Transcript – World PI Week Talks Season 2

Episode 1 - Diagnosis & Screening

Moderator: Sue Saville

Speakers: Prof. Jim Bonham & Prof. Antonio Condino

00:00:08 Sue Saville

Hello and welcome to the World PI Week talks, a podcast series by the World PI Week, a global movement to raise awareness of primary immunodeficiency diseases, PIDs, which takes place on the 22nd to the 29th of April each year.

In this new season for 2022, we will focus on the main themes of this year's campaign, which are early diagnosis and newborn screening, treatment and care, health awareness and preventative medicine, and then latest research. My name is Sue Saville, an independent health journalist. I'm delighted to be hosting these podcasts, to find out more about PIDs with the help of scientific experts, patients, clinical organisations and healthcare professionals.

00:00:56 Sue Saville

We'll be using the hashtag WPIW talks to promote the campaign. So primary immunodeficiencies then are rare but life threatening chronic conditions, which occur when a person's immune system is absent or doesn't function properly. When a defect in the immune system is inherited, that is carried by the genes, it's called a primary immunodeficiency, and there are over 450 forms of primary immunodeficiency which range widely in severity. Primary immunodeficiency often presents in the form of persistent or recurring common infections.

00:01:33 Sue Saville

Sometimes they lead doctors to treat the infections and then miss the underlying cause, which can leave the patient vulnerable to vital organ damage, physical disability or even death. It's estimated that some 10 million people worldwide are living with primary immunodeficiency, and 70 to 90% of people with these conditions are still undiagnosed worldwide. But with the right access to healthcare, lives can be saved.

So for this first podcast, let's find out more about the value of early diagnosis and of newborn screening with the help of two very distinguished guests. We have with us Professor Jim Bonham, who is the President of the International Society for Neonatal Screening, who supports screening programs in more than 80 countries in the world.

00:02:23 Sue Saville

And before this, he was the clinical director at Sheffield Children Hospital and leads the first expanded newborn screening pilot program in the UK. Also with us, Professor Antonio Condino, Professor of Immunology at the Institute of Biomedical Sciences at the University of San Paulo in Brazil and Director

of the Jeffrey Modell Center for primary Immunodeficiencies in Sao Paulo. He helped to set up the newborn screening program for primary immunodeficiencies in Brazil. Welcome to you both. So let's get started. If I could start with you then, Professor Antonio Condino, what then is early diagnosis of PIDs? Why is it so important? What difference would it make for patients to get this diagnosis?

00:03:07 Antonio Condino

Hi, Sue. Thank you. It is very important to make the early diagnosis because those babies have a very profound immunodeficiency, and they will get severe infections that may bring sequelae or even cause the early death of the patient during the first year of life. So we want to make the diagnosis as soon as possible, prevent infections, and in the case of severe combined immunodeficiency, it is necessary to look for the bone marrow transplant as early as possible.

00:03:49 Sue Saville

So then that's the importance. Professor Jim Bonham, what are the main challenges in terms of getting access to early diagnosis?

00:03:58 Jim Bonham

Well, I guess the availability of newborn screening. These children appear normal at birth, so of course they can escape clinical detection. But if you do the right test at the right time shortly after birth, then these patients can be identified and successfully treated.

00:04:13 Sue Saville

So can you tell us more then, about newborn screening? What is it? How is it done? What does it involve?

00:04:19 Jim Bonham

Yes, so it began 60 years ago with a pie in the air by the name of Robert Guthrie, locally known as Bob Guthrie. And he had a niece with a devastating condition called phenylketonuria, and in that condition, children poison themselves by the accumulation of phenylalanine, which causes irreversible brain damage. And of course Bob Guthrie wanted to be able to recognize that early, to allow the treatment, which had just been described, to be put into place earlier to avoid that irreversible brain damage. And he set about devising a test.

But perhaps even more importantly, he set about devising a method of sample collection that we still use today, and often goes by his name actually, the Guthrie card or the Dried Blood spot card.

00:05:09 Jim Bonham

And that allows us to take just a couple of drops of blood onto a filter paper, with the name and address of the patient attached, and that can be sent to a testing center. And he did that back in the early 1960s. He was so convinced that this was important that he sold up and bought two VW Microbuses.

