of the University of Heidelberg we have five minutes per patient. In five minutes per patient you can't do a good job. Thus patients often go home with their unsolved problems. Considering this situation we think it's important to have centers as Dr. Beyer is establishing, as he manages to have time for the patient. But it's a financial problem, too. The time it takes you to care for one Thalidomide affected patient, in this time maybe you would examine and medicate 10 other patients. I think this is a very important point, too.

Hinoshita：OK. Is there anyone who has any good positive plans or schemes to support the thalidomiders in the near future? In United Kingdom, the government or the Thalidomide Trust has given much financial support. But in other counties, that's not enough or well organized maybe. How to solve this problem? In your opinion, no comment?

Kayamori：I don't have any idea, but we don't know about the financial problem in Japanese thalidomiders. That's a secret. That one is difficult to know. So in terms of money, we don't have any idea for Japanese thalidomiders. I have no idea that they are lacking of money or have enough money to have a treatment.

Hinoshita：Do you think it necessary to build up some specialized center for the thalidomiders?

Kayamori：No, I think most of the thalidomiders are against that opinion. Because they are comfortable in living in outside of Tokyo. The important thing is that they are in their own houses in which they are living for a long time. The rest of their life must be spent there. That's the best way. So even we build a new hospital where we have comprehensive treatment for thalidomide victims. I don't think it a good idea for Japanese thalidomiders.

Hinoshita：OK. How about in Australia? Thalidomiders are satisfied with pain control and with living in Australia now?

McCredie：No , they have exactly the same problems as we heard from the patients today. They complain of pain, complain of premature aging, and all comes with that. And I feel they would be very well with (???@04:34:46) came out few years ago. We review all the thalidomiders, and they were given substantial sum of money which has helped them. But that' time limited that lasts for another 10 years, then it cut out and they wonder what will happen on them. Meantime our government has decided to create disabilities scheme on which the thalidomiders would be able to draw. That's not gain these (???@04:35:18) into 29 team. And so that's something in the future. The cynical thalidomiders think government is putting off data of instituting that hope that some of them are (???@04:35:33). So it's not (???@04:35:37) in our country. We also have the problem about huge area you could fit the whole of Europe inside Australia and then have some space left over. And our population is around the edge of it basically with big (???@04:35:54) in the middle. UFA is terribly expensive. And the thalidomiders which there are roughly 60 are scattered through the towns and villages and so on. And so it's very difficult to create a clinic that they can deal with them. And the hospital, I don't think would be a feasible thing, and a close patient said one of the problem is that a lot of young doctors are not aware of the problem and (???@04:36:31). And so dropping out of the medical education.

Hinoshita：OK. When it comes to pain control, there was hot discussion before, namely whether surgery is good or not. But anyway, since we have such an international symposium let's exchange

information about the good way to operate or the good way to control pain. Please let us know Dr. Peters and Dr. Beyer because you are specialists about those. Please.

Peters: Yes, I think pain control, pain management should be multidisciplinary, that is important and multifunctional different methods, drugs may or must be only one part of. And physiotherapy, acupuncture, several other technics around the pain, and the operation is only the last step of long journey through a pain control.

Hinoshita: OK. Do you agree with Prof Peters?

Beyer: Yes. From my point of view, I totally agree with this, and I have two eyes on it. One eye as anesthetist, one eye as pain consultant. And my clinic I established when operation is needed, there should be a conference interdisciplinary different doctors. And orthopedic surgeons are very cautious with doing something which does not fit and normally working day. So they take care of it and plan it very well even rehabilitation afterword plan very well because if we have our patient out hospital and he exceed the time of day, it will lower the economic at the end of the year, and they will be remembered to this point weekly by the day managing director. So they take care of this, and I think it's not a decision of one. Specialists should make a decision in a couple of specialists.

Hinoshita: How about the cost-performance problem.

Beyer: What? I didn't get that.

Someone: Namely, was this cost too much for this result or performance?

Beyer: How many costs I produce by doing what I'm doing?

Hinoshita: Yeah.

Beyer: I have no clue. I tried to calculate this. There are so many people involved in this. It's really, really hard to estimate, and if you pay one trained consultant, you pay 180,000 euro. If you have a physiotherapist part time, you pay maybe 40,000 euro. So you can exceed easily limitations they usually have. And up to now, my managing director allows me to do so. But I don't know how long it will go.

Hinoshita: Yeah. A tough role. From a different point of view, Dr. Morrison, do you have any comment on this pain control and the premature problem?

Morrison: I think one of the things I'd like to develop on our website is a pain leaflet specially tailored for our individuals. The British Pain Society has a good one. Unfortunately it is sponsored by Grunenthal. As I have mentioned I think peer to peer support is very good and quotes from other beneficiaries as to how they have been helped could be included in any such leaflet. So I think if we try to get very good information on the website as well as showing them what interventional therapies can help e.g. hugging a pillow at night can help those with short arms, pacing activities during the day to help with fatigue.

Hinoshita: In Japan, we don't know exactly the information given by the Thalidomide Trust or the

English staff in UK. In other western counties, European counties, do you know the solutions or some good information given by the Thalidomide Trust? Do you see such information and understand it? Please, Dr. Ghassemi.

Ghassemi： I think the most information actually goes to the EX-Center in Stockholm. They don't deal only with thalidomiders but also with dysmelia. Unfortunately the information is not spread out over the country. Many times when I had my study group and they complained on something I wrote the letter to the general practitioner because they are also a matter of financial problem. So I wrote to doctors, hoping that they will send these people to the EX-Center. But I know that it didn't happen. So I gave my opinion to the EX-Center by myself actually and gathered more information about what they're doing and they also want the information to be strict. So I have a good idea when I go back home to Sweden what to do actually after this.

Hinoshita： Anyway, you have various opinions or ideas to control pain and support premature problems in the thalidomiders. But anyway I think it is important to ask to exchange good information or better innovation if someone or some center might find or spread in each country. So let's exchange good information between these countries. Then let's take good measures or ways to control pain or support the thalidomiders. So, just after you go home, let's introduce our website addresses or so mutually, OK? One more comment.

