



IPWSO
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IPWSO Health ECHO abstract

December 7, 2021: Orthopaedics in PWS

Please note this document is abridged from audio transcription of the Zoom session. Some errors resulting from the transcription process may be present.

IPWSO hosts: Georgina Loughnan (GL) Tony Holland (TH)

Presenters: Ralf Stücker (RS), Winnie Ong (WO)

Video link

Prof. Rd. Ralf Stücker, [Management of orthopaedics in Prader-Willi-syndrome](#)

[Q&A Following Ralf's Presentation](#)

Q: I am in Switzerland, and it's very interesting to listen to your talk, thank you very much as it's really great also covering the whole age spectrum and to a different perspective, so young children, adults and two different techniques. You mentioned that in the early onset of scoliosis the muscular hypotonia is one of the major factors associated, and you didn't mention it too much afterwards. So, I'm very interested in this association of scoliosis muscle hypertonia, the muscle treatment training and so on. What is your experience, for example, is the incidence of scoliosis in the older age, so people and young adults also associated with high muscle hypertonia or inversely related to growth hormone treatment and physiotherapy for example? And you said there is no association to obesity. Obesity, in my experience is also related to the overall treatment concept. And so, it may be related to physiotherapy and other muscle strength trainings. Is your experience, experience really such that obesity is not related to scoliosis? So it is a multiple question thing.

RS: Thank you very good question. I think they're all good questions. And we don't know exactly what are the risk factors. For the very young child, we know that hypertonia is a risk factor and you're right, probably for the older patients, the obesity

And hypotonia are also risk factors but they have not been clearly detected as risk factors because of the unit higher numbers to really look at risk factors will determine risk factors. However, I still think that obesity and muscle strength and all these things you mentioned are risk factors. And another risk factor is probably the osteopenia. There are nice studies from Hong Kong area and from China, and they did randomized study in adolescent idiopathic scoliosis and they were able to clearly find an association with bone loss, so osteopenia, and the progression rate of scoliosis. And if that is true

for adolescent idiopathic scoliosis probably true for PWS. So, I think all of what you mentioned are probably risk factors which need to be addressed. Although they were not clearly detected as risk factors yet.

Q: So this may lead me to another question related to puberty. If you say lower bone mineral density is related to sclerosis and this adolescent and young adult group of patients often have late onset of puberty, where treatment is often delayed because of multiple factor reasons we already discussed in this group. What is your idea? Could it be an argument, in a sense, that we don't have to wait too long to introduce sex hormone replacement in these adolescents, also in view of having a positive impact on the scoliosis and scoliosis progression, or is this going too far?

RS: I think everything which is related to strength and muscles and decreased bone mineral density is probably is probably good to use. We know that the progression of scoliosis is also related to growth. Typically, if the growth rate is very high progression rate of scoliosis is high, and if the growth rate is low progression is very low, that is the reason why in between 5 to 10 when the growth rate of the spine is only one centimeter from T1 to S1 per year growth that the progression rate is usually low and many curves can be controlled with a brace. But when the growth rate increases, the growth spurt, then this is often the time when the brace is no longer able to control the curve and you need to consider surgical treatments.

Q: Which could be, if I understand you correctly, this new method of tethering, maybe.

RS: Well, when you do the tethering it's what we call an anterior approach, and for many children with PWS, it's not really applicable because you have to go through the thorax and we know that the lung could collapse during surgery and there may be negative effects on lung function, and this is why many colleagues of mine still think that this may be a contra-indication of PWS. However many PWS patients have scoliosis in the lumbar spine, not in the thoracic spine. And as you know if you have to fuse the lumbar spine, the whole mobility of the spine is gone. So this may be a growth, preserving and mobility preserving surgical technique for some patients with PWS, with scoliosis in the lumbar spine.

Q: Thank you very much for very clear presentation. I want to ask you about the patients who are a little older, those who are 40 and 50 and 60, who have scoliosis and who also have kyphosis, and they have not been treated with bracing or operated on. My experience with this group is that many of them suffer from back pain, pain around the neck, and they are over bent, because of muscle hypotonia. Do you have any experience with this age group?

