to more specifically address these health

5 problems.

6 The next slide shows the framework

7 for the Portland Environmental Hazards Center, which

8 is a joint effort between OHSU and the Portland VA

9 Medical Center. There is an epidemiology core. We

10 coordinate with the Persian Gulf Registry. We have

11 a multidisciplinary team of clinicians,

12 epidemiologists, biostatisticians, and also some

13 scientists who specialize in the area of biological

14 markers. We have a protozoa disorder study.

15 And then we have research projects

16 that are laboratory-based in the areas of

17 neuropsycho- -- neuropsychology, neuroendocrinology,

18 neurotoxicology, and genetic toxicology.

19 The epidemiology core -- I want to

20 give you a little more detail on exactly the

21 population that we're accessing to identify the risk

22 factors for unexplained illness. We're focusing on

417 1 veterans from the northwest United States who were

2 deployed to the Persian Gulf region during the

3 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

418

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 tele- -- 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

419

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.

420

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-

depth components on exposures in the Persian Gulf, military history, family history, lifestyle factors, and occupational -- current occupation and occupational history.

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

421

specifically looking at the deployed population. The inclusion of these items on this survey is designed to assess the general reproductive health of a limited sample of deployed veterans. We do not have specific hypotheses regarding exposures in the theater of operations and reproductive outcomes.

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.

Now, while these data could be

potentially leaked with -- linked with pregnancy outcome data from other studies, our study alone, as shown on this overhead, does not have the power to do anything statistically to detect differences between deployment groups.

We project that we may have the sample size to compare rates of infertility among responders in the different deployment strata, and perhaps to do some analysis of spontaneous abortion rates if female veterans and spouses of male veterans are combined. This would be preliminary analysis only; we would not have the sample size to do any multifactorial types of analyses.

Even with obtaining these reproductive data, as Dr. Correa mentioned today in the very well designed semiconductor study at Johns Hopkins, we will not -- to verify the spontaneous abortion rates would be quite a challenge in a population-based survey like this. So verification would be extremely difficult.

And also, we have no time-specificity. These are pregnancies that basically occurred after the veterans returned home. We really don't have pregnancies that occurred while the exposures were taking place.

From our population-based survey

423 1 design, we've been able to obtain a sample of
2 veterans, of whom 90 percent have not previously
3 sought medical attention in the VA or DOD
4 registries. This population is highly mobile, and
5 requires intensive follow-up of non-responders to
6 achieve representative samples.
7 From the responders to our survey,
8 we're recruiting 250 subjects reporting symptoms of
9 unexplained illness and 250 health controls who will
10 participate in the clinical evaluation component of
11 our study. The response rate for the clinical
12 evaluation component has been very positive: 80
13 percent of the questionnaire responders have agreed
14 to be contacted for future studies, and enrollment
15 rates for the clinical case-control study are
16 approximately 80 percent. That's for veterans
17 living within fifty miles of our Center. We'll have
18 to do satellite clinics as we move out into other
19 areas of the Northwest. The participation rates for
20 cases and controls are comparable, to date.
21 During our clinical evaluation of
22 cases and controls we obtain samples of blood,
424 1 lymphocytes, and skin to assess DNA damage and
2 repair, in a study being conducted by Dr.Glen Kisby
3 at OHSU. Two questions are being asked by Dr.
4 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?

427

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

428

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. CASSELLS: 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. CASSELLS: 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. CASSELLS: 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

of the Desert Storm and Desert Shield population?

MS. McCAULEY: Yes. Our data are comparable to the general frequency distributions in the DOD database.

MR. McDANIELS: Okay. I was just concerned that with the Northwest population you might have an overrepresentation of Navy personnel and different exposures for them.

MS. McCAULEY: It doesn't appear to be, no. I think this -- the Northwest cohort included people who were stationed all over the United States, but listed Oregon and Washington as their home state of record at the time of deployment, so it's not just people who were just stationed here. So we're not seeing any distinct differences in the branch of service.

MS. GWIN: Thanks very much, Dr. McCauley.

MS. McCAULEY: Thank you.

MS. GWIN: We'll start our next panel now on diagnosis, defining syndromes, determining prevalence, and surveillance.

DIAGNOSIS, DEFINING SYNDROMES, DETERMINING PREVALENCE, AND SURVEILLANCE

COMMENTS BY LEWIS HOLMES

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

433

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

process;
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

17 one of the points I'd like to illustrate, that the
18 structural major abnormalities are the key that
19 we're talking about.
20 Frequency. We carried out at Brigham
21 and Women's Hospital in Boston an analysis of the
22 birth defects identified in children through ten
435 1 years of our active hospital surveillance. You'll
2 see that in this ten-year period 69,000 infants were
3 born, and the overall prevalence rate was just a
4 little over 2 percent.
5 We carried out something that hadn't
6 been done before we did this, which is, break it
7 down by recognized cause. You can see -- everyone
8 always talks about the unknowns. Clearly, there's
9 still a large group that's unknown. The different
10 categories of recognized causes are listed. There
11 clearly is a group of about 25 percent that's in the
12 strictly genetic category. And another large group
13 -- we only put in this category conditions where the
14 data available from large studies were consistent
15 with the understanding of multifactorial
16 inheritance.
17 Now, you'll notice the parentheses.
18 One of the advantages of a hospital-based
19 surveillance program is that you can identify
20 elective terminations for structural abnormalities,

21 a problem that all the data sets that have been

22 discussed so far have had to struggle with.

436

1 We're finding at this hospital about

2 a third now of all the children with major birth

3 defects, the abnormalities have been identified in

4 utero. And so there's a steady increase in the

5 number of elective terminations. If you're dealing

6 with a data set that doesn't include elective

7 terminations, you obviously have an enormous problem

8 of "What am I missing?"