He traveled across the US, and he traveled across Europe, advocating for this spectacularly effective newborn screening test. And since then, just with this particular condition, around about 50,000 babies have been identified in those intervening years and had their lives dramatically changed as a result. And

of course, that's grown now and we see around about 25 million babies in total across the world that are screened by newborn screening, and for up to around 50 conditions in some countries.

00:06:07 Sue Saville

And the program, the pilot that you're leading, what does that involve in terms of expanding and extending this test?

00:06:15 Jim Bonham

Yes, I mean the pilot that I was involved with expanded, we were currently at the time doing four conditions in the UK. We added a further number of conditions to that, to bring us up to almost 10. We're still a little ways off places like the US for different reasons, where they're offering 40 or 50 conditions. But that's what I was involved with then. That's been successful, it's made a big impact to those babies who've been detected. And of course, we're now looking at beginning to screen for this condition that we're talking about today, severe combined immune deficiency and we're beginning to evaluate that too in the UK.

00:06:54 Sue Saville

And let's find out a little bit more about this then, severe combined immunodeficiency, SCID. Professor Condino, from your perspective, how important is it to get newborn screening for a condition like SCID?

00:07:09 Antonio Condino

Well, this is the most severe immunodeficiency. The problem is an impairment, the lack of T lymphocytes and B lymphocytes. The patient cannot mount immune response. The patient does not react, does not produce any antibody. The patient cannot develop an immunological memory. So the consequences are the occurrence of severe infections early in life. That kind of diagnosis we should make and transplant the data up to three or four months of age. Otherwise, the patient will get severe infections and have the risk to die.

Ideally, just to comment about the prognosis, if we transplant this baby up to four months of age, we have a 90% chance of cure. If we postpone it to five or six months of age, we have about 50 or 60% chance of survival.

00:08:26 Antonio Condino

And if we do later than that, the prognosis is very poor. So it's very aggressive, and the only way to treat the patient as early as possible is to make the newborn screening. That's why SCID is a priority for newborn screening.

00:08:47 Sue Saville

And those statistics you give there are quite remarkable then, really emphasizing if you can get in early, get that diagnosis, how much greater are the chances then. But of course, screening isn't available worldwide. Professor Bonham you've looked at screening across the world. How much does it vary?

00:09:05 Jim Bonham

It varies hugely. For instance, at the minute we're screening around about 6 million babies per year for this condition, largely in the US and in around about a third of European countries. But we're seeing other countries adopt this fairly rapidly. So there are regional programs in a number of areas, including Spain, Italy and Brazil that Professor Condino is from, and that accounts for probably another 2,000,000 or so babies per year.

And then there are those countries like the UK, China and other areas around the world that are actively evaluating screening for this condition, and that probably adds another 2,000,000. So I guess that we could look forward, perhaps in the next five years, to expanding that 6 million babies a year tested to perhaps more than double that for this particular disorder.

00:09:57 Sue Saville

For Professor Condino in Brazil, what difference does it make to have this screening if you've looked at survival rates and data across Brazil?

00:10:08 Antonio Condino

Brazil, a huge country, with a population of 200 million people. We have about 2.5 million newborns per year. What we had approved recently, in May 2021; we had approved the federal law expanding the newborn screening program up to 50 diseases. And primary immunodeficiencies are in that group. So we will be screening form SCIDs and for agammaglobulinemia. Agammaglobulinemia is a group of diseases where the patient does not produce antibodies.

We currently have this program already active in the City of Sao Paulo, which is a population of 12 million people, in the state of Minas Gerais and in the capital of Brazil, Brasilia. So in other words, it's about a 45 million coverage of the population. We have in those places where this program is already active, we have a dramatic change of the statistics.

00:11:22 Antonio Condino

Before those pilot programs in Brazil, and before this program was implemented, we had about 90% mortality of SCID during the first year of life. In other words, it's a sentence of death. It's really dramatic. Currently we have about 60% survival, it's dramatic. And we have to push forward, move forward in order to improve that statistics and make it available for all the territory.

00:11:58 Sue Saville

But what then are the problems? What are the challenges in terms of pushing it forward and extending that coverage?

