When your world turns dark

Joyce de Ruiter
Ambassador of the Usher Syndrome Foundation

Joyce de Ruiter was sixteen years old when her parents had to tell her that she'd been diagnosed with Usher syndrome: an inherited disorder which deteriorates hearing and especially vision during life, often resulting in people becoming deaf and blind. "Finally, the puzzle pieces of hearing loss and night blindness had been named, but at the same time your whole future outlook wavers." Joyce tells us about the impact this diagnosis had on her life and how it gradually turned into something she now draws strength and courage from.

Joyce and her brother were hearing impaired from birth and started to experience initial symptoms of night blindness around puberty, which was strange, as it didn't run in the family. A diagnosis was lacking until her then 18-year-old brother's vision deteriorated even further and an ophthalmologist diagnosed Usher syndrome. Joyce was diagnosed with the same disorder when she was just sixteen years old, radically changing her life and future plans. "I wanted to study, work, get married, and have a family. Would that still be possible? When I discovered the study Visual Marketing the fire started burning again, even though the name of the study didn't sound very useful when you have a visual handicap. But I always kept making choices that made me happy and I'm convinced this enables me to do the things I want to do - despite all the limitations."

Rushing life no longer

Joyce has worked in HR, Communications, and Events. "I crossed my own limits for too long, because I felt like I had to cram a whole life into half. After my third burnout at age 30, I was declared incapacitated, also because my vision kept deteriorating. It was another one of those moments: what can I still do, what do I want? My eyes and ears didn't work so well anymore, but there was nothing wrong with my brain."

INVESTING IN A POSSIBLE TREATMENT IS CHEAPER THAN LIVING WITH THE LIMITATIONS

She decides to tell her personal story in the newspaper, on radio, and on TV as an ambassador for the Dutch Usher Syndrome Foundation, in order to underline the importance of scientific research and development of treatments. This is how the speaking profession came on her path and she has been working hard on her business for 6 years, with success: "As an independent entrepreneur, I now speak at conferences and events about change and agility. Usher constantly confronts you with problems and changes that you have to learn to deal with. I link my personal story to insights in psychology about how to develop an agile mindset. With that, I try to be of value to other people. I think that is the most meaningful thing you can do in a human life."

Tunnel vision, literally

Joyce is now 38. Her hearing loss is 70 decibels, but with advanced hearing aids she can still function reasonably well. Her vision is greatly reduced, though. "Last year I still had 18 degrees of vision, which is less than a toilet roll I can see through. My orientation on the street is becoming more and more difficult, I haven't been able to ride a bicycle for years and I feel unsafe in crowded environments; all because of my reduced vision. This is why scientific research is so important. Investing in a possible treatment is ultimately cheaper than living with the limitations. It would be fantastic if a treatment can be found that stops the deterioration and that children do not have to experience any hearing or sight restrictions at all. Of course, we hope that all patients with Ushers syndrome will recover. That is why the volunteers of the Usher Syndrome Foundation are putting their heart and soul into continuing to make research into a treatment such as that at the Radboud university medical center possible."

Learn more:
ushersyndroom.nl

Bringing light to the dark

Erwin van Wijk
researcher at Radboud university medical center

From discovering the gene to, hopefully, developing a therapy which will give patients a positive outlook. Erwin Van Wijk has been involved with Usher syndrome research from start to finish, which is quite unique in this field of work as it shows how rapidly developments are following up on each other. "In the most severe form of Usher, children are born deaf and slowly start to lose their vision before puberty. We developed a genetic patch that may be able to limit the damage to vision, our data and the results of the trials look positive."

"The hearing problems in Usher are not easy to treat because the underlying cause already arose during development in utero", says Erwin. "With my research group, I have focused mainly on the visual problems. These arise during life, so there are more opportunities to do something about them at an early stage. The goal of the research was therefore to slow down or even prevent the deterioration of vision. First of all, we need to know which and how genetic defects lead to problems. Mutations in the USH2A gene are the most common, so we took that gene as the primary starting point for developing a therapy."

Restoring the function of light-sensitive cells

Usher syndrome arises from a genetic mutation which causes the loss or malfunctioning of the corresponding protein usherin. Slowly but surely, the light-sensitive cells in the eye progressively die as a result, and people become vision impaired or at a later stage even completely blind. The question is: How can this disease process be stopped? Erwin: "Replacing the mutated gene was technically almost impossible because the USH2A gene is extremely large. Instead, we taped the region of the gene with the mutation with a genetic patch. As a result, a slightly shorter protein is produced, lacking the mutation. When carefully selecting the region to skip, the resulting 'shortened protein' could work almost as well as the original protein. In principle, this would then solve the problem. In cells we saw that the genetic patch indeed masked the region of the hereditary error. Next, we had to demonstrate that the shortened protein is also functional in the eye."

Zebrafish as part of the solution

Erwin stumbled upon an unexpected animal to establish whether the genetic patch could preserve visual function. "Zebrafish happen to have an USH2A gene and protein that's very similar to those of humans. If a mutation is introduced into this gene, the visual function of the zebrafish is also significantly reduced. They are an excellent model for studying USH2A-related visual dysfunction and for determining the effect of a therapeutic intervention. Indeed, visual function of USH2A mutant zebrafish treated with the genetic patch was highly improved."

INITIAL RESULTS FROM A CLINICAL STUDY IN PATIENTS ARE HIGHLY PROMISING

After this, the first careful steps towards the translation of the results into a use in humans could be taken. First tests in Usher patients with a mutation in the specific region of the USH2A gene showed promising outcomes, resulting in the design of a large multicenter follow-up study in which the results of the initial clinical trial will hopefully be corroborated in a large cohort of patients. If results hold up, a request for market introduction can be submitted to the American FDA and the European EMA."