RS: Unfortunately, I don't have experience because I'm in pediatric orthopedics. I treat patients, up to the age of 18. But I know what you mean. You can still develop scoliosis even if there is no more growth, even when you're 40 or 50, especially those patients who have osteopenia so little bone mineral density. So they still may develop

progressive scoliosis And in those cases when it increases to more than 40 to 50 degrees, surgery is probably also necessary.

Q: I think about, patients who have had the scoliosis since puberty, and it was never treated and years back it was thought often that the operation could be dangerous because of the increased bleeding risk. That was what one was told 25 years ago or so.

RS: But nowadays that's not true anymore. You know the bleeding is not a real problem anymore because we have good methods to control the bleeding during the surgery. That was different 20 years ago.

TH: Can I just ask, when you get a severe scoliosis or kypho scoliosis, to what extent does it compromise other systems of the body? I can imagine it compromises the lung. Does it affect the heart function and abdominal gastrointestinal function to extreme degrees? Is that one of the reasons why correcting this is very important?

RS: Well we know when scoliosis exceeds 60 degrees, it affects the lungs. And if it exceeds 90 degrees, it also affects the heart. But the abdominal contents are not really affected because the kidneys or the liver and they have space enough, and most of the organs then move towards the cavity and are not affected. But the heart is affected so definitely when it when the scoliosis exceeds 90 degrees.

Q: Can I ask another question about the proximal junction kyphosis. This is something, if it happens it's really scary in a way. And what is your experience, how fast does this happen, because if there is the question of putting something like fix into the spine to stabilize the scoliosis my worries is that in a couple of years later on this complication with the proximal junctional kyphosis will come up. Does this complication come early after surgery, or could it come also 10 years later?

RS: My experiences is that it comes very early. after surgery. But you have to think about that patients have a kyphosis before surgery, like let's say 70 degrees, and you can correct that to 40 degrees, for example, then they want to go back to the original position. Also, what you need to take into account is that the patients who have severe scoliosis have severe shortened muscles in the front, like the pectoralis muscles, the muscles between the ribs are shortened, the abdominal muscles are short and this is probably the nice effect of the halo gravity traction, because you stretch this out before surgery, and you have no tethering effect in the front anymore. This is something we learned, that the halo gravity traction with kyphosis really makes the event of a junctional kyphosis much less likely.

GL: It strikes me that it tells us there is a very strong indication of very early physiotherapy and weight bearing exercises and strengthening exercises for children with PWS, to try and improve their muscle strength and bulk, whether they're on growth hormone or not, which will in turn help with the osteopenia, so I think it's possibly something we should all push a lot more.

RS: I think you're definitely right. I didn't focus on the physiotherapy aspect but it's very important in my view to make all the efforts which are available to strengthen not only the trunk muscles, but also the bone early in early in the development, because we know if you don't do that then the likelihood of having severe spinal deformity is very high.

GL: Thank you, Ralf for a very interesting presentation. Although we are only few tonight this generated lots of discussion so greatly appreciated.

Case presentation (abridged)

GL: It gives me great pleasure to introduce Dr Winnie Ong who is a Clinical Geneticist at the Department of Genetics in Kuala Lumpur Hospital, which serves as the national referral centre for inherited metabolic diseases and genetic disorders in Malaysia. She has worked there since 2014. Her Clinical Genetics Fellowship was in the Ministry of Health of Malaysia from 2010-2012, and the Manchester Centre for Genomic Medicine, UK in 2013. Her Special interest is in Dysmorphology and Ophthalmic Genetics.

Case Presented: 17 year-old male, Prader-Willi syndrome - deletion type

Treatment and significant information to date: 1. Was on L-thyroxine (max 50mcg/day) from infancy till 9 years of age for hypothyroidism. Since then has remained euthyroid without medication.