9 This data analysis was completed in

10 '85. So if you look for the data for, say 1995, the

11 numbers in parentheses will be much higher. This

12 table comes from -- this paper is in the materials I

13 submitted to the panel.

14 Race makes a difference. You can see

15 here, not data from us, but from CDC, showing the

16 obvious variation between two large racial groups

17 that are available to them in the greater

18 metropolitan area where they carry out their active

19 surveillance program.

20 Another thing that makes a big

21 difference is excluding minor anomalies and normal

22 variations. These are some that, if written into

437 1 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.

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

439

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

prominent thumbs. And this would be the part of the phenotype that would be easily missed. So here's an example of a genetic condition. If you were considering, as Dr. Brent pointed out, that the exposure might be mutagenic, this would be the kind of thing that you'd need to be able to address in your surveillance system.

Here's another genetic disorder that would be a candidate for being increased among individuals exposed to a potential mutagen. You can see here it's a young child whose external ear is deformed in a way that would be considered mild to moderate, but is -- this kind of severity is often associated with significant hearing loss.

For the surveillance issue, would it be recognized that she had a pit here in her neck? You can see the tape from the surgery that she's had, already had on the other side, where these branchial cleft cysts were being removed. The association with the external ear malformation and the cyst makes this a specific entity. So there has to be enough ability to spot this.

And here's her mother. And even though it's obvious to us, sitting here today, she's got the less cosmetic scar from the removal of her 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

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

3 earlier and earlier, you can imagine it's harder for
4 everyone to get the thorough exam that might be
5 needed to settle the presence or absence of some of
6 these findings.
7 Dr. Olney yesterday was commenting
8 that the key to recognizing the Goldenhars in the
9 cases they surveyed was that someone took the time
10 to do the consultation exam that really was the key
11 to settling that it was, indeed, Goldenhars.
12 The epibulbar dermoid doesn't cause
13 any pain or any problems, but it creeps out in a way
14 that scares you that it's going to impede the pupil
15 of the eye. But fortunately, that usually does not
16 cause problems. I wasn't sure how well that would
17 project, and I put in another slide from an older
18 boy showing the same thing.
19 Okay, so that shows you a lot of
20 specific examples.
21 When we went through our data set, we
22 identified in these years, through about 160,000
445 1 births, six infants with the Goldenhars phenotype.
2 And I think you can appreciate the issue of
3 variability as you look at the pluses across the
4 table here. Yes, microtia occurred frequently, but
5 not in all infants. The tags were also common, but
6 not in all, and so forth. The smallness of the

7 mandible is the key finding -- occasional cleft lip
8 or palate, occasional vertebral anomalies, and a
9 variety of other malformations.
10 You might not have noticed when you
11 quickly scanned this the point I'm making here about
12 transfer status. When you work at a tertiary
13 hospital, you have to exclude the women who hadn't
14 planned to deliver there, because that's a bias of
15 being at a tertiary center.
16 One of the mothers had had prenatal
17 screening that picked up that the child was
18 stillborn, and came simply for termination of
19 pregnancy after fetal demise. The other had
20 hydrocephalus diagnosed, had planned to deliver at
21 another hospital. So if you're establishing
22 prevalence rates, you've got to be able to do that,
446 1 and you'd exclude these two cases from your
2 estimates of prevalence, and come out with roughly
3 four in 160,000.
4 MS. LASHOF: That's a lower incidence
5 than many others we've heard so far, isn't it?
6 MR. HOLMES: Well, statistically I
7 don't know whether most -- the larger data sets that
8 have similar quality in the data will come in at one
9 in 25,000. And we haven't done a calculation of
10 whether our one in 40,000, out of 106,000, is

significantly different from one in 25,000, out of, say, 950,000 births, so -- but I think it illustrates the impact of prenatal detection of, obviously, the stillbirth.

So you come back to this group. What you'd expect to see -- I'd like to make the next point about phenotypic heterogeneity, which obviously pushes a child around in the apparent etiology, depending on how you put the things together.

The first point I would make concerns the well-known disorder of spina bifida, shown here

on the right. We've looked at the data over many years. This is an old slide, but it make the point. Everyone is very familiar with anencephaly and encephaloceles and spina bifida. Most of these conditions are now being diagnosed prenatally. The pregnancies typically do not get to term, so they would be missed if you were not including elective terminations for birth defects.

Down at the bottom is a key point: out of the children being surveyed here, 10 percent had, in association with a neural tube defect, either a chromosome abnormality or were part of a specific syndrome, many of which are hereditary.

14 And so if you were looking at neural tube defects,
15 heart defects, any group you want to name, being
16 able to separate out the chromosome abnormalities,
17 separate out the autosomal recessive disorders, is
18 very crucial before you allege an environmental
19 exposure.
20 Just another example. We're just
21 starting a sample of the apparent association of
22 limb deficiencies and the prenatal procedure of
448 1 chorionic villus sampling. Here is a visual
2 illustration of what a mixed group of infants' limb
3 deficiencies are.
4 My colleagues in epidemiology always
5 like to lump these children together. And our
6 concern is that it's a very heterogeneous group. So
7 if you had in your study limb deficiencies as a
8 single outcome, look at what a mixture you'd have:
9 disorders due to dominant or recessive genes,
10 chromosome abnormalities, specific syndromes, then
11 the much smaller group that would be relevant to
12 your alleged environmental exposure.
13 So just to complete the point about
14 etiologic heterogeneity, let's go back to the entity
15 that I mentioned earlier, the microtia, which is a
16 feature of Goldenhars. And this child actually is
17 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

449 1 the 160,000 births, fourteen with just isolated micro- -- 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