Ding-Greiner： Yes, speaking only about pain control is not enough, there are more problems. You need cardiologists, gynecologists, urologists and all kinds of physicians, but there are not enough Thalidomide affected people to run a big hospital exclusively for them. So I think Mr. Beyer's project of a virtual clinic is very good because there are all kinds of physicians accessible as needed. Also they are physicians who are interested in Thalidomide embryopathy and the long-term outcome. Patients know where to go, they can just give a call and get a reasonable treatment. I think it is very important to focus not only on pain but on the problems that are coming now as they are getting older. There are more deficiencies at present than 20 years ago and all the diseases and impairments of old age make an appearance, too.

Hinoshita： You mean more and more physicians in other fields.

Ding-Greiner： Yes.

Hinoshita： We must be more interested in these problems.

Ding-Greiner： Yes. You can't go to every physician as a thalidomider who has a specific problem. Physicians and therapists need some information about the causes of the prenatal damage, the development of the damage through lifetime. And there is almost no literature about Thalidomide. In our surveys the experts on Thalidomide were the participants. You need time seeing patients and learning about their strategies handling their discomfort and their impairments, they have a lifetime's experience in doing so. The best therapy is conceived together by thalidomiders and their physicians and therapists.

Hinoshita： Thank you. Finally.

Beyer： One short comment. The websites supported thalidomiders in Hamburg or elsewhere also in

English, and the barrier-free version. So you can choose.

Hinoshita： We have a great barrier, language barrier, sorry. In your country, everything is broadcast or spread in English?

Beyer： Usually not.

Hinoshita： Let's exchange messages in English just as we are doing now. Dr. Nakamura, please.

Nakamura： Thank you very much. Very interesting discussion I heard from you all. They are the very specialists on the thalidomiders. I'm very curious about the more mordern technique of the data on pain assessment, for example, functional MRI data. Do you have any those kind of the data on the thalidomider's pain issues? Anyone has any opinion?

Beyer： I have no data from technical investigations like functional MRI. I think up to now, it's not known what means functional MRI for the individual person, I don't know. But I'm collecting date on a questionnaire in Germany like every other countries I suppose. There is a pain society. And they have established questionnaire with many, many items. And I uses patients to, let's say, compare at the end of the day with normal chronic pain patients, and these questionnaire contains, I think everything is needed for the assessment of pain and also demographic data, general health data and social data, and for example, some kind like SF-36 of life quality and activity of daily life. So this data I collect. But I have a very small number up to now.

Nakamura： So, for example, in the orthopedic field and pain control societies to save lumbar and low back pain patients. There are many informations coming from fMRI observations. So I think it could be feasible for you or us to collect the data. On the chronic pain basis in thalidomiders, the investigation, we could get the image of it from fMRI. If we can have very good candidates and collaborators for the assessment.

Beyer： But I think before you put persons in MRI which is inconvenient, you need to have really good reason for this. I think good reason means it changes maybe your decision for the therapy. But I'm not sure about this.

Nakamura： I'm not so acute about the remedy exploitation. But just I want to know the condition of the thalidomiders pain, chronic pains. What is going on there? Is it possible to explore or to extend our understanding form the kind of the general population data or not? I'm just curious about it.

Hinoshita： Thank you very much. Maybe Dr. Nakamura is talking about subjective evaluation of pain control. It is one of the good measures to use the fMRI.

Then let's go ahead to the next question. What kind of orthopedic problems are important now? And how to solve? First, Dr. Peters. Do you have any keen programs you are now most interested in.

Peters： It's a variety of problems there. Muscle problems and joint problems due to osteoarthritis. It's a pain problem, problem of activity of daily living. I think they have to perform several procedures. Physiotherapy programs and pain control programs, even in a few cases, operations, and assisted living

problems for the people in the future. I think that will be a big topic.

Hinoshita： OK. Then first, let's focus on osteoarthritis which does not need any surgery or so.

Peters： We have some those...

Hinoshita： Those pathological changes are progressing now in thalidomiders.

Peters： Is it. Yes.

Peters： Especially the last five years. That's progressing a lot. With conservative treatments, however, it's becoming worse and worse because we have no original treatment to cure arthritis. And I think next years the number of thalidomiders who have to get surgical procedures will increase.

Hinoshita： Yes. Then the percentage of that way in thalidomiders is much greater than in the general population?

Peters： Yes.

Hinoshita： Do you have any comment, Dr. Ghassemi?

Ghassemi： Yes. Actually we have. Because the orthopedic problem is as it is for all of us. It may be not the problem at home, it's at work. I know that some of the thalidomiders just stopped working because this is a way to help them with the many more symptoms of arthritis. And of course as Dr. Peters are saying the operation is the last session or most for those joints. And before that I also could show all studies. Their sport and recreation was quite effective in these groups, which makes even difficult for them to convince them to go to physiotherapy, because it's just like post-polio syndrome or so. They just get more and more tired. And they don't have the trend as they should.

Hinoshita： Is there any other good method to disturb or slow the progression of osteoarthritis or similar changes in thalidomiders? Dr. Morrison, please.

Morrison： I think the controlling of their weight is very important. Individuals who have lost weight have improved their flexibility and improved the pain control. The Swedish study on lifestyle management very much showed this. We have had the team over to talk through their findings in this study and they have a book which they used to help with the study.

Hinoshita： Dr. Peters.

Peters： We perform one more very intensive rehabilitation program for these patients, two or three weeks as inpatients and they have therapy every day. We keep down the pain and disabilities for certain time.

Hinoshita： When I talked with Dr. Graf in Nurnberg, he said if thalidomiders are really painful, they should stop working. And he said they don't need to do hard exercises or training to soften the pain. Do you agree to that opinion?

Peters： I think going away from drugs is not always a solution. Because they will have the pain also besides work, therefore we try to make patients doing rehabilitation to put them out of the normal environment, put them the places where they can do the eerxcises and programs all day long for certain time, two, three, or even four weeks. That will largely give good benefit for them.

Hinoshita： OK, is there any other opinion about this problem, osteoarthritis?

Beyer： I think it's largely dependent on what you are doing on the work. And if you are forced to do things that you don't like or that are very static, for example computer work, or I had one patient to be employed in the street working, and this was definitely not good for the locomotor system. And I think one solution could be to retrieve these people from work and to retire them if they can afford it, and if the pension is high enough for this. And there is a clear evidence that there is a link between sports and recreation and a low number of pain. So you should motivate patients to do so. But not good as a street workout from my point of view. I think it's a good idea to keep them in mobility anyway.

Hinoshita： And then Dr. Ghassemi.

