RARE DISEASES

Shahram Attarian – It's meetings with rare people that impress. In my fourth year of medicine, I took part in a consultation where a Portuguese patient with a hereditary amyloid neuropathy was brought in and examined by the intern. The illness was quite advanced, I was left with a memory of the malnourished state of this forty-year-old patient and the look in his eyes. I told myself that he wouldn't be around in another year or two. Then during my internship in neurology during '95 to '96, I met other people with rare diseases. I saw their shock when told, the violence of their despair and their resentment at the injustice when confronted by this disaster. I was attracted by the challenge of the field of neuromuscular diseases, the lack of knowledge, the absence of treatments and the daily difficulties of the patients. I wanted to be one of those few medical research doctors who dare to explore these rare diseases, sometimes ultra-rare, to be someone who took an interest in these black holes of medicine.

What is a rare disease? A very precise definition of a rare disease is one with a prevalence of 1 per 2 500 people. To give you an example based on amyloid neuropathy that I have just mentioned, then in a town such as Marseille there would be three, perhaps four cases! And so far we have identified more than 7000 rare diseases; in my area there are 700. So it's pretty vast. For my part, I pay homage to our forebears who dared to attack this problem of neuromuscular disease when it was an unknown area: Georges Serratrice, Professor Georges Serratrice was a pioneer in 1968. And then Professor Jean Pouget who set up the clinic for neuromuscular disease in Marseille. They had not only curiosity but also courage. I should point out that nowadays it's easier, we are on a path where things are a bit more clear…. From 2018 onwards we have entered an exciting period. First of all are the therapies that act on RNA then there are the genetic therapies where we have the recent Nobel prize for genetic scissors, a very interesting toolbox that lets us cut and paste! In 2021, some very effective new families of treatment emerged and when we look back, we can tell what a road we have travelled…And I believe that in the near future, we will be able to forget the catastrophic situation of this Portuguese patient whose look was so filled with distress and incomprehension.

Now in my area, 50% of diseases are genetic diseases. We are beginning to find treatments… We need access to the genome, access to cells for the treatment to get to where we want and while the treatments are at present intravenous, will they get to their targets? That's not always so: for the muscles yes, the muscles are very permeable but for nerves, the nervous system is very well protected, there is a barrier and at present treatments do not get through this barrier so that's an obstacle to treatment. So some of the medicines must be inserted by lumbar puncture. In the end, it's these patients who need to be looked after so we must

see what is best for them. For example, we do not feel the patient's pain and cannot evaluate their fatigue! It could be that doctors are less perceptive because we do see paralysis or a deficiency like that which is observable! It may be that what really matters to the patient and their quality of life is not what you yourself think. And nowadays we probe more deeply and ask what is important for you? If there is something in your life that we need to improve, what is it? There will be someone who says that it's walking, another will say that it's writing, a third will say that they themselves would like control of their wheelchair. The difficulty is to shape things round the individual and that takes a lot of time and a lot of resource when you have 3000 patients…. But it's patients who matter. We need to listen to them. Now it's difficult to say this to a doctor, I shouldn't say that with age one learns, but in the end one must listen. It's a good lesson.

4 min 47 s