



COMMONWEALTH OF AUSTRALIA

Official Committee Hansard

JOINT STANDING COMMITTEE ON FOREIGN AFFAIRS,
DEFENCE AND TRADE DEFENCE SUBCOMMITTEE

Reference: Royal Australian Air Force F111 workers and their families

THURSDAY, 16 APRIL 2009

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**JOINT STANDING COMMITTEE
ON FOREIGN AFFAIRS, DEFENCE AND TRADE**

Thursday, 16 April 2009

Members: Senator Forshaw (*Chair*), Mr Hawker (*Deputy Chair*), Senators Mark Bishop, Ferguson, Fifield, Furner, Hanson-Young, Johnston, Ludlam, Moore, O'Brien, Payne and Trood and Mr Baldwin, Mr Bevis, Ms Julie Bishop, Mr Danby, Ms Annette Ellis, Mr Gibbons, Ms Grierson, Mr Hale, Mr Ian Macfarlane, Mrs Markus, Mr Murphy, Mr Oakeshott, Ms Parke, Ms Rea, Mr Ripoll, Mr Robert, Mr Ruddock, Ms Saffin, Mr Bruce Scott, Mr Kelvin Thomson and Ms Vamvakinou

Defence Subcommittee members: Mr Bevis (*Chair*), Mr Baldwin (*Deputy Chair*), Senators Mark Bishop, Ferguson, Fifield, Forshaw (*ex officio*), Furner, Johnston, Ludlam, O'Brien, Payne, and Trood and Mr Danby, Mr Gibbons, Ms Grierson, Mr Hale, Mr Hawker (*ex officio*), Mr Ian Macfarlane, Mrs Markus, Mr Oakeshott, Mr Robert, Ms Saffin, Mr Bruce Scott and Mr Kelvin Thomson

Members in attendance: Senator O'Brien, Mr Baldwin, Mr Bevis, Mr Hale, Mr Robert, Mr Bruce Scott and Mr Kelvin Thomson

Terms of reference for the inquiry:

The committee will investigate and review claims for compensation from former F-111 deseal/reseal workers including the Commonwealth's response to the health and support needs of former F-111 deseal/reseal workers and their families. The Committee should ascertain whether the response was adequate, whether it was consistent with the findings of the Study of Health Outcomes in Aircraft Maintenance Personnel (SHOAMP) and whether the overall administration and handling of the program was adequate.

The Inquiry will consider the adequacy and equity of the Health Care Scheme in meeting the health and support needs of participants and their families and whether this was consistent with the SHOAMP findings. Matters to be considered will include, but not be limited to:

- The differences, and transitional arrangements, between the interim health scheme and the final Health Care Scheme;
- The timing of cessation of access to the Health Care Scheme;
- The range of treatment and health benefits provided under the Health Care Scheme;
- Whether the current Health Care Scheme is consistent with the range of treatment and health benefits available to persons under other Health Care Schemes;
- The adequacy of arrangements under the Health Care Scheme affected family members (including widows) or serving members; and
- If the Health Care Scheme is not considered to be an adequate response to the health and support needs of participants and their families, consider and report on possible alternatives that are considered to be adequate in light of the findings of SHOAMP and other Health Care Schemes.

The Inquiry will consider the adequacy and equity of the financial element of the Ex Gratia Scheme and whether it was consistent with (i) the findings of SHOAMP, (ii) the Health Care Scheme response (iii) the Tier definitions, and (iv) one off payments to other veteran groups. The Inquiry will consider, but not be limited to:

- Whether the lump sums available under the ex gratia scheme were appropriate;
- Whether the lump sums available were appropriate given the findings of the SHOAMP;
- Whether the lump sums, when considered along with the benefits available under the Health Care Scheme, were appropriate;
- Whether the lump sums available under the ex gratia scheme were appropriate, when considered along with the full range of benefits and compensation available under other Commonwealth or State statutory schemes;
- Whether the lump sums were consistent with the definitions of Tiers of participants;
- Whether the lump sums were consistent with other one-off payments made to veteran groups;
- When assessing the question of adequate remedies whether regard should be given to the establishment of a dedicated administrative assessment and settlement scheme, and
- If the lump sums available under the ex-gratia scheme are not considered to be financially adequate, discuss what compensatory payment would be appropriate in light of the SHOAMP findings, other one-off payments made to

veteran groups, and the full range of benefits and compensation available under other Commonwealth and State statutory schemes or common law damages available under Australian law.

