



## **IPWSO Summit Meeting 'Newborn screening for Prader-Willi Syndrome and other chromosome 15 abnormalities'**

### **Introduction**

Following suggestions made at the virtual meeting to celebrate the 30<sup>th</sup> Anniversary of IPWSO held in August 2021, we have organized the first 'IPWSO Summit Meeting'. These global conversations will explore key issues relevant to the needs of people with Prader-Willi Syndrome (PWS) and their families. Some will be controversial and such discussions will help IPWSO develop its own policies. Others will consider new advances in diagnosis and treatment and the positive and negative aspects to such developments. One challenge that is likely to be relevant to this and future Summit Meetings will be the fact that access to early diagnosis and to expertise varies very considerably globally and there remain significant health inequalities for people with PWS across the world and also within individual countries.

The format of these meetings will be to have short presentations by experts on the topic and then an open discussion. The first of these Summit Meetings is on newborn screening for PWS. We welcome your suggestions for future Summit topics.

### **Context**

One of the most significant advances for people with PWS and their families has been the possibility of an early and accurate diagnosis. This has allowed new parents to have some understanding of their babies' immediate difficulties, to then care for them in an informed way ensuring the best possible start in life, to undertake those interventions that are either needed or best begun early in life (e.g. growth hormone, diet, physiotherapy), and to inform planning for the future. The expectation is that, wherever the baby is born, medical staff will recognize the symptoms of possible PWS when the baby is observed to be floppy at birth and fails to thrive and will then arrange genetic testing to confirm the diagnosis or not of PWS. However, in countries with limited health care systems and where there may be other major health priorities, diagnostic testing for PWS may not be available at all or may be available only to a small proportion of the population depending on socio-economic factors or on whether the family live in a metropolitan or rural setting. This may be the case even in countries with advanced health care services. Where a diagnosis for PWS is not made early in life, parents are likely to struggle to make sense of their child's difficulties, and early intervention and targeted support will not be given, resulting in the child not having the best start to their life, with likely sub-optimal longer-term outcomes for both the child with PWS and their family.

Virtually all infants born in Australia, Europe and the United States are screened for over 25 rare disorders as part of state-sponsored newborn bloodspot screening programs. Each program predominantly uses biochemical tests on dried newborn blood spots (NBS) collected on filter paper from a few drops of the baby's blood within the first days of life. With further significant advances in genetic technologies and potential therapies the screening of infants at birth for many known genetic abnormalities becomes both possible and potentially advantageous. In some cases such genetic screening can identify the presence of the disorder before signs and symptoms become apparent.

One example is that of Angelman syndrome (AS), which like PWS is due to abnormalities involving chromosome 15. There is the potential of experimental treatment using gene therapy (in clinical trials), the aim being to re-activating the *UBE3A* gene on chromosome 15, whose silencing is the primary cause of AS. A similar treatment has been developed for another rare disorder – Spinal Muscular Atrophy (SMA), resulting in SMA now being added to newborn screening programs around the world. As PWS is like AS, in that it is a chromosome 15 imprinting disorder, it could also be identified at birth using the same screening tests that are being used to identify AS.

With these new genetic tests and treatment technologies becoming available further expansions of existing newborn screening programmes for every infant born are being considered, largely by high resource countries around the world. Governments are having to decide whether or not every newborn child should be screened for some or all of these conditions. It is important that global support organisations, such as IPWSO, are aware of such developments. In this Summit, the place of newborn screening for PWS and other chromosome 15 conditions (such as AS), along with screening for other rare disorders, will be discussed and the questions listed below considered.

### **Questions**

1. Should genetic testing for PWS become routine for every newborn baby regardless of whether or not there are any clinical indications to suggest the presence of PWS?
2. What are the advantages and disadvantages of such an approach if used to screen for PWS?
3. If the advantages outweigh the disadvantages, what priority should be given to a newborn screening programme globally, accepting that there are at present significant inequalities experienced by children and adults with PWS within and between countries?
4. Will different technologies identify different genetic types of PWS, and other conditions associated with chromosome 15 and if so, how does this impact on their suitability for newborn screening for PWS?
5. Should IPWSO take a view on these issues and if so, what might that be?

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Marguerite Hughes, CEO of IPWSO.

Tony Holland, President of IPWSO.

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