22 side has very small preauricular tags. When we did
450 1 many years ago a study of the prevalence of minor
2 features, you can see how very common these are,
3 whether it's the tags in front of the ear, on the
4 ear lobe, or in other regions.
5 So in summary, what I've done is make
6 a pitch for the need for folks involved in looking
7 at the birth defects, who are sensitive to the many
8 etiologies of common birth defects and would be able
9 to exclude the much more common and less significant
10 minor physical features.
11 If out of this, these hearings, there
12 is a proposal made to examine Gulf War-exposed
13 children, or fathers who were exposed in the Gulf
14 War, or mothers, I would stress the fact that we've
15 learned the hard way from other studies of exposures
16 that simply coming up with an exam protocol doesn't
17 solve the problem. Because folks, well-meaning,
18 who've got the same definition in front of them,
19 we've shown in other studies they don't find the
20 same frequency, because that internal definition
21 overrides whatever is written on the paper. And
22 you'd need to be sure you had a small number of
451 1 examiners, and they'd need to be given the
2 opportunity to see whether there really is anything
3 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

 1 hour getting the pedigree" approach, versus focusing 2 on the immediate family. If you look in the reprint 3 I enclosed with this, there's a list of the 4 frequency with which the child, even with genetic 5 disorders, is a total surprise to healthy parents, 6 and there is no family history. And there are 7 X-linked causes of malformations, but most are

dominant and recessives. And the immediate family is the key.

And so what I would -- what I do when I do this kind of work is have an individual designated who will do the pregnancy history review with the mother, do the pedigree, confirm it with both parents, pursue anything in the close members of the family that seems worth pursuing, but not go into exhaustive detail on distant relatives, because that really doesn't help you very much.

And that individual can be trained to do this work. A college graduate who is motivated, interested, and organized is a starting point. Obviously, the more experienced the person, the more help they would be. But you don't have to have

someone who is coming at this with a lot of postgraduate training.

MS. LASHOF: To confirm the diagnosis of Goldenhar, how extensive would the exam --

MR. HOLMES: How many features have to be there?

MS. LASHOF: Who would we need? Would we have to bring every case to you, or send you to each one to examine them to confirm? It 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

454

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

15 obvious difference in severity or something like
16 that in the group. And then let the experienced
17 individuals do the exam.
18 Because if you look at what we've
19 learned from other environmental causes of birth
20 defects, there should be some specificity to the
21 phenotype. And if there isn't, that's helpful. And
22 you know, they'd examine the children blindly,
455 1 figuratively speaking, and then --
2 (Laughter.)
3 -- the data would be pulled together
4 and you'd be able to speak to that point.
5 I think geographic constraints are an
6 issue. You'd want to -- if you have a group of
7 folks that are in the Pacific Northwest, there are
8 lots of people who are well-trained clinicians,
9 could do this in the Pacific Northwest.
10 The thing I'd want to caution you
11 about, which I mentioned earlier, is, we tried in
12 other studies to have everyone agree on an exam
13 protocol, and that doesn't solve the problems of
14 variations from examiner to examiner. That's just a
15 real fact of life in this work. I doubt that it
16 would be a fact of life for the outcomes I showed
17 for Goldenhars. Saying whether an epibulbar dermoid
18 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,

457 1 and a majority of that time has been managing
2 surveillance activities in our branch. And in the
3 last few years I've been working with state health
4 departments on developing and implementing a
5 surveillance program.
6 I was asked by the staff to talk
7 about surveillance methodologies for birth defects
8 and talk about what we do at CDC and what's going on
9 in surveillance in the United States with state
10 health departments and other programs.
11 You've seen some of these slides
12 before, but I think it's important to talk about why
13 we're interested at CDC in birth defects and
14 prevention, in that you know that birth defects are
15 the leading cause of infant mortality.
16 I think it's important to point out
17 that -- how many children are affected each year
18 with a major birth defect. We talk about 3 or 4
19 percent, but that's a large number of infants that
20 are affected each year. So depending on how you
21 define a birth defect, 120- to 160,000 babies a
22 year.
458
1 Thirty percent of these infants are
2 admitted to a pediatric hospital. And the medical
3 cost associated with this is phenomenal. A recently

4 published article estimates that $8 billion lifetime
5 costs are associated with eight major -- eighteen
6 major malformations. So a baby born in 1992 -- that
7 will be with those eighteen malformations, the
8 lifetime cost will be that $8 billion.
9 And more importantly, I think now, is
10 that we're finding some prevention for birth
11 defects, most notably the recent discovery that
12 folic acid could prevent a large portion of spina
13 bifida and anencephalics. So I think that's the
14 positive note that we need to start with.
15 A definition, I think, is important
16 for "surveillance," and this is, I think, a
17 definition that CDC uses for a lot of their work:
18 it's the ongoing collection, analysis, and
19 interpretation of birth defect data essential for
20 the planning, implementation, and evaluation of
21 public health practice.
22 You asked me to address what we do at
459 1 CDC. This is kind of a flow diagram that points out
2 some of -- the building block is surveillance,
3 collecting good quality data, and then going to
4 epidemiologic studies, which you've heard a number
5 of. But let me back up to the surveillance systems.
6 In CDC we started in this activity
7 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.

460 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,

12 the prevention.

13 I want to go over basic -- some basic

14 building blocks for what makes a good surveillance

15 system, some of the characteristics of a good

16 surveillance system.

17 Most importantly is that you identify

18 all the data sources you can to identify children

19 with birth defects, and as Lew, I think, has talked

20 about very, very well, that you need an accurate and

21 precise diagnosis. This is most critical -- not

22 just a birth defect, but all the birth defects --

461 1 and it's described very well.

2 And you need a classification system

3 that is meaningful. Major birth defects is one way,

4 all birth defects -- but more specifically getting

5 down to the specific birth defects or birth defects

6 that might be associated together.

7 A large database, that's important

8 for getting the numbers. I mean, you raised

9 questions about powers. So building a large

10 database is important.