Ghassemi： That was almost as you were saying because in Sweden there is a possibility if your work is too static and you cannot manage that. There are always ways to adjust your work to your anatomical ability. And I think after that, mostly after that because people are trying not to retire as much as they can because of the mental healthiness, you know. You want to be in contact with social life. That is why and just not to feel pain even more if you are sitting at home all alone after these helps from this day and from your local job basically if he doesn't work. Then I think it's a good way to just offer them as, yeah.

Hinoshita： And Ms. Newbronner.

Newbronner： Yeah. We just support that you know it is working UK, I think we have found that for the people who feel that they have no choice but to give up work because of the health problems and loss of function, that can be very negatively associated with poor social life and socialization. I think when Dr. Beyer said that people are helped to either change their work or give up working more positive way, and perhaps replacing that with recreation or volunteer work which they can regulate more easily. Then you can have very positive benefits but it can be negative when people feel they have no choice and they forced to give up work and possibly don't have the resources to continue a good quality of life.

Hinoshita： To completely stop jobs is not always a good way. Thank you. Is there anyone who would like to comment? OK, Dr. Kayamori.

Kayamori： Just I'm facing troublesome cases with tendinitis which really causes intractable pain. So I want to know any idea. How about Dr. Peters? Do you have any good idea to treat tendinitis which is intractable and really painful? Is there any good treatment for that?

Peters： In most cases you can only do is to do preservative treatment with bandages. Our thesis, for example, is local physiotherapy and physical therapy. Combination. I think for anatomic changes you should do (???@5:01:20) to stabilize the overused joint, and sometimes if it's a working hand of the

patient, you get into other trouble. And you must try with physical therapy and physiotherapy and local pain control.

Kayamori： But the patient has had intractable pain over 30 years, she is working as a housewife. She is using the hand 24/7 or around the clock. So no rest. So do you have any experience to have surgery for that?

Hinoshita： OK, Dr. Ding-Greiner.

Ding-Greiner： I think the best support you will find first in assistance for relief. If physiotherapy doesn't help any more, then surgery is left as the last chance.

Beyer： So one last comment, I have seen quite a few patients and went surgery for this problem and at the end, they always had more pain. And it's just a matter of surgeon to say, "I can help you." "I will help you." But I have never seen it worked out

Hinoshita： We may have some candidates of thalidomiders who should or might be operated for the hip joint program. But some of the specialists including Dr. Kayamori or Dr. Greiner or so would say the operation would be the final solution. Then, refrain from operating him or her for the time being to wait. Do you agree to the idea or opinion on the hip joint program? Dr. Peters, please.

Peters： As for the hip joint operation should be always the last solution for every patient. You should use all conservative treatments before. And then it finished and there is no choice at all, then you can discuss it with patients and see the benefit and risks.

Hinoshita： OK, when it comes to this program, almost the same opinion as ours.

Peters： Yeah.

Hinoshita： Thank you. Is there any other comment or discussion about the orthopedic problems? Please, Dr. Schulte-Hillen.

Schulte-Hillen： I would like to ask a question concerning total hip replacement. Do the hip implants allow for the same range of motion as normal hip because thalidomiders deeply depend on a big range of motion?

Peters: That can be a problem in a single case if you find very much literalated mobility of the hip, but otherwise most of them are normal range and the normal collective motions of the patient. The mobility can a bit go down. For example if you have (???@05:04:51) of 60, 70 degrees internal external retention can have as the thalidomiders, you born to achieve that was a Fischer joint. Otherwise you have the risk of luxation.

Schulte-Hillen： So this has to be taken into consideration when we're talking with the patients before they decide to have hips replaced. Sorry. For example, somebody comes for this feet probably not going to be able to do so after total replacement

Peters：That's correct, yes.

Schulte-Hillen：Thank you very much.

Hinoshita：OK, there is little time left for the question 2. Then go ahead to question 3. How should we solve the specific pain problem, so called post-thalidomide syndrome in thalidomiders? But as for pain control, we have already discussed it so much. So is there anyone who would like to give some comment on the post-thalidomide syndrome? Please, Dr. McCredie.

McCredie：I think some of you would look at these slides, right? If you look at the first picture, that's a picture of us. You and me. It shows what happens to our peripheral nerves during life of normal people. And just plotting number of fibers on the vertical against age on the horizontal, and the horizontal line itself represents the symptom threshold. And if our curb of numbers of those nerve fibers drop on low back, we will going to pain, tingling, and numbness. And when we're normal, we have a physiological episode in the middle age whereby that the number of nerve fibers drops off and it cause through life with the reduced number but still painful. So we don't get symptoms. Now we look at the second picture, it's the same one, the normal above that underneath with work what happens in the thalidomiders in their embryonic stage, they have damages to the sensory nerves. So they end up going through life with reduced number. That's like having not enough money in a bank. And when I get to middle age, they suffer the exactly the same proportional drop off and no fibers as we normal people do. Only with them because they started with a low number, the pain threshold was originally lowered, and that is why you get pain. So we (???@05:07:37). That' s what we told in our medical school.

Hinoshita：OK. If I follow your opinions straight, the sensory and the motor system of the nerves would go quite worse in their later lives of the thalidomiders. Right? Do you feel the great damage of the peripheral nerves in your consultation with thalidomiders in each country? Dr. Kayamori.

Kayamori：From my experience, I don't think peripheral nerve is involved. So, in my opinion, peripheral nerve is judging from nerve conduction study. I don't think peripheral nerve is involved. At first, axonal of type of peripheral neuropathy used be one of the side effects of thalidomide. But I don't have any experience having patients with peripheral neuropathy.

Hinoshita：Dr. Morisson, maybe you are interested in peripheral nerve neuropathy.

Morisson：As I said, we have a neuro-orthopedic surgeon, a doctor who is used to treating patients with post-polio and used to examining for generalized neuropathies. So far, there is no evidence at present any of our beneficiaries have a clinical generalised neuropathy. They do have compressive neuropathies (but there may be some possibility of an underlying more generalized subclinical neuropathy which the nerve study showed).

Hinoshita：Just now, some other doctors are studying the peripheral nerve.

