



IPWSO
International
Prader-Willi Syndrome
Organisation

IPWSO Health ECHO abstract

February 16, 2021: Diagnosis and genetics

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) and Tony Holland (TH)

Presenters: Kate Baker (KB) and Esther Maina (EM)

Video links

Tony Holland: [Welcome and introduction to Project ECHO](#)

Kate Baker: Prader-Willi syndrome: Clinical presentations and genetic diagnosis

[PART 1: Clinical presentations](#)

[PART 2: Genetic diagnosis](#)

[Group chat](#)

KB: "Type all the features of this baby picture here that you think might suggest to you that they have PWS." (Ref): from timestamp 07:45 in Part 1 video.

Chat responses:

- hypotonic
- hypotonia, feeding tube, monitoring, pectus excavatum
- Posture suggesting hypotonia
- Low muscle tone
- muscle weakness, feeding problems
- Tube feeding suggesting poor suck
- feet position and hypotonia
- feeding tube
- abnormal hand/foot position
- difficulty feeding as per feeding tube
- NG feeding, hypotonia (legs splayed apart), drowsy
- Widespread legs suggesting hypotonia
- hypotonia NG tube Fair posture small hands feet
- small hands and foot
- tube, eyes, face, hands and feet

- hypotonia, feeding difficulty
- feeding tube
- Feeding tube suggesting difficulty eating, triangle shaped mouth
- Open-book position, hand-feet attitude, tube -feeding
- a floppy child that do not cry
- they look up, but they not crying and no pain sensitivity
- Other children with hyperphagia were not floppy as babies as we see in PWS

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

Q: Is there evidence that the number of UPD diagnoses are linked to females having children later in life?

KB: I'm not aware of a link there. In theory, it's segregational.

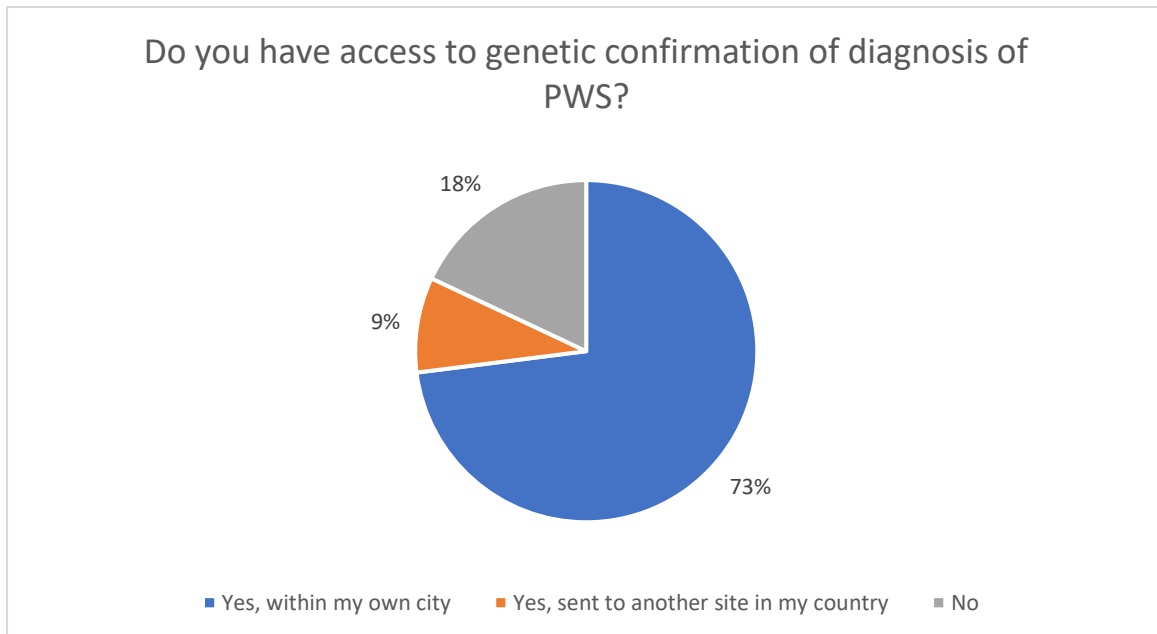
Now there are 2 different forms of PD one where it's the segregation problem pre-conception and one where it's a post zygotic problem and in either situation you end up with 3 of the chromosome fifteens and then what's called Trisomic Rescue where, I explain it to parents as "the father's copy jumps out to say to save the baby."