11 It's very important that data be

12 timely and that it can be used and addressed in a

13 timely fashion, if you have a concern that you're

14 not looking at it two, three years down the line --

15 kind of the situation we're doing with the Gulf War

16 now.

17 You need to disseminate the data and

18 get it out to the public in a timely manner, that

19 people can use it and look at it.

20 Probably one of the most important

21 things about a good surveillance system is, you have

22 to have personal identifiers to do follow-up. And

462 1 this always causes a lot of concern, but you have to

2 have this to link to other data, to link records

3 among babies, among visits, and so on.

4 And because you have personal

5 identifiers, you need to develop a very well-

6 developed confidentiality system to protect the

7 patients' privacy.

8 What are the limitations of

9 surveillance? Well, the quality of the data, the

10 data we get, depends on the resources we expend.

11 And I'll show you a couple of different approaches

12 that we use at CDC. So the harder you work at it,

13 the better the data is going to be.

14 The case identification in a

15 surveillance system is dependent upon the quality of

16 the medical record. And Dr. Holmes has address

17 that, too. If we don't get down -- written down on

18 the medical record an accurate and precise

19 diagnosis, we can't collect that data.

And I think, you know, we need to realize that we're not going to identify all cases. Our goal is to try to get to 100 percent, and in most cases we don't reach that goal. But we do very well at it in some cases.

Talk about a case definition. And this varies greatly among some of the states, as I'll talk about later. But this is very important. And Lew just went over this again: you need to define what you consider a major malformation in your surveillance program, what you're going to include in the program. You need to define what a minor malformation is, and whether you're going to include it or not. There are certain conditions that aren't included, as Dr. Holmes talked about: the hemangiomas, polydactyly, and things like that. If that's the only defect, a lot of times we exclude those from our surveillance systems.

Other surveillance in special settings may include other birth defects that aren't in. At CDC we do major birth defects. Some states require all malformations, because they're interested in delivering services to children. A number of state programs include biochemical and 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

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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

466

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 metropolitan area.

You can also go to existing data

sources. In this country now most states have a statewide hospital discharge database that will identify all hospital discharges, and you can look at newborns in that database.

There's Medicaid data that you can look at.

And now more and more the insurance and HMO systems are building databases, and they're interested in trying to look at this, especially for prevention activities.

Trying to address some of the different kinds of surveillance methods that are -- that are going on now or that have gone on in the past. And one that was alluded to earlier and a lot of you know about was the Collaborative Perinatal Project. This was an ideal project. This would be an ideal surveillance system, if we could do it. You have a standard protocol: you go examine every baby. This program followed 50,000 pregnancies, and I'll come back to this and talk about the rates that came out of that program.

You can review -- and this is probably one of the most comprehensive surveillance systems now, is to review medical records of potential cases. And this can include records from nurseries, NICUs, the specialty clinics that I

13 talked about, laboratories, and then all kinds of
14 screening programs. And I will come back and talk
15 about this with the Metropolitan Atlanta Program.
16 You can use hospital discharge
17 summaries and disease indexes to identify records.
18 Some states use that kind of approach. You can use
19 existing hospital discharge data.
20 The National Birth Defect Monitoring
21 Program, I'll talk about was a program like that.
22 And the uniform billing data is
468 1 something that exists currently.
2 Other approaches to ascertaining
3 birth defect data is, a number of states now are
4 developing legislative mandates. Probably the vast
5 majority of the programs have a law that mandates
6 birth defect reporting, and it requires hospitals
7 and physicians to report. In most of these states
8 that do that type of approach, they use some
9 supplemental interaction with the hospitals to
10 increase reporting.
11 And then you have states that link
12 data sources. They may have the hospital discharge
13 data, they may have the Medicaid data. Vital
14 records is one. So they link all these data sets.
15 And then, as I said earlier, we've
16 got vital statistics.

17 And then, a number of states are
18 developing specialized surveillance programs for
19 selected conditions. And that's looking at neural
20 tube defects; they're focusing on just one or two
21 malformations.
22 What kind of -- the data can vary
469
1 greatly with the intensity of surveillance effort.
2 And I wouldn't focus so much on the absolute numbers
3 on this slide, but the great variation of rates
4 depending on how much effort you put forward.
5 If you examine "Infant," you can get
6 a rate. The Collaborative Perinatal Project had a
7 rate of about 8 percent for major defects, had a
8 rate of around 15 percent for all defects. So lots
9 of minor malformations were identified.
10 Comprehensive hospital surveillance,
11 something like we do in Atlanta and they do in
12 California, the rate will be -- around 3 to 4
13 percent of babies will have a major defect. And
14 then you can start seeing the hospital reporting
15 systems. The rate, depending upon their methods --
16 some were 2 and a half to 3 percent.
17 And then as I alluded to earlier,
18 birth certificates don't do very well; they only
19 identify about one percent of the babies with a

20 birth defect.
21 So it can vary greatly, and so you
22 really know -- need to know how the data was
470 1 collected.
2 In metropolitan Atlanta, as I said
3 earlier, we started in the -- in the late '60s. And
4 Atlanta served as a prototype for a lot of other
5 surveillance systems now that are -- that are
6 operating in the U.S.
7 We monitor all births in metropolitan
8 Atlanta, around 40,000 births a year, and we look at
9 all live and stillborn infants who are diagnosed.
10 And we really focus on major malformations that are
11 diagnosed up to first year of life. And we use a
12 very intensive type of case-finding where we go to
13 multiple sources to find the cases in the hospitals
14 and specialty clinics. And we've used this database
15 over the years for doing a lot of epidemiologic
16 studies.
17 Another system that I think ought to
18 be looked at, especially when you come to my kind of
19 recommendation at the end there, is -- the Birth
20 Defect Monitoring Program might be an example of
21 what the DOD might look at for hospital discharge
22 data. This is a program that we had operational
471 1 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

472 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,
473 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 --

476

MS. LASHOF: Yeah. I mean, even with what Dr. Araneta is trying to do, she's going to the 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
479 1 category. So in about seven or eight of those
2 states you could do that approach. I don't know
3 what the numbers would be. We could probably try to
4 figure that out. But then you could go to those, do
5 a case-control study with them.
6 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?

