PEDIAPOD JANUARY 2024

Linda de Vries

I'm Linda de Vries. I'm a retired neonatologist. I used to work in Utrecht for almost 30 years. I am now an emeritus professor and I've got a guest appointment in Utrecht and at the University of Leiden where I still do some research.

Geoff Marsh

How are you enjoying being a professor emeritus? Do you now have less responsibility but can just be involved in whatever interests you? What's that like?

Linda de Vries

Yes, it's exactly what you say. You don't have the responsibilities anymore and you can be a little bit more choosy to say, yes, I would like to do this, or I wouldn't like to do this. So I think it gives you a little bit more free time. I also miss being able to do a follow up clinic and talk to the parents and see the children growing up. So it's a mixture.

Geoff Marsh

Can you give us a potted history of how it is you arrived at your current position as a neonatal neurologist?

Linda de Vries

Well, I have to take you back a very, very long time, 40 years ago now. When I was doing my pediatrics, it was becoming possible to also do an elective abroad. So we're talking about the early 80s. My father used to be a GP and then he got interested in hematology and he went to learn this specialty at the Hammersmith Hospital in London. He was there for a couple of years just before the Second World War. When I was finishing my pediatrics, my father had passed but I got in touch with his mentor and he said well, maybe the Hammersmith is a very good hospital to go to for you as well because Victor and Lilly Dubowitz are working here and you may be interested in coming to work with them. So I initially did my six month elective there at the Hammersmith hospital and then I went back to Utrecht and did my neonatology. Then Victor rang me and said he had an open position for a PhD project, and would I like to apply, and I did. Then I actually spent four years there and that really got me very, very interested in the field of neonatal neurology.

Geoff Marsh

Is that what set you down your path in terms of research or were you always wanting to do research as well?

Linda de Vries

When I was there the first time I got interested in learning how to do ultrasound of the brain and Malcolm Levine was one of the first people in the world who did cranial ultrasound in preterm

babies. He taught me how to do it and when I came back for my research, we were just able to diagnose white matter injury using cranial ultrasound so that became the topic of my PhD. In those days we were also starting to be able to do MRI in these preterm babies, so this was all very kind of new and exciting.

Geoff Marsh

Would a contemporary neurologist recognize the images that were coming out of those early forms of MRI and cranial ultrasound?

Linda de Vries

Oh yes well, I mean, it's a world of difference. What you got in those days, they started off with linear ultrasound and you were not able at all to see the white matter. So we really only looked at IVHs and only when there were big cysts in the white matter were we able to recognize them. So the resolution of those ultrasound images has really changed a lot and it's still improving actually with the new equipment that we are getting. And then with the MRI- I always tell this to people and they kind of look at me really surprised- in the beginning when we went to the MRI, we only got single slices. So like now you'll get 1000 slices when you've done your MRI in around half an hour. In those days, you would sit next to the baby for 45 minutes and then you would go back to the unit having only got three slices. And so if you were lucky, you were just having the slices where the brain injury could be recognized. And of course there also the resolution was very different, we couldn't do any advanced imaging techniques like we can do now, like connectivity and DTI. Those were just plain T1 and T2 images.

Geoff Marsh

But they were enough to get your PhD?

Linda de Vries

Oh yes, definitely. It was all very new and the PhD covered that the white matter injury was more important for outcome compared to an IVH. We always thought in the beginning that an IVH, even when it was quite small, would matter and If you had a large IVH then you often died and that you would have a poor outcome. But then once we were able to recognize white matter injury, we found out that white matter injury was bilateral and it often caused a lot of problems to the brain in the future, to the child in the future, developing cerebral palsy was very, very likely. So this difference was kind of the beginning of the PhD and then we looked at postmortem data of those children and we also looked at longer outcomes at two and five years. And of course, looking at risk factors for these conditions as well and trying to reduce the incidence. Actually between the 80s and where we are now, these severe cystic white matter injuries have really dropped in incidence from kind of 6% to less than 1% at present. So it did work to get things better over time.

Geoff Marsh

That must mark the earliest period of us being able to make any predictions about these high risk children?

Linda de Vries

Yes, absolutely. I think in those days it will still kind of 'wait and see' and we don't know. Parents went home with their babies and huge uncertainties and I think what I learned at the Hammersmith and what I also worked on over the next years when I went back to Utrechtl was to kind of get early prediction so that you could start working with the parents and the children very early on and start physio very early and also kind of get rid of that uncertainty. Of course, you know, sometimes you're still uncertain, you don't always exactly know what is going to happen but the prediction improved a lot over time.

Geoff Marsh

So you finished your PhD in London and you went back to the Netherlands where have you been ever since?