2. S/C insulin and oral metformin for Type II diabetes since 14.5 years-old till present, but compliance is an issue, hence diabetes is poorly controlled (HbA1c 13-14%).

Did not have the opportunity for growth hormone therapy (not readily available in Malaysia) even though under endocrine follow-up since childhood.

Past medical history: Congenital hypothyroidism - was on L-thyroxine till 9 years-old.

Bilateral undescended testes - orchidopexy done

Obstructive sleep apnoea - was on nasal CPAP (air) during sleep from ages 6 - 9 years

Dental caries (rampant) - dental works/ extractions; treatment for malocclusion.

Physical: Hyperphagia an ongoing problem.

Obesity - from 3-4 years-old till 12+ years-old, improved significantly since 13 years old with progressive weight loss till now (currently weight 52kg at 10th centile)

Hepatomegaly, fatty liver and elevated liver transaminases - persistent but stable

Dyslipidaemia - mild

Mild scoliosis

Skin picking has been a big problem since early childhood till present; previous psychological therapy & behavioural modification attempts not very helpful. Many scars especially on limbs.

Psychosocial: Progressive behavioural difficulties from age 10 years onwards:

temper tantrums, especially regarding food, rebellious and stubborn, aggressive eg. hits siblings/other children, lies

Manipulative and persuasive

Low self-esteem, bullied when in mainstream school, not many friends (selectively choose friends) - better after switching to special educational needs school at 10 years-old

Despite the above, remained a happy boy generally then.

Loss to follow-up from ages 13-15.5 years

Escalating/ worsening behavioural problems main concern at present:

Food-seeking behaviour - wakes up early in morning (5-6am) to steal food, will unlock food pantry/ raid the fridge/food cupboard) when other family members still asleep.

Lies and denies when parents confront him of this.

Dangerous behaviour - becomes extremely angry and aggressive especially when it's related to food issues/ food restrictions, throws furniture/objects, threatens parents (mom especially) with a knife.

Temperamental and aggressive/rough with siblings eg. hits younger brother when parents not around

Occasionally will get hit by his father.

Refusal to attend clinic reviews, hence defaults most clinic appointments given, including with psychiatrists, endocrinologists

Compliance with treatment/medication - sometimes caught eating extra dose of metformin when he wants to steal food.

No actual hallucinations/ delusions/ abnormal speech noted.

Patient is aware of his diagnosis and seem to understand what's needed treatment/management of PWS individuals. But uncertain exactly how good is his insight on things, especially now as unable to engage him to describe his feelings very much. His refusal to see doctors frequently (especially psychologist/psychiatrist, endocrinologist) makes his treatment even more difficult and challenging.

Impact on family:

Mom largely the main carer - no longer able to contain him (both physically and emotionally/psychologically), exasperated, exhausted, fear for safety, worried & sad.

Dad long hours at work, not very involved with his medical and psychosocial problems. Dad has never attended our clinic review sessions. Physically beats patient when unable to cope.

Siblings - affected physically and emotionally, disrupted and chaotic family environment.

Food issues - mom has to sometimes throw away 'red' group of foods at home to prevent patient getting to them, strain on family with food restrictions.

Medical/Allied Health Support: Previously very active and enthusiastic with physical activities - enjoys zumba, cycling, swimming, horse-riding; much less motivated now, especially with the frequent lockdowns (movement restrictions) due to the Covid-19 pandemic.

Encouraged to join the activities and support of the PWSA of Malaysia, especially with other teenage PWS individuals, but not much participation or interest. Closest to mom, but now parents have difficulty in getting him to express his feelings as he gets older. Not many friends.

Key questions for the participants to consider with regards to this case.

1. What helpful approaches to manage his escalating behavioural difficulties especially with:

a) His anger, aggression and dangerous behaviour (eg. threatening with knife)?
- would you consider these episodes as psychosis?

b) His refusal to go for clinic/medical review and follow-up appointments with healthcare professionals? - challenging to initiate and institute treatment for him.

c) The balance between food control and behavioural angst?

d) Helping the family? (there's no established respite care in Malaysia, neither are there shared homes for PWS individuals)

2. Any helpful advice/tricks to manage his skin picking?

Thank you very much.