Morisson：Yes. Seeing people to assess them. At present there is no evidence of a clinical generalized neuropathy. As I have said the nerve (peripheral neuropathy study) says that there is some evidence of concern regarding the possibility of a subclinical neuropathy but they didn't do progressive studies with age. The study was static (at one period of time only). They didn't know whether the nerves had been

damaged at birth. And been that way ever since. But often nerves decline with age so without doing a study over a period of time we do not know. So whether they will in the future develop a clinical generalized neuropathy we don't know. At present, we are safe that if there is an issue it is subclinical. We need to be cautious about trying to raise awareness of this area as there is very little we can do to help and we know compressive neuropathies are common and are treatable. Hence we may miss something that is treatable if we focus on any underlying issue. So it is important to look for compressive neuropathies and causes which can be treatable before looking at options for pain management. We are looking at this are with further research in mind. We will see what happens.

Hinoshita：How do you think of or feel for peripheral neuropathy of thalidomiders in your clinics? Dr. Ghassemi or Dr. Beyer, Dr. Peters?

Beyer：I think two ways of neuropathy. Maybe some patients have experiences for a long time, and they have compensated anyhow, terms of balance problems or weakness, maybe it's new to neuropathy. And now they come to point where this compensation does not work any longer. And for neuropathic pain, I would say if you have nerve tightened syndrome, it's neuropathic pain. If you have cervical spine, it's neuropathic pain. if you have (???@05:12:05), it's neuropathic pain. Maybe you have found a special solution by operation maybe.

Kayamori：It is true that patients complain of numbness and extremities. I mean the foot and the hand. Patients complained such problems so that I did the electoral physiological examination. But I couldn't find polyneuropathy. So that's the problem. As patients complain of numbness and pain in the hands and the feet, but we have to consider another reason, not neuropathy. That's my opinion.

Beyer：But you still find some patients who has a patchy operation of the spinal tracts. And it was also mixed with multiple sclerosis. But the clinical way is completely different, so I assume it isn't thalidomide damage which was compensated for a long time. And now this compensation does not work any longer. And it's neuropathy. And I think the hand and the foot are the part of the body you can see it first, because it's a last (???@05:13:40), could you say so? Germany, we say so.

Hinoshita：Dr. Ghassemi.

Ghassemi：I always say some of our patients have done the surgery for the release of the median nerve at the carpal tunnel. And I believe this is the most performed surgery actually in this group. And having the surgery on the early age, unfortunately I don't know if they had the sensory problem before the surgery. I don't have more experience of that actually in my clinic.

Hinoshita：Then, let's go ahead to the next question. Number 4 will be lifestyle disease. Obesity, cardiovascular disease, and stroke markedly increase in later lives of them. What do you think of them? Dr. Greiner, you have partly talked about it.

Ding-Greiner：I think you have to treat these diseases in every person, there shouldn't be differences in society. Thalidomiders have a problem going to see a doctor because they were in hospitals as children where they made bad experiences. Hospitals in the 60s were not a good place to be. So a lot of them say that they don't want to see a doctor. It's one side of the problem. But at present a lot of them are dying as Dr. Schulte-Hillen told us. Something has to be done. I don't think we can solve all existing problems.

The very important thing we can do is to give them good living conditions and a good health care. The time which is left for them to live should be a good time for them.

Hinoshita： OK. In Japan, our research group have examined more than 100 thalidomiders to check if they have a lifestyle-related disease or not, or the level s of their cholesterol, triglyceride, fasting blood sugar or so. So far in other countries, you didn't check such parameters. Then will you be interested in the lifestyle diseases in the near future in Germany or in United Kingdom? How about this?

Peters： We checked it all in our study, too, but I didn't present these data because of a large number of data.

Hinoshita： OK.

Morrison： Everybody in the UK is invited for a health check by the GP once they are over 45. So these individuals will be invited and it's usually the GP who deals with those problems. If an ECG or MRI showed that even if their blood pressure was normal but that body is not coping with the blood pressure (target organ damage) then their blood pressure needs to be treated or an opinion from the specialist is needed. Obviously this is a group who may not like doctors or taking medication and our blood pressure study may not reach those individuals as they may not wish to take part. It was for these individuals in particular we were doing the Blood Pressure study. We will see what our study shows.

Hinoshita： Do you feel if thalidomiders have more cardiovascular attacks or incidents? I mean compared with the general population in UK or in Germany.

Morrison： I'm suspicious, a lot of them on the helpline seem to be on blood pressure treatment. So I wouldn't like to say without more research but I have a suspicion that this may be an issue. But obviously lifestyle factors are very important. And they need to be considered when treating the individuals.

Hinoshita： How about in Germany, Dr. Greiner?

Ding-Greiner： We have similar problems, but we have no means to force thalidomiders to make a checkup, everyone is free to do it or not. I guess, if we had physicians and therapists with good knowledge of Thalidomide damage, maybe it is easier for them to go to a consultation. But the big problem begins with taking blood. Lots of thalidomiders told me that it is not possible to take blood under normal conditions. There are a lot of barriers for affected people for going to seek medical help.

Hinoshita： Dr. Morrison, please.

Morrison： I think if you are highly suspicious of a problem and feel they are at high risk a way forward is to put them on treatment with medication that doesn't need blood tests to monitor it. Or you can refer give them to a specialist who can do this.

Hinoshita： How about in Australia? There may be less thalidomiders in the country. How about cardiovascular attacks or stroke, something like that.

McCredie： I've heard of only three or four who have died. Two are certainly from coronary diseases. And one of them was stroke. With any (???@05:20:00) total 60 thalidomiders in my country, so there is maybe some little (???@05:20:05).

Hinoshita： Dr. Shiga? You have examined it.

Shiga： In Japan, there are many patients with fatty liver and hypertension, but in this medical checkup, we can check thalidomiders. But I heard that many thalidomiders don't want to go to hospital, so some of them don't check the blood pressure. So it is difficult to order them to go to the hospital. I think it is good information about checking the blood pressure is good for you by internet or some leaflet and so on. The information is good thing I thought.

Hinoshita： All right. Do you have any other comment? Anyone else? OK, then let's go to the next theme. Number 5. How about the anatomical problems or bone defect? How about depression and/or other mental problems? First, anatomical problems or bone defect. Dr. Tajima, do you have any comment? He is a radiologist.

Tajima： I want to talk about undescended testis. Someone talks about undescended testis. This is a very important problem. That can cause testicular malignancy. So we have to follow these patients. Also I think spina bifida is another important problem. It has been reported that spina bifida patients have strong influence on neurological deficits. So someone who have neurological symptoms we have to follow and perform CT or MR in the area of lumbar spine or sacrum. How about spina bifida in your country?