00:12:05 Antonio Condino

The size of the country, which is continental. So, our inspiration is the United States. The United States started in 2008 and finished in 2018. It took ten years for the United States to implement this program. And perhaps that is going to happen as well in Brazil, because the country is so huge and heterogeneous. In the southern regions, we have very wealthy places and no problem to do it. But in the North of Brazil, in the poor areas, then it's going to be a real challenge to do that.

00:12:45 Sue Saville

And then is it all the question of resources? Professor Bonham, with the efforts you're making through your International Society for Neonatal Screening, is it resources that are needed or what actions is your organization leading to try to help here?

00:13:00 Jim Bonham

It is partly about resources, and particularly, as Professor Condino has just said, in low and middle income areas in the world then it's perhaps largely about resources. In developed countries, it's about awareness and it's about really thinking about newborn screening as part of health priorities.

So the way that we're tackling this in ISNS, in the International Society of Neo-Natal Screening, is in terms of low and middle income countries, then we're reaching out to those countries together with partners such as the International Federation of Clinical Chemistry, as part of a global task force to address the expansion of newborn screening in areas that find it difficult to implement that. And we were really encouraged last year.

00:13:45 Jim Bonham

We did a questionnaire across the world, and we had responses from 84 countries wanting to either expand newborn screening or introduce newborn screening. And from those 84 countries we had 425 responses. Some of those were responses offering help, and some of those responses were asking for help. So at the minute, we're at the business end of trying to match up those who are willing to offer help, advice, education, but also some elements of financial support to those who desperately need that.

00:14:22 Sue Saville

You talked about awareness there. Is that meaning that there's a need to educate public, perhaps healthcare professionals, so that the early symptoms are recognized more speedily?

00:14:33 Jim Bonham

Yes, I think in the developed world there are difficult and tricky decisions to make about which conditions are included within newborn screening programs. So what we're also doing, in ISNS, is to try and provide information that will make good policy decision making possible. And we're particularly working with IPOPI, a parents support organization working in the field of primary immune deficiencies, the European Society of Immunodeficiency, and we've created an organization called Screen4Rare.

And, as the name would suggest, it's about promoting screening as part of the policy for the early detection of rare diseases. And what we want to do within that is to provide good quality, unbiased information to support health policymakers in sometimes difficult decisions to know should we include this condition or should we not include it. And if we should, then why should we do that?

00:15:34 Jim Bonham

And of course, some of that is about health economics because it makes sense to detect these children early. It makes sense for the child, it makes sense for the family. And very often, it makes economic sense within the country health care provision.

00:15:51 Sue Saville

Thank you. And Professor Condino, what would you say is needed if other countries are aspiring to try to extend screening? What would you say is needed to make this happen?

00:16:02 Antonio Condino

Well, so it's the combination of resources, financial resources, money. You have to invest in that line of care. And it's good to remind that newborn screening is not just about lab test result. Actually, it is a line of care. Once you get an altered newborn screening test, you have to move forward and make the confirmation, and treat the patient, and manage the family. You have to explain the family what to do. So it's a complete line of care. So it's a matter of money, mentality and political wish as well. So the politicians and the civil society, they may be willing to do that. So it's a common work, it's a joint effort work.

For us, our law was approved last year in May, as a result of a 10 year campaign. And it's implemented in four steps, to finish in 4 years. So I just said about the 10 years in the United States, here it is scheduled for 4 years. But knowing the size of country, for me as a citizen it is going to be acceptable for 10 years because the country is very huge. But the main barrier, we already overcame and we have the resources, we have the political wish and the society is winning for that. So, it's going to work eventually.

00:17:39 Sue Saville

I love that positive note. Thank you both very much indeed for those insights. Professor Antonio Condino, Professor Jim Bonham, thank you very much indeed. You've set out why it's so important that we get the early diagnosis, the value of newborn screening and that positive will to make this happen. Of course, it's so important to remember that access to health care is a basic human right, and every PID patient is entitled to the correct diagnosis and then quality treatment and care.

So in the next episode of this podcast series, we're going to look more closely at treatment options such as immunoglobulin replacement therapy, stem cell transplants, gene therapy, and the role of vaccinations. So with access to the right health care, lives can be saved.

So until next time, do help us promote this campaign using the hashtag WPIW talks. For me, it's goodbye for now. Thank you.