Segregation during meiosis is a chromosome problem that one would think of within the ballpark of Aneuploidies, which might have an age related link. But I don't know that for sure.

GL: And can anyone else contribute to that please?

TH: We published a paper some years ago in which we looked at the ratio of UPD and deletion in relatively young children, so recently born versus older people, and what we found is that the relationship of the disomy form or the ratio of the disomy increased in the younger group and it was the younger group that then tended to have mothers that were a little older than the older group when they were born, which did suggest that there was a maternal age effect on the risk of disomy therefore changing the ratio a little bit between disomy and deletion causes.

Poll Results

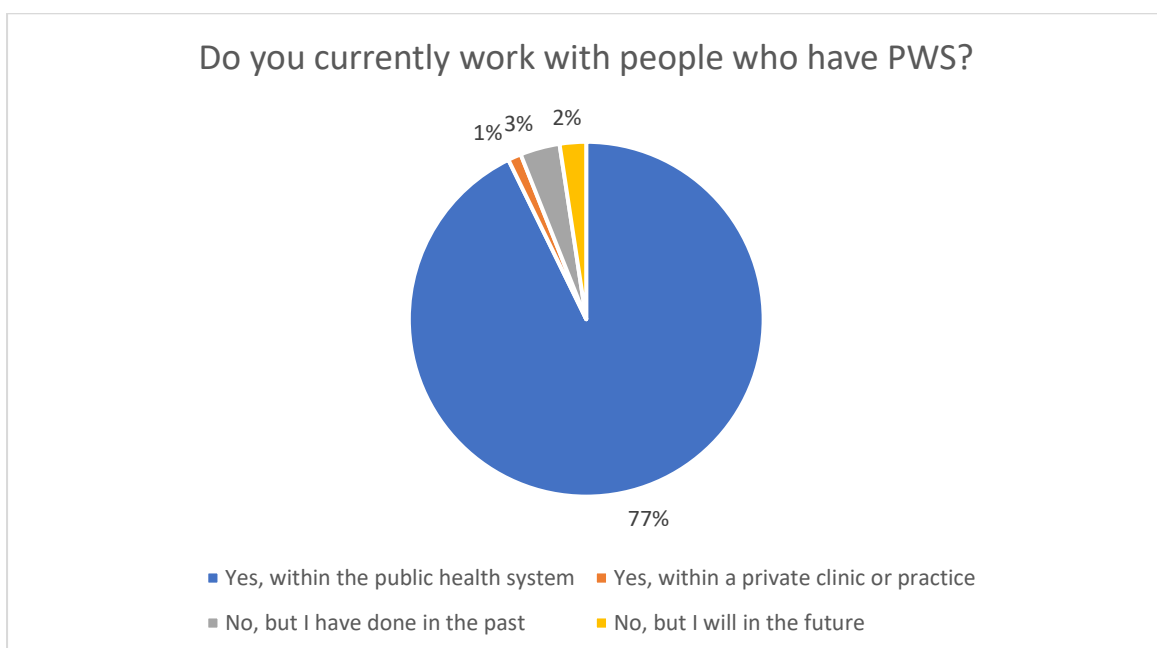


[Group chat](#)

Q: In the survey no one send to BIRD in Italy?

A: Bulgaria : We send to Italy sometimes

If you do not have access to genetic confirmation of diagnosis of PWS and would like to find out about free diagnosis through IPWSO, [see our website for more information](#).