The Inquiry will consider whether the overall handling and administration of ex gratia and compensation claims was appropriate, timely and transparent for both participants and their families. The Inquiry will consider whether, but not be limited to:

- Cross agency cooperation was effective;
- The documentation and records held by both Agencies as they relate to deseal/reseal activities was adequate;
- The standard of evidence required to substantiate a claim was reasonable and, if not, whether alternative standards of proof may be used when making an eligibility determination;
- There has been equitable treatment of service personnel, public servants, civilian employees and contractors involved in deseal/reseal activities;
- Staffing resources were adequate to produce a timely result;
- There were unreasonable delays in the process, taking into account the complex nature of issues; and
- The overall handling and administration of ex gratia and compensation claims was appropriate and timely.

WITNESSES

BOWLING, Professor Francis, Director, Biochemical Diseases Unit, Mater Children's Hospital1

Subcommittee met at 12.19 pm**BOWLING, Professor Francis, Director, Biochemical Diseases Unit, Mater Children's Hospital**

CHAIR (Mr Bevis)—There are a number of items that have been presented to the committee as exhibits since last year when we last met in a formal hearing. Perhaps tomorrow when this hearing commences more fully I will record for the benefit of the record those various documents, some of which are newly created and others of which were sought and received by the subcommittee after its last hearing.

Professor Bowling, we appreciate you making time available. We were happy to rearrange our affairs today to ensure that you were able to be with us. Do you have any comments to make on the capacity in which you appear?

Prof. Bowling—I am a specialist in metabolic diseases at the Mater Children's Hospital and I am also Professor of Medical Biochemistry at the University of Queensland. I appear as an expert witness into the basis of some of the conditions that have been observed in the airmen.

CHAIR—Although the subcommittee will not require you to give your evidence on oath, I do advise you that these hearings are legal proceedings of the parliament and therefore have the same standing as proceedings of the respective houses. Do you wish to make an opening statement for the benefit of the committee?

Prof. Bowling—Yes. The evidence I would like to present is quite technical. If the committee likes I can make a very short visual presentation to try and explain some of it.

CHAIR—Sounds good.

A PowerPoint presentation was then given—

Prof. Bowling—The first part is simply an introduction to the science. I will try to explain only two or three ideas. You will understand their importance as we come to the matter itself. I have also prepared for the committee a lay summary that you may like to use. I think that has been distributed. Then there is the formal technical report, which can be heavy going.

I am an expert in what we call inherited metabolic disorders. These are inherited defects in the body's chemistry. Because of that I have a particular understanding in certain very special parts of the cell. The part of the cell that I want to focus on today is a little organ known as a mitochondrion. Some of the studies which we have done, and which I will explain in more detail, suggest that there are changes in the mitochondria in individuals who have been exposed to the fuel and possibly the solvents.

I want to give you an idea of what a mitochondria is because you will hear it referred to repeatedly. My first diagram is just to make my point about the mitochondria. Within our cells there are many special compartments that do their own tasks. One task is done by what we call the mitochondria. The reason that they are getting this particular mention is that mitochondria are unique. In prehistoric terms we believe they were probably originally parasites. So they have

their own ability to survive in some ways independently of a cell. They are a strange thing to understand. The reason that this is important is that many years after the exposure the mitochondria are a place where you might find injury that occurred many years ago.

The mitochondria exist in their own right within cells. In fact, they are passed into every cell from the primary cells in the bone marrow in what we call the stem cells. Stem cells are present throughout your life. If you injure a stem cell it will remain injured for many, many years—possibly your whole life. The mitochondria come from those stem cells. All other blood cells are turned over regularly. If you damage them a few months later you will not see any evidence of the change. But mitochondria can show you things that have happened a long time ago. That is the key point about them.

This diagram is just to emphasise that point. This is a photograph of a stem cell passing on its mitochondria to another cell, which will eventually be released into the blood. That is just to explain that principle to you.

