Transcript: Children and Challenges: Treating Pediatric HIV

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Over 2 million children are living with HIV/AIDS around the world. Dr. José Ramos talks with Peter Staley at the European AIDS Conference in Madrid about the challenges facing HIV-positive children and their health care providers, including treatment challenges with fewer approved antiretroviral options and limited dosing information. To see the video click here.

Peter Staley: Hello this is Peter Staley with AIDSmeds.com, and we're reporting from Madrid all week with the European AIDS Conference, and we're here this afternoon with Dr. José Ramos. José is from Madrid. Thank you for welcoming us to this beautiful city. You're the chairman of pediatrics at the University Hospital of Getafe in Madrid. Didn't quite get that pronunciation right, but I'm working on it. I heard you speak this morning about children and HIV. It's an issue we haven't covered on AIDSmeds.com yet, but it's a huge problem. First, frame it for us. How many children in the world are HIV positive?

José Ramos: Well, it is estimated that around 2.3 million children are infected worldwide, nowadays. So it's a huge problem, compared to Western countries, in which the proportion is lower. In developing countries, particularly in the sub-Saharan countries, the problem is huge.

PS: So most of the two million are in sub-Saharan Africa?

JR: Yes, it's estimated that around 2 million are in sub-Saharan Africa.

PS: Is it getting worse or better?

JR: Well, the situation is very difficult now, because even if things are improving a lot everywhere—and in the Western countries we are very lucky to have the advantages that we have for HIV—in sub-Saharan Africa it is estimated that only 2 percent of children are treated nowadays, and of those who would need treatment, less than 10 percent of children are treated. And if we consider the pregnant women in whom we know there are many measures to prevent the vertical transmission from the mother to the child, very few women are treated for a number of reasons.

PS: Now you spoke about the differences about how HIV acts differently in children than it does in adults. Can you explain that?

JR: Yes, that's very important, because most infection in children occurs from the mother, from vertical transmission. So the virus infects when there is an immature immune system, and the virus disseminates to all over the body very easily, including the central nervous system. So it is

estimated that without treatment, around 50 percent of children in resource-poor settings die by the age of two years. So there is a much faster evolution of the disease than in adults.

PS: Besides progressing faster, what is the difference in viral load and CD4 count between children and adults?

JR: This is very important, too, because there are different surrogate markers in children compared to adults. Children start off with very high CD4 cell counts, that physiologically go down. And the drop in the CD4 counts in HIV-infected children is much more pronounced than in adults. It's not rare to see children who lose more than 1,000 CD4 [cells] in the first year of life without treatment. Whereas viral load is also different, because normally, after primary infection in adults, a mature immune system may control, somehow, the viral load replication. After 6 or 9 months, there is what is called a set point that determines the speed of progression. Whereas in children, this set point takes much longer to occur, 5 to 6 years, and remains usually at least one log more [about 10 times higher] than in adults. So this may explain somehow why the rapidity of the disease is greater in children compared to adults.

PS: I think it would be very surprising for many people to hear how much more difficult it is to actually try to treat children with HIV. We don't have many drugs that have been tested in them. Explain how the drugs work differently in children and why it's such a challenge.

JR: Well, despite having a much faster progression of the disease, there is a shortage of data in children, a shortage of antiretroviral drugs and this is due mainly to the fact that we need specific studies of pharmacokinetics, tolerance, toxicity across all ages. A newborn has nothing to do with an adolescent, and we have to make specific studies for both ages. In addition, it's recognized that HIV infection in children has a bimodal pattern, with 15 to 20 percent of children having a very rapid disease progression. So endpoints used in adults cannot be used in children, and we need pediatric formulations that are easy to take—a liquid formulation, in general—and we need compounds that can be taken or swallowed by children, which is not the case with many antiretrovirals.

PS: And it's a real challenge to figure out what dose to give them, correct? Because they're changing weight quickly and variants within children are a lot greater than within adults

JR: That's right, and that's the reason why many children are under-dosed with the antiretrovirals commonly used, and this is why perhaps we are pushing to have TDM, therapeutic drug monitoring. That is not feasible in developing countries, but at least in Western countries, it should be a very important tool in clinical practice. Because there is a lot of variability among many antiretrovirals, and we need to know the set dose is, and also what dose we are giving to the child.

PS: Most of our audience is American, and therapeutic drug monitoring, which actually tries to measure how much of the antiretrovirals are getting into your body, into your blood, into your cells—we actually don't know much about that in the states, because it's not as common as it is being used here in Europe. But you do use it on children.

JR: Yes, but as a research tool, it's not as commonplace. The national health system doesn't pay for it now. But I think at least in the first two, three years of life it would be a very, very useful tool because there is a lot of variability and sometimes when we get an undetectable viral load with

the drugs we are using, but you have the surprise when measuring blood levels that the child has very low blood levels. And sometimes this patient fails after some time, and you always blame it on adherence. And sometimes this is not the case—it's a problem of under-dosing.

PS: What is the most common regimen that we put children on first?

JR: Well, that's an important question, and again, we are having difficulties with the dose of many drugs, and with the availability of many drugs. For example, efavirenz is a very good drug.

PS: Sustiva…

JR: Yes Sustiva is a very commonly used drug in adults, but we can't use it below three years of age, because there is a lot of variability, the liquid formulation is not bioequivalent to the pills, so it's not allowed below three years. So below three years, we generally use lopinavir/ritonavir.

PS: Kaletra…

JR: Kaletra, right. It's a very powerful drug, but it has the problem of the taste. The taste is not good, the syrup, because of the ritonavir component, and sometimes it's difficult for children to take the medication.

PS: They make a smaller pill, though, for certain ages?

JR: Yes, I think it's a very important advance, particularly in resource-poor settings. But again, it cannot be used in children who can't swallow capsules. But the dose would be okay for children over 7 kilos. So if a child is able to swallow this new tablet formulation, it would be a major advance.

PS: Well, your work sounds incredibly frustrating and challenging, but much needs to be done. And we thank you very much for taking the time to talk with us about this very important issue.

JR: Thank you very much.

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