Hinoshita： Two problems. First, undescended testis. Next, spina bifida, right? So first, let's focus on undescended testis. Maybe Dr. Peters has mentioned about abnormalities in the sexual organs among your patients.

Peters： That's not a rare condition as we thought all of the undescended testis have to be treated in childhood. But spina bifida, I think it's not more common in thalidomiders. I think it's not a typical anatomical problem of the thalidomider.

Hinoshita： How about it, Dr. Greiner? Undescended testis and spina bifida?

Ding-Greiner： Participants told me they had undescended testis, they were operated in childhood but it was too late. The doctors didn't take notice of it. Patients have higher risk of developing cancer of testes. We have in our fist survey of 2012 about 10 to 20 percent of participants who were childless of this and of other causes.

Hinoshita： You noticed the number of the patients with undescended testis increased in thalidomiders. More increased than in the general population. Anyone else? Spina bifida or something else. Anatomical problems.

Schulte-Hillen： To my knowledge, spina bifida is not a part of thalidomide syndrome. Undescended testis is, I say in Germany, at least 30 to 40 with that condition, and we have at least one who developed carcinoma of the testis, and survived.

Hinoshita： OK. Thank you. Is there anything else which we didn't know as anatomical abnormalities that you know just found?

Peters： I think slight hypoplastic changes of the knee joints often not seen, and that's also primary damage of the thalidomiders. But in a lot of cases it's not seen and not diagnosed. And they might result in severe secondary knee arthrosis.

Hinoshita： OK. Do you have any idea for those cases how it was derived of or it was caused by the thalidomide itself?

Peters： I don't think so, like the hip dysplasia as the same dysplasia of the knee joint.

Hinoshita： I see.

Schulte-Hillen： Two years ago, we found out that many of the thalidomiders with the ear damage also have complete missing of (???@5:27:07) acoustic organ which means particularly dangerous for the people with short arms because they cannot go out themselves when they fall. They changed the law in Germany. This defect is generally accepted as part of the thalidomide syndrome and compensated for.

Hinoshita： We also expect there might be more anatomical deficit or problems in the face or near the mouth or near the ears, bone defect or something which nobody have ever discovered, maybe. So Dr. Maruoka. Now we are starting to check the mouth and the jaw joint in our medical checkup. Do you have any comment?

Maruoka： So far, I've never seen such a disorder. But from now, I will investigate such types of disorder.

Hinoshita： All right. Is there any anatomical problem? OK, please.

Ghassemi： I have one of our patients, actually a woman. It was shown that she didn't have any internal genitalia. So no uterus. That's only thing I know which is the only person also I know. And you don't know if it's because of the thalidomide or not.

Hinoshita： I see.

Schulte-Hillen： Can I answer to the question?

Hinoshita： Yes, sure.

Schulte-Hillen： Malformation of the internal sexual organs is considered as part of the thalidomide syndrome. And we have quite a few of them (???@05:29:05) I think that's the name for it are completely missing aplasia or complete atresia of...

Ghassemi： Because that was complete aplasia.

Beyer： That is in Germany definitely part of the thalidomide syndrome.

Hinoshita： Aplasia of the gallbladder is also famous, you know. Next number 6 question. There're still many problems to be solved on the thalidomide embryopathy, TE. Does your country fully train young physicians treating TE? How about this?

Beyer： I think in Germany there are a very low number of specialists because in the normal clinics today, nobody would like to spend the time or exceeding the time for this topic. And I found out I do my clinic together with orthopedic surgeons which are under the state of registra or special registra and what they are normally doing is assessment for hip replacement or shoulder surgery, and they are doing this very quick and very fast. And they like to come to my clinic to make an assessment of people whether they can assess the whole people with all joints because I forced them to do so. And they always get one and half hour and they are off duty or reward this time. So they like it. And I tried to help them little bit by what I found out how to classify the dysmelia because nobody has analogy of this.

Hinoshita： OK. Ms. Newbronner.

Newbronner： We also found in our survey in the UK that many thalidomiders had problems with a lack of knowledge of thalidomide damage or the specific impairments when they saw health professionals. And I think people are realistic. They appreciate their doctors or other health professionals cannot know everything especially if they are generalist. But I think what often people say is that they would like people to listen more carefully to their own knowledge of their bodies. And so to have that time as Dr. Beyer said to discuss things more thoroughly with them. And also not to rush to treatment but to seek advice ether from the Thalidomide Trust or from specialist. So I think it's about taking that time and listening to the thalidomiders themselves. Because it is not possible of every doctor and every nurse too understand thalidomide.

Hinoshita： Maybe It's a universal or general problem over the world. If we examine the thalidomiders, it will take much longer time for that patient. Dr. Graf in Nurnberg did say the similar thing to us when I visited him. No many orthopedists or specialists who don't like to gladly examine the thalidomiders. Now we have Japanese people with TE in this place. So Ms. Masuyama, what's the situation in Japan? Do you have any reliable physicians or physicians who would listen to your complaints or problems in Japan?

Ms. Masuyama： Well I am not an expert on this topic, so this is my personal impression actually. But on the Ishizue foundation I am working as supportive or supporting staff members. So through this capability I have seen or contacted many people with the TE. And actually some people were deteriorating their physical conditions rise quickly. I have seen such people in most recent several years in particular. And I hear some physicians just declined their treatment for such people because some physicians are feeling that this is a completely unknown condition for them. And further it's an unknown condition even to ourselves. Generally speaking, physicians might be afraid if this is a completely new condition which might require surgery and if the patient might be dying after the surgery. So there might be some cases actually I often heard of that some patients were actually referred back and forth among different physicians.

Hinoshita： Anyway, to support thalidomiders even if a little, our research group of Japan has determined to make some medical network. I mean the specialists or physicians who can take care of the thalidomiders. I mean in other word, you are preparing a list of the specialists or physicians who

can take care of them. Now I am arraning it. In a few months we can complete the list up. But anyway, sorry to say however, I have asked more than 70 doctors, and only 30 or 40 doctors have said yes to be involved in that network so far. Anyway, is there any comment? Dr. Nakamura.