481 1 MR. EDMONDS: Right.

2 MS. LASHOF: And then what -- are 3 there any routine studies that you're doing on a 4 selected group of birth defects?

5 MR. EDMONDS: Right. That goes --

6 MS. LASHOF: Or how do you then 7 follow up, and what additional information do you 8 get from the parents for exposures, et cetera?

9 MR. EDMONDS: Well, the risk factors 10 surveillance study -- we're funding two of the 11 states, California and Iowa, and then in Atlanta, 12 where we're interviewing the parents of a number of 13 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

those studies.

MS. LASHOF: So that at this point you can say that having this surveillance system in effect has enabled you to identify specific risk factors that we can do something about?

MR. EDMONDS: Yes. I think -- yeah, the Vietnam study.

MS. LASHOF: We don't have that many success stories.

MR. EDMONDS: No, we don't.

MS. LASHOF: To get them out --

MR. EDMONDS: I think the folic acid study is one that came out of that.

MS. LASHOF: Pardon? Which one?

MR. EDMONDS: Folic acid --

MS. LASHOF: Uh-huh; yeah.

MR. EDMONDS: -- I think, came directly out of that. Our study was one of many that pinpointed that folic acid was effective in preventing neural tube. So that's one of the success stories.

MS. LASHOF: What percentage of neural tube defects do we now believe are due to folic acid deficiency?

MR. EDMONDS: Fifty percent.

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. CASSELLS: 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

folks that are trained as -- they usually call themselves dysmorphologists, meaning they focused on understanding the causes of birth defects, and they're sensitive to the outcomes we're talking about. Those folks are all over the United States, and you could just identify individuals geographically that might be interested in participating in this kind of work. I would recommend that over the system used in the NCPP, where people like me were given the form to do for $10 or something like that.

MS. LASHOF: Started you off on a whole new career, though, didn't it?

MR. HOLMES: Yes.

MR. CASSELLS: But is that -- is that data at all useful, given those caveats?

MR. HOLMES: For minor features, no. We've looked back -- when we did our tabulation of the 70,000 births in terms of the frequency of the

various major malformations and the etiologies we recognized, we wanted to know whether other data sets had seen similar abnormalities. And it was impressive to see that between '65, when the NCPP ended, and when we were doing this in '85, the number of entities we could

7 diagnose, which are on table 2 in that reprint you
8 have, has grown tremendously. And Dr. Brent
9 referred yesterday to the Mendelian inheritance in
10 man, this catalogue that has over -- since the
11 mid-'60s has shown this incredible growth in the
12 number of phenotypes identified. So the problem
13 with the NCPP is, its folks didn't know these
14 entities existed. So their descriptions might be
15 all right, but you're not sure.
16 MS. LASHOF: Okay. Thank you very
17 much.
18 We are running a little behind time,
19 as usual. We will resume at ten after and try to
20 make up at least five minutes. So ten after the
21 hour.
22 (Recess at 10:55 a.m. to 11:12 a.m.)
487 1 MS. LASHOF: I think we'll try to
2 resume our hearings now.
3 And I'm very pleased to welcome Dr.
4 Thomas Garthwaite, Deputy Undersecretary of Health
5 from the Veterans Affairs Agency.
6 GENETIC SERVICES, REFERRAL, AND OUTREACH:
7 DEPARTMENT OF VETERANS AFFAIRS
8 COMMENTS BY THOMAS L. GARTHWAITE
9 MR. GARTHWAITE: Thank you, Dr.
10 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

493 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

well.

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?

494

QUESTIONS

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

12 came to this meeting Sunday night and sat through
13 all the testimony yesterday and today, and feel that
14 I've probably learned a fair amount, as I think
15 everyone here has. I'm not sure I could conclude a
16 lot, not being a geneticist, or someone really
17 expert in that, but someone with a background in
18 internal medicine and endocrinology.
19 I'm not sure what clear and helpful
20 piece of information I could give them other than
21 that there are still significant issues to be
22 resolved and that there are significant -- that
495 1 there are considerable attempts being made to try to
2 resolve those; perhaps put into perspective those
3 good studies that show that there's not a -- that
4 the risk of a birth defect is real in everyone who
5 has a child, but at least so far is not demonstrably
6 that much greater in studies, although I think you
7 still have to put those limitations on the studies
8 that are done.
9 I think it's common in science to
10 have to have imprecise science, and try to help
11 people make real-life "now" decisions. And I don't
12 know what we can do to help clarify the issue. I
13 mean, I come away from this with the sense that
14 there's not yet clarity, and --
15 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

496

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

was that geared to?

MR. GARTHWAITE: It was to all the

Persian Gulf coordinators and all the

497

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.

498 1 MR. GARTHWAITE: Sure. Before I left
2 as Chief of Staff in Milwaukee VA, we had a
3 traveling show throughout the State of Wisconsin
4 where we brought in the best experts we could, and
5 held open forum meetings advertised in every media
6 that would listen. And we got pretty good
7 attendance, and I think, you know, some reasonable
8 interchange between the best experts we could find
9 on the subject and Persian Gulf veterans. I think
10 we have to continue all those kinds of efforts
11 because no one way is good. We have a large number
12 of people who sign on to our Web site, but that's no
13 good for a whole bunch of people without computers.
14 Television advertisements aren't good
15 for people that don't watch a lot of TV. And I it's
16 just we have to use multiple media to try to reach
17 as many as possible.
18 MS. LASHOF: Did you have other
19 questions about the outreach, Tom?
20 MR. McDANIELS: No.
21 MS. LASHOF: I didn't mean to
22 interrupt you.
499 1 Marguerite?
2 MS. KNOX: Yeah, I just wanted to ask
3 your opinion, Dr. Garthwaite. Yesterday you said
4 you stayed and you listened to testimony. What were

your feelings on that, knowing some of the comments made about the VA system?