Discussion following Winnie Ong's case presentation

GL: I think it's a very interesting case and it's probably one that we may all be able to identify with it at some stage during our careers working with people with PWS. So do we have any suggestions for Winnie?

TH: The dilemma here is that there isn't a simple or straightforward solution. If there was, I'm sure you would have done that. And it really ultimately I think is about how one helps the family adjust the environment and work with him in a way that can somehow contain these behaviours. And it's very easy to say that and of course it is very difficult to do.

I think, rightfully as you have said, one needs to eliminate other possible causes, and I think you have eliminated the possibility that his behaviour has deteriorated because of, for example a psychotic illness. It seems unlikely from what you say that something like sleep apnea is making things very much worse, although if he has put on weight again, that's a possibility.

I think the other thing to say is that just getting older and becoming an adult in itself is an issue because we often talk about this idea of a disability gap, the cognitive disabilities that he had, although his impairment is relatively mild, they are going to be more marked in adult life than they are in childhood and that's going to be a problem for him. But perhaps we can come back into discuss again how one might work with the family.

Comment: My idea when I hear this is that the family and the boy haven't had enough support. One thing is that he has had access to food. So, the kitchen door should have been locked when he was growing up, I think. But this is only a speculation, that the family expects more from him, that he can manage himself, and he cannot because of Prader-Willi, the behaviour that we see here is so typical when the children have not had enough support and everything is late, they need so much more control to relax. So, I'm very sorry about it and I remember in one of our presentations, there was a question from a sister about how to manage the behaviour. So, I think when we see these cases in Europe, sometimes it helps a lot when they move to a PWS home, and I know that you do not have this possibility. So in some way, it is support to him, and the family. First of all, no access to food, no access to medication at all. And then, more support and then praise him for everything he does well and never ask him about if he stole food because he will deny it, and then it will cause a temper tantrum. It's wasting your time blaming him for what he did, because he will deny.

WO: I think for this family apparently food seems to be the trigger for a lot of his outbursts. So I think they have tried very hard to keep his weight good but in the process, it has it has triggered a lot of this unhappiness. I think they're wondering whether if they are not so strict would that help lessen his outbursts. But I think that's probably not the way either because then you're probably going back to the obesity problems and he's actually been doing quite well with his weight.

Comment: The weight is related to the diabetes, which is not controlled. So, if this diabetes was controlled (it would be better.) With an uncontrolled food intake, he will most probably have more of these breathing problems and complications coming one after the other. So, not having the opportunity to bring him into a controlled environment or situation where everything is like controlled, my view is really what is the aim? Because if there is not a medium or long term solution for him, which controls the main things in the everyday situations, mainly food and medication, then he will die. And I think he will die quite soon related to the diabetes.

When you presented your case, I thought the only solution I would have is if the parents or the adolescent is willing to enter into a home. And if you don't have such an institution I don't have any idea how to, how to discuss this other than thinking about what is the aim.

Comment: Do you have any possibility to give this a family personal help, because he cannot move to a home, but is there any possibility that someone from outside can come and help them, support them to support him, take him out to activities without parents, and so on, is that any possibility?

WO: I think if it is a non-healthcare professional, we could probably engage the PWS Association. I think they are always willing to help and some of these individuals are very motivated, we might be able to engage some of them. We don't have a home that we can bring him in and as I mentioned, probably some of us who are close to him, we could try again and see if we could mediate a session, maybe not in the hospital where it's quite threatening for him, perhaps, but somewhere outside, and then we can try and engage him from there maybe.

Comment: What I think about is someone coming into the home and setting up the structure, make him a day plan with a white board so that he has a plan for every day, that is not to be discussed at all, and fixed meals, so that you try to build up the structure that you have in a PWS home. From this story, the mother is exhausted, and the brothers and sisters are about to run away.