Nakamura：I would like to know what the different face of the investigation of the thalidomiders. We have got many new informations regarding the biological assessment. So I would like to ask Dr. Morrison if you can. I know that UK has started the genome-wide analysis. 100,000 genome projects here supported by NHS. Dr. Mark Williams studied that project. I mean the investigation of your British people, to gain the British people's standard genome profile.

Morrison：You mean regarding blood pressure?

Nakamura：Yeah. Oh, everything. Genome-wide analysis.

Morrison：You mean over 45?

Nakamura：Yeah. Everything. I hear 100,000 genome projects, it said.

Morrison：All right. I don't know.

Nakamura：Uh-huh.

Nakamura：This is my personal view, but the conventional investigation is come to the kind of the limited now. So we should employ much more innovative methods to investigate the pathology of thalidomiders. So if possible, we need to consider genome-wide analysis of the gene information, and to compare that kind of data with the general population. That might be giving us very good clue to know or to extend more about the pathology and pathogenesis of our concerning condition. So just I want to know your British status because I hear that your British data are very good, greatly advanced on the GWAS genome-wide analysis.

Morrison：No, I don't know about it.

Nakamura：OK.

Morrison：I couldn't comment.

Nakamura：Thank you.

Hinoshita：Is there any comment or opinion? OK, Dr. Greiner, please.

Ding-Greiner：I guess the secret to be a good doctor for thalidomiders is to forget part of everything you know concerning your ordinary patients, to listen to the patient because those patients and their ailments are different from other people's as the cause is an intoxication with Thalidomide. You have to invest a lot of time listening to them and thinking about possible causes, about which therapy might help, and the most important problem is which kind of therapy or support help they will accept.

Hinoshita：Thank you. Is there any comment or opinion? Finally we'd like to go to the next question. Today, we gathered from several countries. Can you show us strong or good points as well as bad points and the support system and the social system to assist thalidomiders in your own country? Could you show us in detail in each country? Then Dr. Greiner? No, sorry, Dr. Morrison.

Morrison：I think there is financial pressure to reduce everywhere costs to support individuals. Theoretically our individuals should be able to claim from the government in addition to the compensation they receive to help their daily lives. However, a lot of them are having the amount they receive reduced. And hence we are trying to support them and to help them answer the questions and to fill in the questionnaires to help them get the money they should be entitled to. And it's partly why we have increased our team to try to give more individual support. We've also discussed assessing everybody in the trust with a needs assessment to look at all the different factors and trying to see where we can help. So I think the good thing is we have the Trust to help. The bad thing about it is the waiting list and prioritizing individuals.

Newbronner：I think the other thing in the UK is in our social care system. Actually a relatively small proportion of thalidomiders in the UK get social care support - less than 20 percent. This is partly because they're working and they have more income, so they are not entitle to it. But also many people don't want to be part of the social care system. Because they had bad experiences in the past of being told what to do or having restrictions placed on the kind of support and care they can receive. So I think firstly want to have control over the personal kind of support they have. And I think particularly people who are upper limb affected. The social care system doesn't really understand that is a disability is impairment, they don't understand people will use wheelchairs. But they have limited grasp of the implications of upper limb impairment. And we have the Trust's work to comprehensively document upper limb impairment, something called Upper Limb Statement that colleagues are really working on. I think it is something that eventually could be turned into information for health and social care professionals. So they perhaps will better understand just how many problems life presents people with upper limb damage.

Hinoshita：In your country UK, you have the great financial support from the government or the Thalidomide Trust. It is good point and also now you are making up a list to specialized medical centers, Wrightington Hospital and the Royal National Orthopaedic Hospital (RNOH) to treat thalidomiders especially for pain control or surgical operations, right? These are good points I think. Anyway, let's go to Germany, and who would answer.

Beyer：So, I think the support by the thalidomide trust (Conterganstiftung?) is really poor in Germany. There are no definite medicals as decision-makers from my point of view, and I see you say to grasp of what disability means to people is not very good there. And everything has been built up in Germany is without the support of the trust (Conterganstiftung?), I would say. It's just a kind of treasurer for the money which is...

Hinoshita：So you mean you are lacking of decision-makers to financially support individual thalidomides?

Beyer：Yeah, I think there is no central navigation by the trust. You have to do everything on your own, and invent on your own, and you have to ask for money. It's not easy. And there is no one who is

doing a kind of central navigation.

Hinoshita： But you have the Conterganstiftung.

Beyer： Yeah.

Hinoshita： Conterganstiftung is not functioning well you mean?

Beyer： I think the Conterganstiftung, they just take care how to spend the money without really having medical knowledge. And they decide by formal things, not by medical things. This is my personal view. So thalidomiders need to go to hospitals and ask if they could imagine to build up a clinic or something. They have to do on their own. They are not supported by anyone. I think there is a lack in Germany. If you compare it with the rich country and if I look through England or through Sweden, I think it' s much better.

Schulte-Hillen： I would like to respond to that.

Hinoshita： Yes.

Beyer： One of the members of the medical committee of the Conterganstiftung of the thalidomide trust in Germany, and by law that the task of the thalidomide trust was to distribute the money. And they have developed beyond that and they are starting to assemble database for physicians. We are capable of, we have special knowledge and they found database for content management. So, for example where to drop that from the thalidomiders, for example where to measure the blood pressure. As you know Germany has changed in the last decade. Big changes in the health system, and everything is managed-care. People we have one of 5 big diseases like diabetes or breast cancer and hypertension very well taking care of. This went to great extent Germany was forced be the European Union to find that is called national union for people with rare diseases. And thalidomiders have one of those rare diseases considered as one rare diseases. And we are just starting, you might say.

Hinoshita： OK. Thank you very much. Is there any comment from other German doctor? Dr. Peters or Dr. Greiner.

Peters： I think it's improving because financial support has improved in the last years. But it's the way, the way it's not the end up to now. I think one of the main point is future secondary damages. It has to be notified, seen as a problem. That's not a problem in the focus at the moment. I think that will be noticed as the next step. Secondary damages are important. That decrease quality of life. That has to put it in the financial support, I think for the people. That's not up to now. And we have to build up a network for specialists all over the all country. That will be one of the next aims.

Hinoshita： Anyway, you yourself just started to build up a good center for the thalidomiders? Then also Dr. Beyer vigorously deal with pain control in thalidomiders. Please spread those movements to all over the nation. Anyway, next, how about in Sweden?