MR. GARTHWAITE: You mean with regard to the patients who testified early in the morning?

MS. KNOX: Yeah. Early in the morning. Were you surprised?

MR. GARTHWAITE: Well, for someone who has been in the VA for twenty-two years, and who has treated hundreds of veterans, and whose office was down the hall from the patient representative, I wasn't surprised. But I would also say that, you know, any time that a veteran comes to the VA and is less than 100 percent satisfied with their visit, I feel badly. We see -- we have probably 25 million outpatient contacts, visits, a year.

MS. KNOX: Uh-huh.

MR. GARTHWAITE: It's not going to be possible to make all those visits perfect, but we

500 have to strive to do that. In listening to the various comments, I think -- I was struck by the fact that we need to try to help the individuals who made those comments in any way possible. They all, too me, seemed to have real issues and real problems. The hard part is to know which of those real issues and real problems are a direct result of 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.

MS. KNOX: Yeah. It's disturbing at times.

MS. LASHOF: Let me ask you a question about the Agent Orange legislation that you're struggling with. And I can imagine that there are a lot of issues that have to be addressed. And the decision to go ahead and reimburse for -- or consider it related to service, was made on the basis of the IOM report which suggested a limited -- a limited or suggestive category, and further

research will go on. I'm not familiar enough with all of the research going on. It's hard to keep on top of all of this, but to keep on top of all of the Agent Orange research -- but are there further studies going on to try to determine whether that category will move from limited/suggestive to definite, or move from limited/suggestive to negative, unrelated, and -- well, that would be the first question. Are such studies going on to try to refine that category?

MR. GARTHWAITE: I understand there are, but I would -- you know, I would really need to ask someone specifically the nature of those studies to be able to provide that information to you. But 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

vote on the legislation up to speed, has some appeal. I appreciate those comments.

MS. LASHOF: Good luck.

MS. GWIN: Well, my questions lie sort of along the same lines. You stated at the beginning of your testimony that you're prohibited by law from offering services to families of veterans. So we have a situation that, even if we did determine a link between Gulf War service and families' illnesses, your hands are tied until there's an act of Congress. Is that correct?

MR. GARTHWAITE: At the current time that's my understanding of the interpretation of the statutes.

MS. GWIN: So when you were considering this spina bifida legislation did you give any consideration to going more generic with your request to Congress so that you would be more empowered to help families if there turned out to be a need to?

MR. GARTHWAITE: We've been pushing

506 1 for -- just for veterans, been pushing for an improvement in the eligibility legislation which is, today, very complex and convoluted, very difficult to explain either to employees or to veterans, and 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

507 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

for case in a non-VA setting, could we do that,"
then I think that would be a different matter, and
that would be a more -- would be an easier
legislative initiative because it doesn't imply any
displacement of veterans from VA hospitals. And so
that would just be a, "Does the United States have
an obligation to provide for care for non-veterans
in those circumstances?"
And I think where we had the science
to back it up, we're going forward. I mean, you
know, here I think it's right now a more difficult
issue in terms of, "Do we have the science to push
that agenda?"
508
MS. LASHOF: Joe?
MR. CASSELLS: I understand the
problems with providing care to family members under
the current legislation, but male veterans have
reproductive concerns also. What kind of capability
within the VA system is there for dealing with
those?
MR. GARTHWAITE: I think we do a
fairly reasonable job there, simply because much of
that care is provided by urologists, and because we
have a significant number of well-trained urologists
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
509 1 relatively variable piece of the health spectrum for
2 the United States as a whole, and I would suspect at
3 the VA it's also somewhat variable. I mean, I think
4 you could find some urologists who are good at that,
5 but I suspect that also the predominant reservoir of
6 knowledge in genetic counseling probably revolves
7 around very active obstetric practices and
8 infertility clinics, and around neonatal intensive
9 care units, and less around urologists who
10 concentrate more in prostatic disease, and kidney
11 stones, and a variety of other things.
12 So I'm just saying I think that it's
13 not a -- not everyone -- as has been previously
14 testified, not everyone comes to the table with the
15 same amount of knowledge. You can hire someone to
16 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 case 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

514

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

in overcoming the causes of infertility. Chromosome analysis in cases of habitual spontaneous abortion is also a covered benefit. Like many other health care plans, TRICARE does not cover non-coital reproductive technologies such as artificial insemination and in vitro fertilization, but some of these fertility programs are offered to a limited extent in certain military hospitals, primarily tertiary teaching hospitals.

516 1 When an eligible beneficiary becomes pregnant a primary care manager or obstetrician oversees the course of her antenatal postpartum care. If a patient has questions or concerns about the health of the fetus, genetic counseling and testing such as amniocentesis, chorionic villus sampling may be covered. High-risk pregnancies are managed in accordance with accepted practice guidelines. Under the Civilian Health Care Program, ultrasound testing is a covered benefit in a high-risk pregnancy situation.