The reason I became involved in this problem is that there was an airman who died following working in the program and presumably following exposure to either the fuel or solvents. More careful investigation was done following an autopsy study. This investigation, I understand, was principally the work of Warrant Officer Hind, who is also trained as a medical technologist. He had the insight to realise that a lot of the symptoms suffered by this airman could be compatible with mitochondrial disease. When the tissues from this airman were studied it was found that he actually did have an inherited disorder in his mitochondria. It was not affecting him greatly because he was able to work as an airman. He basically had a productive life even though he did have an inherited disorder. Because he died following exposure it led to the hypothesis that the exposure itself may be causing injury to mitochondria. With that understanding I was then asked to consider this possibility and advise on how it may be further investigated.

One of the first things I did was to look at a group of airmen who had been specifically referred to me because they had symptoms. The symptoms are briefly summarised here. The symptoms that I have listed on the left are those that these men were experiencing. The symptoms on the right are characteristic of mitochondrial disorders. Symptoms alone do not prove that they had mitochondrial damage. But it again suggests the possibility of mitochondrial involvement in the airmen who had been exposed. At this stage we had two independent factors suggesting that mitochondria might be involved in this story. I might also add that these symptoms are not in themselves diagnostic and are also not specific. There are many other causes of these symptoms, but they do belong to the mitochondrial family.

The other reason that we chose to look at mitochondria is that many of the components of both the fuel and, to a lesser extent, the solvents are also known from laboratory studies to cause injury to mitochondria. It is mostly the elements of the fuel which have been shown in laboratory studies to damage mitochondria. There was another piece of evidence suggesting that mitochondria may be involved.

The studies that we undertook were very small pilot studies. They were investigation studies to test this idea that mitochondria were involved. Three studies were undertaken. In each of them we chose to look at the elements from mitochondria that we call proteins. Each mitochondrion has about 600 proteins. We looked at mitochondrial proteins from airmen who had been exposed

and from a matched group of controlled airmen or other individuals who had not been exposed. In each of the three experiments we saw small changes in the exposed airmen's samples. They were independent experiments and each experiment measured something slightly different. But each experiment showed the proteins in the samples from the exposed airmen were different from those in the airmen in the control group who had not been exposed.

I must emphasise that in each study the changes were small and by themselves would not be regarded as sufficiently significant to warrant a full scientific publication. So the changes themselves were small but definitely there. The reason that I believe they may be significant is that in three separate experiments they occurred each time. A single study by itself would be regarded as scientifically weak and should not be over-interpreted. But when you have done it three times by three different methods and you are still seeing the same sorts of change the evidence then becomes stronger that this may be of significance.

The technique that we used to look at the proteins was state of the art at the time and also relatively inexpensive in a laboratory sense. The reason for putting this slide up is to say that that science has moved on and there are now far more sophisticated techniques available for looking at these proteins. My own laboratory currently uses the more modern method for looking at those proteins. But we did not use that method in this study; we used the older method. The reason for mentioning that is that I believe that if we used the more powerful analytical tools that we have today we could possibly see other changes that we have not seen with the older method.

The next slide is very complicated. It is there to remind me of another key point in what we have found. We have found mitochondrial proteins that are increased in the exposed airmen's samples. We have not yet identified these proteins. This is an important next step, because if the proteins are identified and we know their functions we can then probably assign a logical relationship. If they were there for the purposes of repairing cell injury we would say they are coming from an injured cell. We need to identify the proteins and see that they are all linked together. Statistically it is still possible that in 600 proteins in a mitochondrion you might randomly get five that are increased. But because we got the same five in each of the airmen we tested I think that random chance becomes much, much less likely. I believe that there is a change that we are seeing.

This slide is to make the point that we need to further understand these proteins. There is another value in understanding them. I would make no guarantee at all of any treatment. But at least if we understand it there is always a possibility of treatment. If you do not know what you are dealing with it is very hard to do anything about it.

The final comment that I would like to make has to do with caution in over-interpreting the finding. The finding has been small each time, but it has been consistent. This diagram, which is complex, but I will try to simplify it a little. If you look along bottom, that is the quantity of material that you might be measuring. The height at the side is the number of individuals who have that quantity of material. If you look at the red test and the green test right in the middle, they actually lay on top of each other. So if the green group were the healthy group and the red group were the damaged group, the test would not have much of an ability to see a difference. However, if the damaged group were the red group and the healthy group were the purple group over to the side, they are quite separate and you can then see a difference.