Ghassemi： In Sweden, the good point is that thalidomiders actually are not forced to work 100 percent. They can choose if they want to work 100 percent. But they can actually choose to work only 50 percent

if they want to. I need to say the time when they need to work. And the bad point is as you said, it's (???@05:49:46) also they have to stand in line. Because they are also connected to the local practitioner, general practitioner. If they are lucky to get contact with the EX-Center they will do that. And I think it's the problem with any (???@05:50:19) and more severe that they are forced to. And I think the information will also go from their president of the association that actually can ask for that at least give the information to the general practitioner.

Hinoshita： OK. In Japan, the number of the specialists or the experienced doctors for thalidomide embryopathy has been decreasing, such as Dr Kayamori. Some of the doctors are interested in and dealing with the thalidomide embryopathy. The Ministry of Health, Labor and Welfare has been interested in supporting thalidomiders who are over 50 years old. But any totalized medical network has not been built up so far. In my idea, as I said before, we should make up the medical network with the physicians who have been interested in the TE and can take care or treat the thalidomiders over the nation. And also we noticed that at least in Japan, we have increasingly more patients or thalidomiders with lifestyle-related diseases such as hypertension, obesity, fatty liver or some kidney dysfunction. We also should focus on such lifestyle-related diseases from now on. Is there any other comment, Dr. Shiga or Dr. Kayamori about the situation in Japan? No?

Shiga： No.

Hinoshita： OK. How about Dr. McCredie? Is there any additional comment?

McCredie： I think in our country because of the geography and because a lot these people are computer-literate with great help if some of the information (???@05:53:10) today for instance or some other plans. So if the upper limb people coming out of the thalidomide trust if some of those things need more help enormously.

Hinoshita： Thank you. We did not discuss the mental problem, depression or something else. Anyway, Dr. Imai, do you have any specific comment?

Imai： Allow me to explain in Japanese. I work at the same hospital with Dr. Hinoshita. I'd like to say a few words as psychiatrist. I'd like first talk about pain. If drugs and surgical treatment are effective it should be treated. However, it's a big problem that pain would often become chronic. When the pain becomes chronic, people feel that without such pain, I could do more and I could do this. In addition, people are likely to think too much about pain. And consequently their way of thinking would easily deviate. Then psychological treatment may become important. And when that happens Cognitive Behavioral of Treatment, CBT, would be effective. That's I think very useful. CBT would correct this biased thoughts in foundation. What is important is that you should not tell them "You are in such situation. Therefore, do like this". You shouldn't not say in that manner to the patients. You need to encourage patients to recognize their biased recognition on their own. Therefore the treatment is to support patients understand the bias problem. That's the first topic I'd like to talk about. Second according to the Thalidomide Trust in UK and the report in Germany, there are researches on the mental problems in which more than 200 people had been surveyed. And I think it a very good data that you have identified many people with mental problems. But I am a little concerned I am in the practice and I'm afraid because we are not speaking up the information from everybody. For example, in the UK, only 75 percent of the patients had been surveyed. They have complied with a survey. But I believe there are

many people with obviously mental problems who were in the rest of the surveyed. Therefore, what is important is that we tried to pick up the people with mental problems who have fallen in out of the survey data. Another point, there is the German survey where more than 50 percent of the people among disabilities their percentage of mental problems seem to be very high. But as the anesthesiologist reported, how to use benzodiazepines or minor tranquilizers should be very careful because people want to move away from pain. They frequently tend to rely on alcohol or such psychotropic drugs. And we have always this problem in Japan. It may be also true in non-psychiatrists. Whenever patients claim insomnia or anxieties, we would very easily prescribe benzodiazepines. It's been the case today, but when benzodiazepines are prescribed very easily dependency becomes a problem. So that's one thing we need to be careful about in drug treatments. And that is also for pain whenever there is a problem, you need to think of other treatment, alternative treatment. Now about statistic depression or emotional problems and anxieties, we have seen fairly good number of patients complaining these symptoms. And they are not just transient symptoms, but they are probably secondary pain based on that they are victimized. So these are often secondary to what had already happened and if you can treat with the patients or be involved with the patients, I think those are the problems which may be deduced. And now, we will also need to work on this more.

Hinoshita： Thank you very much for the comment. OK, Dr. Beyer.

Beyer： So one comment. Maybe it was misleading what I was talking about, but I do not recommend benzodiazepines at all. I have met patients who wear benzodiazepines for over 20 years. And they are nearly untreatable in terms of pain. So I would never prescribe this. I'm against it.

Hinoshita： OK. So, finally, any comment about mental problems? Anything, anyone else? OK, thank you very much. Now it's 7 PM. Then let's finish this hot and fruitful discussion now. Please get back to your seats, the original seats for the symposiasts. Thank you very much.

Staff： Thank you very much, all the participating doctors on the symposium. So could you return to you own reserved seat now? Thank you.

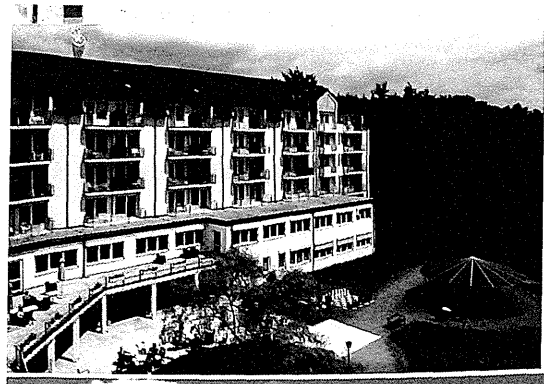
So, Dr. Hinoshita would be giving us the closing remarks. Dr. Hinoshita, please.