For fetal testing, the general guidelines for sharing the costs of care purchase from civilian sources, if a pregnant woman is thirty-five years or older, if the parents of the fetus have had a previous child or personal or 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
517 1 patient in determining the appropriateness of
2 providing the test. If these tests detect a fetal
3 abnormality, then the obstetrician will provide
4 genetic counseling, or refer the beneficiary to an
5 authorized provider for genetic counseling.
6 The Department of Defense is
7 Congressionally prohibited by Title 10 U.S. Code,
8 Section 1093, from providing payment for abortions
9 in either the direct care system or for care
10 purchased from civilian sources in all cases, except
11 where the life of the mother would be endangered if
12 the fetus were carried to term.
13 Once born, a child with special
14 health care needs will receive a full range of
15 medical and related health care benefits from the
16 Department of Defense to the full extent of his or
17 her eligibility. In addition, the child with a
18 disability and incapable of self-support remains
19 eligible for care in the medical health services
20 systems as a family member of an active duty member
21 or retiree even after the child reaches the age of

22 majority. The TRICARE program is the child's

518 1 primary source for medical care.

2 Based on two recent studies, both of

3 which I've provided to the Committee, we believe

4 TRICARE has had a positive impact on access to

5 pediatric health for all of our beneficiaries.

6 In addition to the coverage of

7 medical needs under TRICARE, the Department also

8 provides or arranges for special services in other

9 ways. For example, the Exceptional Family Member

10 Program provides for the screening of children with

11 potential special health care needs and the

12 coordination of duty assignments for the active duty

13 sponsor to insure that all services of the

14 exceptional family member can be met at the gaining

15 duty station. This program is designed so that the

16 active duty member who moves an average of once

17 every three years will locate to a duty assignment

18 that has the appropriate medical and non-medical

19 support structure available. For children with

20 special health care needs, this means access to care

21 either in the direct system, such as to a base or

22 medical center, or in the civilian community with

519

1 civilian medical care costs shared through the

2 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.

520 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

521 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

anomalies. This briefing will consists of two parts. The first part will be a discussion of normal procedures for high-risk pregnancy or infants with congenital anomalies, and the second will be

specific to Gulf War veterans.

With a high-risk pregnancy, each woman at her first prenatal visit will receive a packet of questionnaires that deal with a variety of issues including general information about the patient, past medical history, past obstetrical history, nutritional assessment, social history, genetic and infectious screens, as well as occupational health screens. Physical examinations, standard laboratory screening, and ultrasonic examinations are done.

All assessments, laboratory tests, and ultrasonic examinations fall within the guidelines set by the American College of Obstetricians and Gynecologists.

If, based on these screens and/or physical examination, the pregnancy is felt to be high-risk, the patient will be followed by -- in a complicated OB clinic at the local medical treatment facility, or referred to a perinatology group in or outside the local medical treatment facility. If,

during ongoing prenatal checks, the mother's or

525 1 fetus's condition changes, referral of the pregnant

2 woman to the appropriate complicated OB clinic or

3 perinatology group will be made.

4 Perinatology groups consist of a

5 perinatologist, geneticist, morphologist,

6 nutritionist, and various social support personnel.

7 All known dysmorphic fetuses are referred to the

8 perinatology groups.

9 After delivery, if the neonate is

10 found to have dysmorphic features or congenital

11 anomalies and require immediate medical

12 intervention, that neonate will be referred to a

13 neonatal intensive care unit. If the neonate is

14 medically stable, the infant will be referred to a

15 geneticist, dysmorphologist, for outpatient

16 evaluation.

17 Infants and children outside of the

18 neonatal period who have congenital anomalies are

19 referred to a dysmorphologist and/of developmental

20 pediatrician for ongoing subspecialty care. General

21 pediatric care is provided by the patient's primary

22 care provider.

526 1 Gulf War veterans. Gulf War veterans

2 represent a special subpopulation of potential

3 occupational health risk. The Department of Defense

has developed a specific program, the Comprehensive Clinical Evaluation Program, to evaluate and treat medical problems that may have arisen from exposure in the Gulf War. This program is well delineated, starting with initial screening at the local medical treatment facility, and referral to a regional medical center when appropriate. Entry into this program is voluntary and may be determined -- excuse me -- may be terminated by the veteran at any time. If a pregnant woman who is a Gulf War veteran, or whose partner is a Gulf War veteran, expresses concern that their health or the health of their fetus may be adversely affected because of the Gulf War, the appropriate person or persons will be referred to the local medical treatment facility administrative head for the CCEP program for enrollment. If a patient has a concern that their child is suffering from a condition that was caused by the parents' exposure in the Gulf War, this family will also be enrolled.

Evaluation, or Phase 1, will consist of answering a standardized questionnaire assessing health risk, occupational exposure, and reproductive history. An in-depth medical system-directed evaluation and complete physical exam will be done by an internist or family practitioner. Basic

screening laboratory tests are drawn. If no unexplainable findings are found, then Phase 1 evaluation is complete.

However, if the physician feels that subspecialty evaluation is indicated, then the patient is referred to the regional medical center for entry into Phase 2. In the case of a pediatric patient, evaluation of that patient would be done by a pediatrician or a family practice physician.

I hope that this brief review has clarified the U.S. Navy's policies on children with congenital anomalies. Thank you for this opportunity to meet with your committee.

MS. LASHOF: Thank you very much.

The last speaker is Colonel Jarrett.