The reason for putting this side up is that if we were to use this type of testing to look at individuals who had been exposed, we would not find a perfect test. It is an almost impossible request to find a test that will discover damage done 20 to 30 years ago. Whatever test is used, it will have some weaknesses. The weaknesses may cause you to miss a proportion of individuals who are affected. They could also cause you to diagnose a group who are equally healthy. If you use a test like this today, the test will have an inherent weakness. I think the test itself will be useful, but it will have those weaknesses and those weaknesses would have to be understood by the committee, because there will not be a perfect test. I have an executive summary and I may not go into that immediately unless you would like me to. Perhaps it would be more appropriate now to allow you to ask me questions about the report or to explain it in more detail.

CHAIR—Thank you for that overview in a manner that we could come to grips with. Having read some of the materials and a number of studies, a commentary about this and reports on studies, I understood that there was some evidence about these chemicals having particularly deleterious effect on mitochondrial DNA in laboratory tests with human cells but getting a difference result when tested with mammals, with mice.

Prof. Bowling—Yes.

CHAIR—Can you explain that?

Prof. Bowling—The nature of the fuel materials in particular is known to be very disruptive to DNA. There is a strong body of evidence to show that it is. The DNA within the mitochondria is an unusual material because it is inherited in its own right from its own parent mitochondria. It is not part of our regular DNA. It behaves differently. The rules for nuclear DNA may be different for mitochondrial DNA. The question of whether mitochondrial DNA can be damaged by these solvents, it may very well be.

I am not aware of any experiments. I simply have not looked to see whether it would or would not be. The reason that I have not looked is that the very first study that we did was on the assumption that if the mitochondria or their DNA were damaged then there would be fewer of them to find in the cells. The first experiment we did was to count the amount of mitochondrial DNA in cells from exposed versus controls. We found a very small difference. It was such a small difference that we did not believe it was significant or could be trusted for any form of testing. Our very first study did not show any difference in the amount of mitochondrial DNA between composed and control individuals. I cannot offer any explanation for that.

The further studies then looked at the proteins that make up mitochondria and these proteins mostly come from the stem cells. My suspicion is that if there is a persistent injury over many, many years it is probably to the stem cells. Of course, they are in many tissues, including the bone marrow.

CHAIR—If these chemicals—the fuel, the solvents or whatever—are causing damage to the mitochondrial DNA within a living human, how would that manifest itself? What symptoms would illnesses produce?

Prof. Bowling—In the diseases where we know we definitely have damaged mitochondrial DNA, the symptoms are those that I have on the earlier slide that I presented. As you can see,

they are a very broad group of symptoms, but the more typical mitochondrial response, when its DNA is damaged, is for the mitochondria to decrease in number. They are not able to sustain themselves if they have had significant injury. They usually simply disappear. We could not find any difference in their number.

CHAIR—I had a look at that as you mentioned it and was trying to identify whether or not the symptoms listed on the slide relate to the sorts of symptoms that are identified on the diagram of the human body. Frankly, I am none the wiser having looked at it. For example, I see something like night blindness, so I look at the reference to the eye. It does not say ‘night blindness’. It said optic atrophy, retinal atrophy and so on. That may or may not be night blindness.

Prof. Bowling—I have to apologise for the slides. But the diagram is out of a standard textbook, so it is essentially a reference material. The other is a list of symptoms as I describe them. Unfortunately in medicine there are as many words for things as there are different conditions. I could go through each example if you want, but the particular one is that if you have retinal damage or retinal degeneration then one of the first things you will lose will be your night vision.

CHAIR—So with the symptoms identified in exposed personnel there is some high correlation or low correlation.

Prof. Bowling—Yes.

CHAIR—There is a high correlation between those symptoms they identify and the health issues associated with mitochondrial DNA degradation?

Prof. Bowling—Yes. The symptoms I have listed are all to be found in mitochondrial disorders. There is a high correlation. The caveat, of course, is that this was a group of less than 20 airmen who were referred to my clinic because they had symptoms like that. I cannot make a general statement about the whole group. Those symptoms only apply to the small number of airmen that I saw.