Challenge presentation (Abridged)

GL: Esther Maina is a biochemist and a senior lecturer at the Department of biochemistry at the University of Nairobi, in Kenya. She was previously based at the University in Birmingham, UK, and her research interests include the molecular genetics of PWS. In Kenya she's been preparing collaborative work for researchers, clinicians and families of children with PWS, aiming to improve the awareness and reduce stigmatisation. She's hoping to eventually define a molecular diagnosis protocol for Kenya, and Africa, and connect parents and caregivers in Kenya with support groups around the world.

EM: Kenya is a country of 47,000,000 people. As of May 2019, we had a census and so with that kind of number one would really think that there so many are cases that have been missed going on the 1 in 10,000 to 1 in 30,000 incidence rate in the world, so for me that was one of the driving issues.

As a geneticist, I was pushed to think that being back in Kenya, we can actually do a genotype phenotype correlation issue and be able to narrow down the region. My first job when I got back home, was to try and first understand if there's even knowledge of PWS (in Kenya).

I went first to the clinicians and I talked to clinicians in general. I used a questionnaire to try and ascertain from clinicians or pediatricians. What is their knowledge of or understanding or encounter with PWS?

A problem I had was that I didn't get any communication with the clinicians to determine whether they may have encountered PWS. Maybe some insecurity in actually accepting that maybe they haven't looked out for (PWS) or no one has had that interest because you realise we were in a very different setting and the problems in the developing world are significantly different from the first world. I did actually raise it up and say that how many of our little ones are we losing by virtue of not doing all the necessary things?

I decided to go to special schools where we have children with genetic disabilities and disorders. The difficulty in that is there is a lot of stigma. I tried to interact with pediatricians but information was not forthcoming.

I did share the questionnaire with clinicians in Uganda and Tanzania. I'm still waiting for the answers, but I think the same is true for those other 2 East African countries.

For issues of stigma I found out that there are 2 sides. There is a social stigma and cultural beliefs. The cultural beliefs actually took precedence because rare genetic disorders or even rare diseases which cannot be explained in ways that we are able to understand become a cultural issue. There've been parents were informed that there is some witchcraft, so there's a lot of cultural issues and this goes down to issues of

knowledge. There has been zero dissemination of even just rare diseases and disabilities, physical disabilities. Parents socially do not like that their children with special needs interact with other children with other family members or even go to the doctors. It becomes a family secret.

There is a young lady that I met who is Kenyan and she has Prader-Willi syndrome and that we know because the diagnosis was done in South Africa. She does go out for her clinics to South Africa and to see the endocrinologists and to get some psychiatric care and obviously relate with the clinicians who know what Prader-Willi is about because she was not able to get that assistance in Kenya and so I think this is a benchmark.

Thanks to everyone who responded to Esther's request for feedback on her questionnaire to clinicians in Kenya and wider Africa. Esther says, "I am grateful to everyone who has submitted their fantastic corrections. I will endeavour to re-write the questionnaire and hope fully get the much-needed information."

[Q&A following Esther Maina's presentation](#)

Q: Hi Esther, Do you think the cultural roadblock you are facing spans all levels of society, ie cultural stigma in both educated and uneducated families?

EM: I would say that that it is actually separated by issues of Education. Because the more educated a parent is, by extension in our, in our society, they are more highly positioned in society and even, for lack of a better expression, more affluent. They are and so they can actually access diagnosis information by going to South Africa. But you realise the majority of Kenyans. I would even say to the tune of 90% have no ability and many of them are of basic education, but not at that level of education or affluence.

Going back to issues over social stigma. Even the affluent, educated ones tend to hide their children. So it is actually a very confusing situation. Unless they are now given the knowledge to understand what (PWS is) about these affluent families, tend to hideaway, their children and so we never get to to hear from them.

This young lady is from such an affluent family. But one of the parents is a clinician and so they are the ones who led the young lady to speak to (experts) but I'm sure there are so many others because of the social stigma and the cultural beliefs. I think it is coming from an issue of lack of knowledge. If it is disseminated properly and normalised it can be overcome.

Q: Esther, is there any other disease which was previously 'blocked' by the Society, but is now known and de-stigmatised?