Linda de Vries

When I finished my PhD in London, there was a pediatric neurologists from Leuven called Paul Casaer and he suggested to me that if I wanted to spend my life in neonatal neurology, then it's also a very good idea to know more about pediatric neurology, so why didn't I come to him and do a pediatric neurology training before going back to the Netherlands. So that's what I did and after leaving London I was there in Leuven Belgium for two years to train as a pediatric neurologist. Then I went back to Utrecht and yes, I spent the next 30 years there.

Geoff Marsh

So do you think that that was good advice about doing a stint in pediatric neurology and not getting pigeonholed in one particular area of Pediatrics?

Linda de Vries

Yes, I think it was very, very useful for me. And also it was very useful because when I worked in London as a neonatologist with a special interest in neonatology neurology, I also used to do the follow up clinic and I think having done my pediatric neurology, I was also much better equipped to be able to do the follow up clinic in these infants who had been admitted to the NICU.

Geoff Marsh

I'm going to ask you to just swallow your humility and tell us what you think your major contributions have been to neonatal neurology?

Linda de Vries

OK well, it's a hard question but if I had to pick one, I think that I spent a lot of my time working in the field of PHVD, which means 'posthemorrhagic ventricular dilatation' which we tend to see a lot in preterm babies that have a large IVH and then after a couple of weeks they develop enlargement of the ventricles. People tended to wait a very long time to treat these preterm babies because they didn't have any clinical symptoms like vomiting, or apneas and their heads didn't grow immediately. So rather than waiting for these clinical symptoms to occur, we always in Utrecht and in the Netherlands, tried to treat these babies earlier and by treating I mean, putting in a ventricular reservoir and trying to avoid that subsequently to this, they also need a VP shunt. We always thought that the ventricles getting larger without doing anything would give the pressure on the surrounding white matter and lead to more sequelae in these infants. So then we did a randomized control trial and there we either waited for the clinical symptoms to occur or we treated them before these and performed the lumbar punctures and put in the ventricular reservoir earlier, and we were able to show that these children were doing better later on. So I think that was something which changed the policy in many centers. Unfortunately, people are still using the 'wait for clinical symptoms'- kind of policy, but in many centers they changed the policy and they're now treating earlier and I think that's beneficial to the child.

Geoff Marsh

And what do you think are the big issues still confronting research in neonatal neurology?

Linda de Vries

Well, one of the big issues that I think is still there is that doing research with other centers all over the world, especially when they're outside the European Union, it is so hard nowadays to get the ethics permission. You may easily spend a year before you can do a project with somebody in another center. Even in the Netherlands if you want to combine data you may spend a lot of time getting data sharing agreements and some people even say that they find it so difficult that they prefer not to be doing it anymore. So I think that that is a negative issue. Another positive issue is that we are moving the needle so fast. I mean, so much has happened with the introduction of hypothermia in full term babies, we were for the first time able to start treating babies rather than just giving them support, actually doing something positive. I think over the next few decades we will see that we are much more moving away from prediction of outcome to being able to treat babies. I think things like stem cells and additional medications when you cool babies- all of these may make a big impact on the future of neonatal medicine.

Geoff Marsh

How far are we with that?

Linda de Vries

Well in Utrecht just after I left we were able to complete a small study of ten babies who had neonatal stroke. They were given nasal mesenchymal stem cells transmitted intranasally, non-invasively. And now hopefully, they are going to do an RCT with stem cells in this population as well. So there's hope that stem cells are going to work also for the babies who have hypothermia and also maybe for the preterm population, but it's a long journey. Of course, people are also very hopeful about the contribution of AI, Artificial Intelligence, that is going to be really able to help to analyze the MRIs of big cohorts more successfully, to be able to predict or to diagnose things like septicemia in the preterm baby more quickly and more reliably as well. So AI is probably also going to make a huge contribution and one of my colleagues from Utrecht also looked at this in relation to the use of amplitude integrated EEG. That was just published in The Lancet and that was also showing that it was helpful. So I think that is also another very exciting field.

Geoff Marsh

What would your advice be to future generations?

Linda de Vries

Well, enjoy it. It's a wonderful job and things are happening every day. Make sure that you're going to work in a team that is working well together. If you look for a mentor, make sure that you've got some kind of nice connection with them, that your mentor is also giving you enough time to ask questions and to be there for you. Make sure that you collaborate with people within your team but also with other specialties and people abroad. Make sure that you have got a balance of your normal life and your working life because the risk of getting burnout nowadays is quite high because you're really being approached by all these different issues like emails and WhatsApps and whatever every day. Life is much faster than it used to be and I think that is also making it more complicated for the younger generation.