GENETIC SERVICES, REFERRAL, AND OUTREACH:

DEPARTMENT OF DEFENSE

COMMENTS BY ROBERT JARRETT

MR. JARRETT: My comments in large part will reiterate much of what has already been said, and I think that is due to the nature of the -- the integrated nature of military medicine. It has become much more of a tri-service effort. Our community hospitals and regional referral centers are often intermixed. For example, Captain 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

16 military and the civilian sector. And these
17 physicians are either board-eligible or
18 board-certified in their area of expertise, and are
19 subject to the same certification requirements as
20 their civilian counterparts.
21 When appropriate subspecialty
22 referral care is not available in the military
530
1 medical center, patients are referred to appropriate
2 civilian tertiary care facilities, often university
3 medical centers.
4 Women with uncomplicated pregnancies
5 are followed by family practitioners and
6 obstetricians. The care they receive follows ACOG
7 guidelines for health assessment screening,
8 diagnosis, and treatment. When obstetrical history,
9 laboratory, physical finding, or imaging criteria --
10 for example, ultrasound -- identify a high-risk
11 pregnancy, patients are referred to subspecialists
12 in perinatology. Those consultations may also
13 include consultation with neonatologists,
14 geneticists, pediatric dysmorphologists, pediatric
15 surgeons, or other subspecialists, depending on the
16 problems identified in that pregnancy.
17 For example, if a prenatal ultrasound
18 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

532 1 medically indicated for these infants. When
2 in-house resources are not available, patients are
3 referred to civilian experts, usually at university
4 medical centers. Infants with no clearly
5 identifiable syndrome are presented as case reports
6 and discussions at national meetings.
7 Many children with congenital
8 anomalies continue to have special health care needs
9 beyond the neonatal period. When these children's
10 needs are identified, the Army's Exceptional Family
11 Member Program coordinates the assignment of
12 soldiers to locations where their children's medical
13 needs can be addressed.
14 Thank you.
15 MS. LASHOF: Thank you very much.
16 Questions? Marguerite?
17 QUESTIONS
18 MS. KNOX: Yeah. I just have one.
19 Are you collecting any data on the number of
20 abnormalities, and maybe what they are, that you've
21 seen?
22 MR. JARRETT: The Army, as such, has
533 1 no unified approach to the collection of data on
2 children with birth defects. All of our newborns,
3 whether they're routine newborn or are in a newborn
4 intensive care unit, they all have charts, and the

charts have discharge diagnoses which go into a central database. But that's a database that's not -- that's a database that looks at all diagnoses across the board, and it's not subject to easy queries. So in answer to your question, at the present time we don't have a unified system for looking at birth defects.

MS. LASHOF: Tom?

MR. McDANIELS: For the panel: for active duty personnel who have reproductive concerns because of Gulf War service, what could the medical corps do? What type of information could be disseminated, general information about birth defects, to counteract, I guess, the negative spin, or maybe some of the misinformation that's out there about the incidence of birth defects to offspring of Gulf War veterans?

MR. JOHNSON: I think the answer to

534 that is that you give them the best available information, which is usually research-driven information, as we do with any risk assessment, be it immunizations, or otherwise. And you try to educate them accordingly.

MR. McDANIELS: And that would be, like, specifically through message traffic, through 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. McDANIELS: 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. CASSELLS: 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 --

that's the ones that I have here today.

MR. CASSELLS: 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

537

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. CASSELLS: 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. CASSELLS: 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

2 active duty, and has a child who's getting care
3 through the military hospital, when they separate
4 from the military? What happens -- you described a
5 transition period. You described a system where
6 possibly there's an extension of benefits for a
7 period of time. Can you describe what the options
8 are for that family before they're forced into a
9 civilian health insurance plan?
10 MS. TABLER: Well, during the period
11 of transition, which I said can be up to 120 days, I
12 think, depending on the amount of active service, or
13 longer if the family elects to pay premiums in what
14 is called the Continued Health Care Benefit Program.
15 Any medically-necessary health care related to birth
16 defects or congenital abnormalities, any of those
17 things, are still available as part of their basic
18 benefit. And included in that would be the services
19 under our Program for Case Management. And the
20 purpose of that program is really to find the best
21 array of family-centered services for that person.
22 And it is my belief that as a --
540 1 anyway, that as a family approaches the transition,
2 the point at which they will no longer be among --
3 be eligible for care in our system, that our case
4 managers will be working with them. For example,
5 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. CASSELLS: It's based on the percent of disability --

MS. LASHOF: The percent of disability --

MR. CASSELLS: -- and the family --

MS. LASHOF: -- determines whether the family gets care?

MR. CASSELLS: The family continues to get care.

MS. LASHOF: Okay. It's complicated.

MR. JOHNSON: And there are also some other categories: designees of the Secretary of Navy, Air Force, Army that could get care, even though they're not now on active duty.

MS. TABLER: Dr. Lashof, if I may

543

make sure -- I didn't answer 'cause I wasn't sure, but if a person is medically retired from the service, then they remain eligible for CHAMPUS as a retiree. I believe that's correct.

MS. LASHOF: Okay. Thank you. I gather we're going to have a separate briefing on compensation --

MR. CASSELLS: We are.

MS. LASHOF: -- so maybe we won't push you any more.

MS. TABLER: Okay.

MR. CASSELLS: But I do want to follow up on that eligibility question. What about the instance of administrative separations, either for disciplinary action or other reasons? Are those transition --

MS. TABLER: I don't know the answer.

MR. CASSELLS: And those transition programs are available to the families?

MS. TABLER: I believe so. Yes.

MR. CASSELLS: In most instances, in those circumstances --

MS. TABLER: Yes, they are.

MR. CASSELLS: -- everything is lost.

MS. TABLER: Voluntary -- I believe the transitional benefits are available to voluntary and involuntarily separated persons. I'll confirm that and get it back to you.

MR. CASSELLS: Thank you.

MS. LASHOF: Okay. Any other questions? If not, thank you very much. That completes our formal testimony, and it's a question whether the Committee has any other issues that they want to bring up to discuss before we adjourn.

Do you have any, Holly?

MS. GWIN: No.

MS. LASHOF: No. I'll remind you that our next meeting is July 8th and 9th in Chicago, and the subject is --

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

545 1 all then. And if there are no other questions --

2 Robyn, any last-minute words of wisdom?

3 MS. NISHIMI: No.

4 MS. LASHOF: No? Okay. Thank you

5 all very much. Thank you, all of our participants.

6 And the meeting stands adjourned.

7 (Whereupon, at 12:15 p.m. the meeting

8 was adjourned.)