EM: One of the positives of these issues is that in general, mental disorders are there no longer as stigmatised as highly. It is actually spoken of widely and people have also opened up and I'm liking that that that the conversations that are going on that people

are actually able to say that they are suffering from depression and no one sort of talks about witchcraft and so I think by and by is an issue of the disseminated information and it being given to people so that they have an understanding that it is nothing they have done. It is not a family curse or witchcraft. You know, We've seen that in mental disorders and is really good because among teenagers that we were having a lot of suicidal or suicide incidences so that is one of the things that it's actually changing so I'm hoping it's the same for genetic disorders.

Tony Holland Summary

The first message is the issue of clinical features that should actually raise your index of suspicion that this baby, or this child, or this adult might have Prader-Willi syndrome. So the clinical aspect is your route into deciding to do the genetic testing.

We must recognise that although there's certain core features to Prader-Willi syndrome, there will be variation between children, across children, across adults, and so on, but there were certain clues that Kate mentioned, certainly with the adult, what she described as the frog leg posture the feeding tube, maybe the head size. These sorts of things raise your index of suspicion, give rise to a differential diagnosis. In the context of providing safe neonatal care, you have the opportunity to ask yourself, "Does this child have a genetic disorder or an acquired disorder? What is the indication for genetic testing here?"

Also, Kate emphasised the fact that with Prader Willi syndrome, you get an evolution of symptoms over time. So you get, particularly, the change from being a not eating to the development of the hyperphagia and obesity if you're not controlling access to food. Later, the development of evidence of endocrine deficiencies and then the emergence of more psychiatric and psychological problems and then the into adult life, perhaps some of the social impairments, emotional problems and learning disabilities become more recognised and more of a problem.

Recognise that of course, if the diagnosis is not made in childhood, it's going to be important to know what should raise your index of suspicion in later life and therefore seek a genetic diagnosis at that time.

Kate then went into the different genetic forms of Prader-Willi syndrome, most specifically the deletion, the UPD and the imprinting centre defects and then set out what she described as the genetic diagnostic pathway where you have an index of suspicion that this child or this person might have Prader-Willi syndrome, the relevance then in terms of the particular genetic sub type with respect to genetic counselling and the importance of genetics, in terms of really having made a firm diagnosis, being able to inform the parents and those providing care how best to support their child in in the future.

Esther's presentation highlighted a country of close to 50,000,000 population, one of the most rapidly growing populations in the world, where really, there seems to be a complete lack of people with Prader-Willi syndrome and you don't know how to explain that other than the fact that people are not recognizing it and the diagnostic pathway is not undertaken.

She explored with us some of the challenges she had trying to engage with clinicians and how they really failed to engage with her. She then went on to discuss some of the particular problems of stigma when she tried for example, to go to special schools, and how families may keep their children away from others because of concerns of stigma, particularly if they have a clear disability, and how that is relevant to understanding rare disease is more generally within Kenya.

She felt a link with South Africa brought benefit but I think the main message was there's an enormous amount to do in Kenya in terms of helping pediatricians recognise Prader-Willi syndrome, then setting up the genetic and the diagnostic pathways and to do that one really has to try and overcome some of the problems of stigma.

Upcoming Health ECHO sessions

Tue 16 th March	<i>The Care of the Infant with PWS</i> Constanze Lämmer, Pediatric Endocrinology, Diabetology, Nutrition, Somnology and Epileptology.
Tue 20 th April	<i>Endocrinology</i> Charlotte Hoybe, Endocrinology, Metabolism and Diabetology.
Tue 18 th May	<i>Understanding Hyperphagia</i> Tony Goldstone, Endocrinologist, Clinical Researcher.

Planning of future Health ECHO sessions

Thank you everyone who has voted on their preferred topics for future Health ECHOs. It is not too late to have your say. If you have not done so already, please [click here](#) to view the list of suggested topics and vote on which holds the most interest for you.

Thank you very much to everyone who attended the session and participated. We look forward to growing the programme and seeing even more of you on Session 2 in March.

Ends.