Mr ROBERT—One of the challenges we have had dealing with medical information is the complexity and I am not a doctor. So I rely on the medical prognosis. I see our good defence doctor there who has made the case a number of times that the results are statistically not significant. He has gone on to explain that that is due to the small sample sizes. Am I right to summarise what you have said that in mitochondrial disease it is common, almost always—you choose the word—that there is less mitochondrial material in cells, but in the case of the less than 20 airmen you saw this is not the case?

Prof. Bowling—No, the first part of your statement is not true. If the mitochondrial DNA has a small amount of damage to the DNA itself and if that is at a critical point, it may kill the mitochondria. The mitochondrial DNA will normally remain and the mitochondria will remain, they simply will not work. If there is a large amount of damage done to the mitochondrial DNA then a process that we call housekeeping occurs and the broken mitochondria are recognised, cleaned up and thrown away. Then you find less of them. So in mitochondrial diseases that are

inherited, in some cases, we see a loss of the DNA and a loss of the mitochondria. In other cases we do not see a loss—they are there, but they do not work.

The most common test that is used for mitochondrial injury is a test of how well they work. It has a technical name: oxidative phosphorylation. We measure the power of mitochondria to burn fuel. That would be most common test that is used. The difficulty with using that test in this scenario is that it involves both skeletal muscle and live biopsies, which are quite invasive, difficult, expensive and risky. So for a pilot series of studies I could not ethically justify doing liver and muscle biopsies on a large number of airmen. If I had a patient with possible mitochondrial disease referred to me, that would be the standard investigation.

Mr ROBERT—To summarise—forgive me if I get it wrong again—in the less than 20 airmen you studied there was no mitochondrial DNA that had disappeared or been cleaned up, but there was significant evidence that they no longer worked?

Prof. Bowling—There was no difference in the DNA. We did not test that they worked, because to test that they work you have to do those biopsies I mentioned. So we looked at the building blocks that mitochondria are made out of—what we call the proteins. Those building blocks are where we found the differences. We did not look at what the building blocks were doing; we just looked at the building blocks themselves.

Mr ROBERT—And, having looked at the building blocks, you consistently found changes in mitochondrial proteins—

Prof. Bowling—Yes.

Mr ROBERT—which were not present in the blood samples from non-exposed controls.

Prof. Bowling—Yes.

Mr ROBERT—From that, what can you hypothesise?

Prof. Bowling—I believe that the mitochondria in the exposed individuals are reacting to changes or damage in the stem cells. Mitochondria not only do their own work; they are the decision makers for whether an injured cell will live or die. The mitochondria constantly monitor the health of a cell. If they determine that the cell is too unwell, they will deliberately kill it. They have the ability to do that.

Mr ROBERT—If you believe that the mitochondria are reacting to change in the stem cells in all 20 airmen, is that, given the small sample, statistically significant or insignificant?

Prof. Bowling—The reason I laugh at the question is that it gets back to the graph I drew again. It is true that there was a small statistical difference. The problem I have with statistics is that there is clinically significant and there is statistically significant and they are different things.

Mr ROBERT—You think you're having problems with it!

Prof. Bowling—Exactly. The best example I would give you is that, if you measured 100 people's blood pressure and it was 120 and then you measured another 100 people and it was 121, you would say that the blood pressure was statistically different. But in real life 100 and 121 are not different.

Mr ROBERT—What are the odds of 20 airmen over three successive tests all having mitochondria that are reacting to changes in stem cells?

Prof. Bowling—I think it would be less than one in 100.

Mr ROBERT—In my book that is statistically significant.

Prof. Bowling—Yes.

CHAIR—I know which group I would rather be in.

Prof. Bowling—It would be safer for have the normal protein pattern.

Mr ROBERT—Of the 20, did you differentiate between those who were involved in the four formal programs and those in 482, 3AD and 1 Squadron?

Prof. Bowling—No. I can luckily plead ignorance here, for two reasons. First of all, I do not have insight into the programs. I actually do not need to know the programs. More importantly, to ensure that the results we were getting were valid, all of the samples that we tested were not identified. When we tested a sample we did not know from which group it came. I did not know whether it was from an exposed individual from whatever program or a non-exposed individual. We tested them in a blinded manner.

Mr ROBERT—With the odds of less than one in 100 that they would all have some degree of mitochondria reacting to changes in the stem cells, what sort of symptoms would you expect those 20 airmen to be exhibiting?