WO: Yes, I see so you mean go to his house, and do the program at home for him.

Comment: Yes, because otherwise if he goes somewhere only one or two times a week, then when he comes home, then it will be the same situation.

WO: Yes, I think that we might have to explore that I think because things are quite dire at the moment, looking at things, so that's a good suggestion. We might have to see if that's a possibility, I suppose.

TH: In a sense what's been highlighted is that the issue of allowing more freedom with food is not a choice because, as it's been described, that will only lead to more weight increase, and all the complications that come with that. Also I think we see here sometimes this dilemma that having a little bit of choice is very problematic for someone with PWS and I think that is sort of what has happened, is that he's

discovered that by escalating his behaviour, he can get some choice, I think that that's how he sort of feels it.

The problem will be that as you try and get control again, he may well escalate his behaviour in response to whatever you do, there is going to be a very tough period. Because of that you've got to get through that and I think what has been suggested is absolutely right, if you can get someone with some skill and experience to take over some of that responsibility by going into the house, and you get a good structure with good activities that will engage him, and give the mother some relief, then you may be able to break that cycle and get control again. It's really about trying to get full control of the food, get consistency and proper management, and possibly whether there's some work that could be done with mom and dad together because there's clearly inconsistency on how they approach it.

On one level we can understand why dad does what he does, but it's not acceptable. That is only going to make things worse. One's got to look to how the parents can be supported to work together and have an agreed strategy on how they approach these things, an agreed strategy that might prevent the outbursts, but also how they manage them when they start so there's a real consistent approach to managing them.

Comment: I just wanted to add that I think is very important, never blame him. If a person comes into the house then say, "Now Mr. or Mrs. This is coming because she likes you very much and she find that you're a very nice person and she really loves to work with you." Because, if they say "This Person comes in to control you, and we are exhausted." Then you lose. So we should have such a praising approach, then it works much better.

TH: Absolutely. Lots of praise for when things go well, and try and back off when things are going badly.

GL: Can I ask Is he still at school, or is he just about to finish school?

WO: He's still a school but in Malaysia for almost a whole year now because of the Covid pandemic, there has not been any physical school. So a lot of the classes are held either online, or some teachers just give out work. So especially for the non-mainstream schools the activities can be quite variable in terms of how they are run. But he is still school going age so he is supposed to be still with his special education classes.

Comment/Q: I'm Winnie's colleague, I'm also from Malaysia. In our setting, you can come to us and we see them infrequently and the patient goes back to their house. In cases like this, where we need someone specialized to come in and take charge or manage, we don't have the manpower to actually do that. Like Winnie was saying, it's literally asking for help from the Malaysian PWS society for parents, who have got

experience, of coming in to help. Do you have any other suggestion who else can come in to do the day-to-day work with the patient?

GL: Do you have any support workers in Malaysia, people who support people with disabilities?

Comment: We have social welfare, people who deal with abuse and things like that but they don't really work closely with our PWS patients, they don't sort out issues like this.

GL: Would it be helpful if, first of all Winnie you brought both the parents in, just the parents, and had a good chat with them and explained to them why the boy is behaving like he is, that he's not a bad boy, that this is all PWS.

My concern is that if he's losing interest in the things he likes and he's not doing things anymore, and he's quite bright, maybe there is a touch of depression, maybe he's feeling quite down about his own situation, and you said he understands that. Is he insightful, he may be, but that's not going to stop him seeking food and getting angry because that's part of PWS, unfortunately. But if things are consistent in his life, starting with his parents, if they can be very consistent in their management, and their support of him, that will at least reduce anxiety a little bit so that maybe more things can happen in a more positive way. And as has been said, you never blame, you praise him for all the good things he's doing.

It also sounds to me like he needs somebody to talk to. Somebody who is not necessarily a professional, or maybe a professional, but someone he can just talk to on his own about how he is feeling. I think that could possibly help as well.