Hinoshita： The time has now come to close this international symposium. Although a symposium from 10 AM to 7 PM may seem long, in fact it was very short, because today we were made aware that we still have many unresolved problems. As thalidomiders age, we are certain that they will have, and will suffer from more and more serious physical, mental and medical problems which they had rarely experienced in the past. Fortunately, however, today we were able to discuss and shed light on these problems among physicians and researchers from different countries. I think it is very important to bring these discussions home for re-consideration and to make efforts to improve the situation associated with thalidomide embryopathy in each country. Indeed, there are a few experienced, able and earnest clinicians and researchers for thalidomide embryopathy in each country, but they may be outnumbered by the great needs of the thalidomiders.
There is a famous old proverb in Japan. "I no naka no kawazu taikai wo shirazu" (in Japanese). Namely, "The frog in the well does not know the ocean". I hear there is a similar English proverb."He that stays in the valley shall never get over the hill". Namely, "Tani ni todomaru mono ha oka wo koeru koto ha dekinai" (in Japanese). It seems that, to date, there may have been little international exchange on the

various problems of thalidomide embryopathy, at least between the West and the East, or the southern hemisphere. I hope and believe that this symposium will become a great trigger for further international communication and cooperation among different countries. Also, it may serve as a medium to find and develop good measures in the medical, physical, orthopedic, and mental areas or even in other specific fields. In addition, discussing and refining the compensation scheme and the administration policy will help to resolve the current and future problems that thalidomiders face.
Finally, I would like to thank you very much for joining us today. Especially, I would like to express gratitude for the great assistance of the Ministry of Health, Labour and Welfare, Japan, and the many managing staff. I also express our thanks to the guest symposiasts, especially those who came from abroad, for participating in the symposium and showing us very nice presentations. Now I would like to conclude my remarks by wishing everyone here good health, prosperity and safe travels. Thank you much again.

Staff: Thank you very much. Now, today's program is over. So please leave your receivers on the desk. Thank you very much for being with us for a long time today. We wish your safe return journey back to your home. Thank you.

(End)



International Symposium on Thalidomide Embryopathy in Tokyo, 2015

Thalidomide embryopathy - common and rare differential diagnosis

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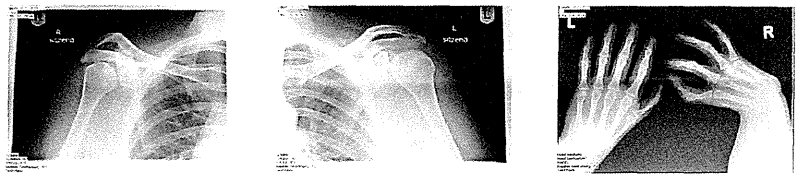
Dysmelia caused by Thalidomide intake of the mother during pregnancy has a certain pattern:

- Longitudinal reduction deformity
- Bilateral damage with relative symmetry
- Aplasia or hypoplasia of the radius and thumb
- Involvement of lower limbs always combined with dysmelia of upper limbs

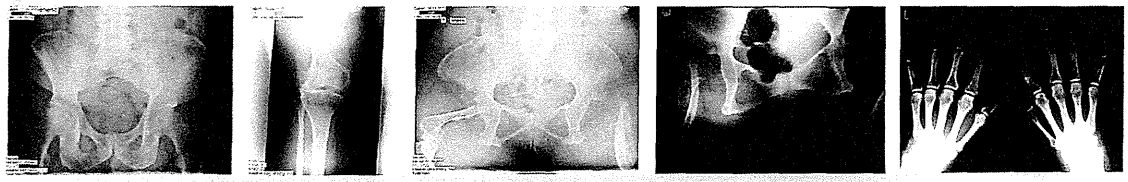
Thalidomide-induced dysmelia

of upper limbs



B. S. *1961:
Longitudiual reduction deformity of upper limbs, right > left with absent right radius and thumb and triphanlangia of the left thumb

of lower limbs and sacrum



P. K. *1961:
Dysplasia of the sacrum with absent coccyx

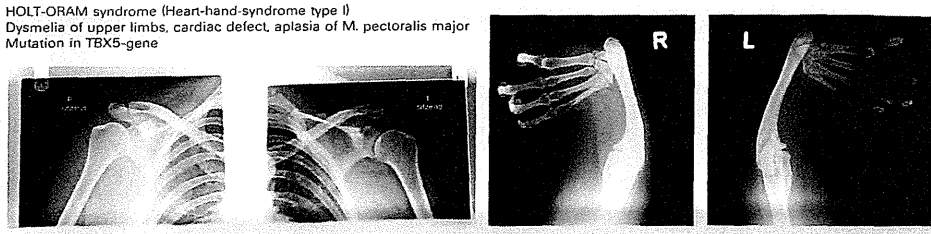
K. W. 1961:
Dysplasia of the right knee with severe secondary gonarthrosis

J. S. *1961:
Severe reduction deformity of upper and lower limbs

D. H. *1961:
Quadruple limb damage: only slight changes in both hands and severe pelvic malformation

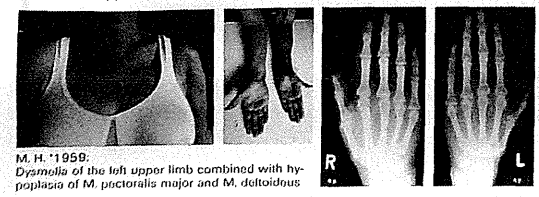
Differential diagnosis

HOLT-ORAM syndrome (Heart-hand-syndrome type I)
Dysmelia of upper limbs, cardiac defect, aplasia of M. pectoralis major
Mutation in TBX5-gene



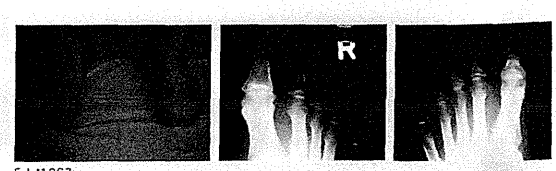
N. F. *1977:
Bilateral symmetric, reduction deformity of upper limbs with abcent radius and thumbs

Poland-syndrome
Unilateral aplasia of M. pectoralis major and mammary gland and Unilateral dysmelia of upper limb



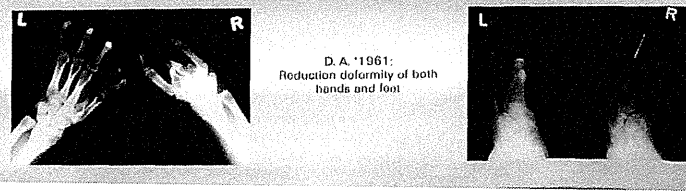
M. H. *1958:
Dysmelia of the left upper limb combined with hypoplasia of M. pectoralis major and M. deltoideus

All transversal reduction deformities



F. L. *1967:
Transversal reduction deformity of both feet with "amputation" of the toes, no dysmelia of upper limbs

EEC-syndrome (Ectrodactyly-ectodermal dysplasia clefting syndrome)



D. A. *1961:
Reduction deformity of both hands and feet