Prof. Bowling—I cannot answer that because I do not know what those five proteins do. If we identified them and I assigned a job to them then I would be able to give you an idea. But, until I know what they do, I cannot guess. There are well over 600 known mitochondrial proteins. They all do different things. Because they all do different things they all have different effects. Until I know what these five do, I cannot guess. Also, it may not be in the normal mitochondrial function; it might be in the mitochondrial reaction to an injury that has occurred. It may be a protective mechanism that the mitochondrion is using to protect itself from other cell injury. Until I can identify them, I cannot extrapolate as to what it means.

Mr ROBERT—Has anyone done any research into what these five proteins do?

Prof. Bowling—Possibly. The reason I cannot tell you what they do is that I do not know their names yet. As I said, the type of technique we used initially was the older style of investigation, and we definitely showed a difference in the patterns. But to take an individual protein from that technique and then identify it and work out what it does is itself a very significant activity. We simply have not got that far. This is the basis of the final slide that I put up. If we were to

continue this type of testing, I would use the newer technology because then I could answer that question.

Mr ROBERT—If, hypothetically, you were to continue this testing and widen your sample size—let's pick 100; I have only picked a number, with no education behind it—what sort of time would you be looking at to complete a study that was statistically significant and able to be documented and written up?

Prof. Bowling—Going back to the patients that I currently test for diseases of the mitochondria, my laboratory with its current staff and workload can do two to three patients per week. This is quite sophisticated testing and it requires a very high level of expertise. Like most questions, the more investment you put into it the quicker you can get the answer. I would be very surprised if we could get an answer within six months with the current state-of-the-art technology. I believe it would be more difficult to fly one of these analysers than to fly one of your new fighter jets. It takes a lot of finetuning and adjusting to get it going. At our current rate of testing, it would be two to three per week. The newer technologies can do it faster than that, and I would guess it would take around six months.

Mr ROBERT—Considering the 20 airmen over the three studies all had an issue with those five proteins, which we do not know the names of, is there any way you could provide the medicine, solution or cure—whatever term fits there?

Prof. Bowling—Generally for mitochondrial disease we have very poor treatments. The only reason for considering that there could be some hope is that, if it is a reactive change we are seeing, it may be in the stem cells themselves rather than in the mitochondria. Until we know what it is, I cannot suggest what the treatment might be. We are generally very limited in our ability to treat true mitochondrial diseases. If the stem cells were injured, there are various cell promoting factors and aids that could be used. But this is all very hypothetical. We would have to identify where the changes were coming from before we could seriously consider that question.

Mr ROBERT—How long have you been working in the area of mitochondrial disease?

Prof. Bowling—On this particular project or in general?

Mr ROBERT—Generally.

Prof. Bowling—Nearly 30 years.

Mr ROBERT—Then let us call you an expert without too much banter. Have you ever seen these types of symptoms before in people who have been exposed to chemicals?

Prof. Bowling—No, but I do not generally see people who are exposed to chemicals; it is not my area. Most of my patients are children and their families, including adults, who would be the ones to have mitochondrial diseases. My only experience with people who have been exposed to a toxin is with the airmen who were referred to me. The only caveat in that would be that I am occasionally referred an individual who has suffered mitochondrial damage because of specific drugs that have been used. In such a case I would see similar symptoms. Usually we find with

drug damage that the individuals have an underlying susceptibility and, when they were exposed to a level of the drug, they succumbed. Probably the most common example would be a loss of hearing in newborns who were given a particular type of antibiotic.

Mr ROBERT—In the reseal-deseal case, the majority, meaning over 51 per cent, of people who received ex gratia payment—in fact, I believe the good corporal behind you, Corporal Janik, is one of them—have had no ill-effects, even though some of them bathed in the stuff, whereas less than 50 per cent have had significant problems, which would indicate to my lay, non-scientific brain that the chemicals, the environment or the lack of oxygen, or all of those environmental impacts, affected some and did not affect others.

Prof. Bowling—Yes.

Mr ROBERT—I think the other medical experts we have heard have also used words to that effect. Are you suggesting that you are seeing the same thing you saw with those people you looked that had an issue with their mitochondrial DNA through drug use—that some people have been found to be susceptible and others can take truckloads of stuff and it does not affect them?