WO: Would you consider like getting him admitted? Not in a medical way, but at least that space, gives them a chance for him to be...

GL: Until he goes back to the home. The home needs to change first because he'll only go back to the same situation. Yeah.

Comment: At this point I was thinking with him, maybe a nice aunt or grandparents if they are fit and healthy, being able to change home for him, you know if they would take over this for a year or two until he goes out of school, and maybe find some kind of controlled work situation, is in my head but if there is nobody, there's no option to change home even in the family, I think this will become very difficult and I think the idea talking first with the parents is extremely important.

WO: Is there a role for vagus nerve stimulation? When living situations cannot get better? It's not easily available and I think we have to try and source for it if there is a role.

TH: I think this is very difficult because there's still limited evidence in this from our two trials, one involving an implanted device and one with the external device, and they work quite effective there. And what vagus nerve stimulation seems to do is make the person more resilient, so they become much more able to cope with a change or

demands or whatever, and better able to control their behaviour. I think it's very difficult if the environment isn't right. Whether vagus nerve stimulation can manage in those circumstances I think is uncertain. The other problem would be, if you use the external device would he be willing to wear it? But he is exactly the sort of person that in many ways we will want to include in the trial that we're hoping to do again about it, so in the future the answer is, it may be if current trials show it to be successful.

If it's approved in Malaysia for treatment of epilepsy, then it may be possible for a doctor to recommend it off label, just like you can recommend a drug off label. But at the moment it's all a little uncertain.

WO: They have the implantable ones for the epilepsy I think, but yes, the external ones might be a little bit challenging, I think.

TH: I think that's the trouble and we really don't have the evidence to suggest, even if he was willing to consent, to go for an implanted one at the moment, I think that's the problem.

WO: Thank you that has been very helpful getting your thoughts and advice. And I think we now know we have to start on changing the environment and the parents and getting everybody to work together as well.

GL: We've had lots of really good discussion but it's now time to hand over to Tony to wrap up.

Tony Holland Summary

I think today's session has just illustrated very vividly, the extreme levels of need in people with PWS. So we had a really excellent talk from Ralf, showing the extreme levels of need with respect to orthopaedics. In his talk he very nicely, illustrated the extent of need in terms of the prevalence of spinal problems in people with scoliosis reaching sometimes as high as 80 or more percent.

He very clearly illustrated the importance of monitoring over time, both in order to intervene early, and how, depending on age and the where the person is in terms of their growth there are different types of interventions. Early on the less invasive or non-invasive interventions and the forms of things like bracing, but then later, the possibility of surgery. I thought what was actually very encouraging was that there were also new approaches that were coming forward that may eventually be applied to people with PWS with great benefit.

There was the traction, the halo gravity traction, for example, the new tethering approaches. And then the issue of dealing with the problem of functional ketosis, that where the head is bent forward so severely. Perhaps the importance to that came out in discussion about addressing issues of bone density. So that is about the use of growth hormone and sex hormone replacements, and then and questions to the

importance of physiotherapy and other forms of intervention throughout the child's life. So we have now a very good recording of the talk, which I think will be very helpful to people across the world to help people monitor the orthopaedic problems of people with PWS.

And then if you contrast that with Winnie's presentation where the focus was on behaviour, so you have orthopaedics and behaviour in one session, and it just shows the requirement for a multi-disciplinary approach to these different aspects of PWS.

It was very nice to hear about the situation in Malaysia, the health services, the role of genetics and the limited number of geneticists you have in Malaysia. We heard about the struggle for some families, particularly where behaviour is a major problem and where there aren't, at present, immediate solutions. I thought your description very well illustrated the real challenge that is not even unique to Malaysia, some of the options may be different elsewhere in the world.

I think it also highlights the importance of how you might try and over the years train people, experts who can go in and support families under these circumstances.

Thank you very much to everyone who attended the session and participated. We look forward to seeing you at future ECHOs in 2022.

Ends.