Prof. Bowling—Yes. We now know that with all the genetic diseases that we deal with there is enormous variability. The variability occurs because some people have other genetic weaknesses that make them more vulnerable. In addition to that, there are individuals who have a separate group of genetic diseases which make them less likely to repair themselves. I know that I can have two patients, or even two mice in a cage, with exactly the same mutation and very, very different diseases. The reason is that in one their protection mechanisms are stronger or their repair mechanisms are stronger. In human disease, that is now a common understanding. An explanation I could give to you for the different reactions seen between airmen is that some of them may be genetically stronger or genetically more able to repair themselves.

Mr HALE—Thank you for your presentation, Professor Bowling. Have there been any studies done on the effect on the children of the airmen who were tested, and has anything shown up in those studies?

Prof. Bowling—No. The studies in which I have been involved have been only in adult airmen, and I have not reviewed the literature from the point of view of children. The reason for that is that the mitochondria are not inherited from their fathers; the mitochondria are inherited from their mothers. In mitochondrial disease, it is especially difficult for fathers to pass on the disease to a child. There are some exceptions to that, but generally that is not the way the biology works.

Mr HALE—Generally it will finish with the actual person that is affected and not be passed on?

Prof. Bowling—Yes, unless it was a female.

Mr HALE—Do you have any other plans for further study into the airmen?

Prof. Bowling—I think the most important contribution that could be made at the moment would be to understand these protein differences to see if they can identify the airmen who are at

risk of illness. When we deal with mitochondrial diseases, because we do not have a gold standard and there is no test that is perfect and that separates those two mountains that I showed you before, we use a series of criteria. I think the criteria for mitochondrial disease could be translated to the problem that you have. I think the history of exposure should be determined: you should know that they have been exposed. The individuals that I would be concerned about would be those who showed symptoms that could be compatible with mitochondrial or stem cell disruption. They may not be diagnosed diseases; I am talking about symptoms such as night blindness. The third thing I would look for, because this is what we do with the mitochondrial disease, is abnormal test results. There are various rules you can make about appropriate history, appropriate symptoms and an abnormal test result. That would be my suggestion. That would identify the individuals who were likely to be or become unwell.

Mr HALE—Is there anything in the day-to-day environment that can affect the mitochondria, like airconditioning, cleaning, filling up the car or smoking?

Prof. Bowling—Cigarette smoking certainly does. In fact, there would be a number of materials. In the studies we did, we tested the samples blindly, but we did match the controls to the airmen as best we could. We matched them for smoking and drinking, medical history and as many parameters as we could think of. There is very little evidence that environmental agents definitely damage our mitochondria, though I might add that one of the most popular theories of ageing is called the mitochondrial theory of ageing—that we all age and die because our mitochondria burn out and we then do not have the ability to generate the energy we need to live. It may possibly be that life itself is the most damaging thing to our mitochondria.

Mr HALE—Too many birthdays!

Senator O'BRIEN—I do not think we needed to know that, Professor!

Prof. Bowling—Unfortunately, you cannot do anything about it.

Senator O'BRIEN—I am interested in the page in your presentation, a copy of which we have before us, headed 'Substances toxic to mitochondria'. We do not have it in colour, but I have made some pencil lines to identify the fuel and desal-reseal solvents into two groups. Do we take it from that slide that each of those substances is scientifically known to be toxic to mitochondria?

Prof. Bowling—Yes. That information is not my data. That is published data from other laboratories throughout the world that have specifically tested each of these materials for their damage to mitochondria. That is why I say that these are ones that are known to be injurious to mitochondria. It does not mean that the others are safe; it is just that there are no published reports that I could find. For the four or five I have listed there, there are published papers from reputable laboratories saying that they damage mitochondria.

Senator O'BRIEN—That is, the fuel identified?

Prof. Bowling—Yes. The fuel, by itself, is injurious.

Senator O'BRIEN—Whereas the other items, which seem to be identified as the deseal-reseal solvents, are not so?

Prof. Bowling—They are not reported to be so. I have not done these studies. All I have been able to do is go to the databases of medically published studies. Those other materials are not published.

Senator O'BRIEN—So you are not saying that they are not; you are saying that you cannot rely on any data which proves that they are toxic to mitochondria.

Prof. Bowling—Yes. I have no data that they are either harmful or harmless.

CHAIR—On that, we have a copy of your briefing notes for the committee. Under 'Conclusions' at point 3, you note that one individual who demonstrated a similar pattern had not been exposed to F111 deseal-reseal but had only been exposed to aviation turbine fuel. Then in brackets you have 'significant accidental ingestion'. That means they have actually swallowed it?

Prof. Bowling—Yes. In fact, I do not have the specific details of the incident. I might have to ask my Air Force colleagues to give the details, but I understand that there was a high-pressure fuel line and this stuff was literally guzzled—it went down his throat.

CHAIR—Okay. But you then say that this indicates that the damaging agent is a constituent of the fuel and not the solvents.

Prof. Bowling—This individual had exactly the same protein changes as the airmen from the deseal-reseal and, as far as I know from the history, was exposed only to the fuel. But this is a single case only.

CHAIR—I guess what it certainly confirms is that drinking copious amounts of avgas is not good for you. You probably do not need to put on a safety warning to tell people that. I am just intrigued. It is another step beyond that to conclude that—in fact, contrary to what you were just saying to Senator O'Brien, it seems to me—the other agents and solvents may not have been involved. Is it not equally possible that both could produce the effects on mitochondrial DNA?

Prof. Bowling—Yes. Also with regard to that particular airman, I do not have the detailed knowledge of his history. He may not have worked in the program; that does not mean that he was not exposed to something else somewhere else. All I can say is that he was not in deseal-reseal. He had fuel exposure and had the same pattern.

CHAIR—Yes. A moment ago you gave some helpful advice to the committee in answer to a question. I am just trying to paraphrase you accurately. I think you said something like you had about three things you needed to do.

Prof. Bowling—Yes.

CHAIR—You said to look at the symptoms because there may not be identifiable diseases.

Prof. Bowling—Yes.

CHAIR—I guess part of the dilemma we have encountered is that the system of compensation upon which everything is based, with very rare exceptions, relies upon identification of the disease.

Prof. Bowling—Yes.

CHAIR—From a medical perspective, can you draw for our benefit the distinction between that point you are making—here are the symptoms; here is the disease—and your advice that we need to look at the symptoms?

Prof. Bowling—The best example I can give is on the metabolic disorders that I deal with. There are two or three international classifications of diseases. In fact, there is one known as the international classification of disease, the ICD-9, or soon-to-be ICD-10. The general view, certainly in health economics, is that, to have a disease that counts, it has to appear in that list. The trouble with that list is that it takes so long to compile these lists that they are out of date when they are written. That is the first point.

There are only a few metabolic disorders in the entire ICD-9 list. I spend my whole life dealing with metabolic disorders, of which there are at least 3,000 known. They are all individually rare, but as a group they are common. Only a couple of those—I have not counted them but there would be less than 10—I consider would be on the ICD9 list. So there are many, many disorders that are simply not there because they have been recently, or relatively recently, discovered.

This is a dilemma. It is a dilemma for me because many of my patients will have a diagnosis that I believe is the diagnosis because I have measured the gene and demonstrated it is damaged and I know they have all the symptoms, but it does not occur in any list of diseases. Those patients have a great disadvantage when they apply for various disability benefits and whatnot because their disease does not exist on the list. One of the great frustrations in trying to help my patients is that their conditions are not there.

This morning I very quickly tried to look for mitochondrial disorders in the ICD-9 but I could not find them. I suspect that they are there, but I could not find them quickly. The symptoms experienced by many of the airmen would fit into the funny group of behaviours—the ‘I don’t know what they are’. That would be the issue.

CHAIR—But, from the work you have done in analysing the DNA, there is identifiable evidence of abnormality and health problems, even if there is not an international standard disease code to give it?

Prof. Bowling—Yes; that is true. I must correct you, though—not from the DNA but from the proteins.

CHAIR—Professor Bowling, you will be given a copy of the *Hansard* to make any necessary corrections, should there be errors. Thank you very much for making yourself available. You are probably aware from the background of this that the committee have been labouring long and

hard over this—a bit longer and a bit harder than many of us thought at the outset. It is important in hearings today and tomorrow to try to wrap up a number of the outstanding matters. Given the complexity of some of these issues, how you have managed to put your evidence in comprehensible terms for us is appreciated.

Subcommittee adjourned at 1.14 pm