

CHAGAS DISEASE Q&A

INTERVIEW BY KAMRAN RAFIQ (ISNTD COMMUNICATIONS DIRECTOR)

Despite large numbers of patients worldwide, in both poor and wealthy regions, Chagas disease remains one of the most neglected of the neglected tropical diseases globally. Treatments currently exist, however diagnosis can be difficult and current medicines need improving. In addition, many patients infected with *Trypanosoma cruzi*, the parasite causing Chagas disease, simply do not receive or have access to treatment and many healthcare professionals are insufficiently informed about the disease. In this interview, the ISNTD asks leading experts on Chagas disease about their views on the current gaps and priorities in Chagas disease control and patient advocacy.

To the wider global health & NTD community, Chagas disease has always been synonymous with Latin America and, within that geography, linked to the associative indicators of poverty - lack of access to medicine, clean water or sanitation, ill-planned settlements and urbanization... However, there are now growing estimates ranging from 300,000 to 1 million cases of Chagas disease in the USA - what is driving this rise?

Pr. Sheba Meymandi (Director of the Center of Excellence for Chagas Disease at Olive View-UCLA Medical Center): The lower figure of 300,000 is most supported in the literature at present. I don't think there has been a rise in cases so much as a better understanding of the epidemiology, at least among Latin American immigrants. Also, while Chagas disease has traditionally been associated with Latin America, it is important to clarify that it is also endemic in the United States. We have 15 species of the vector spread across the southern half of the country, and we increasingly find autochthonous (locally acquired) cases who never travelled to Latin America nor have Latin American ancestry. Local mammals such as opossums and raccoons, and even dogs serve as reservoirs for Chagas disease in the U.S. (as elsewhere).

The fact is we are unaware of the burden of Chagas disease among the U.S.-born population because the disease is not routinely screened outside of blood donation centers. We are better able to make estimates of Chagas disease prevalence among people born in

Latin America because more research has actually been done south of the border. This enables the World Health Organization to create country-specific estimates, which when cross-analyzed with immigration figures (as was recently done in a study by Manne-Goehler et al.) produces an estimate of over 300,000 cases in this population. Our on-the-ground research in Los Angeles was the first major U.S. study of Latin American born individuals, and after screening 4,755 people we found a prevalence of 1.24%. If we projected this nationally, it would support the figure of about 300,000 cases. However, these are not recent immigrants. Our patients have lived in the U.S. an average of 21.2 years. I don't think there has been a dramatic rise in immigrants bringing the disease, but rather we have only just begun to understand the epidemiology and produce these initial estimates.

Dr. Colin Forsyth (Chagas Epidemiologist, DNDi North America): First, I wouldn't necessarily call this a rise; rather, in recent years, the extent of the disease has been quantified for the first time. I want to emphasize Chagas is not some exotic disease invading across our southern border. Chagas disease has long existed within the southern half of the United States. In Texas, researchers discovered the remains of a male with *T.cruzi* DNA and Chagasic megacolon dating from over a thousand years ago. This is the oldest known case in what is now U.S. territory, but it suggests the transmission cycle has been affecting humans for a very long time. We have 11 species of kissing bugs in the U.S. capable of transmitting the disease, and they

are found in 27 states spread across the southern half of the country. The territory they inhabit could expand northward as a result of climate change. However, the disease has remained hidden in the U.S., as elsewhere, for a variety of factors: its indistinct acute phase; its long asymptomatic period; and importantly, the lack of routine screening in the U.S. health system. Plus, a bulk of the people with the disease are immigrants or inhabitants of rural areas, both groups which have traditionally lacked easy access to healthcare.

Once routine screening of the blood supply was implemented beginning about 10 years ago, cases began to turn up. However, we have still only identified <1% of expected cases. A recent study by Manne-Goehler and colleagues, based on immigration rates and the WHO's 2010 estimates of the prevalence of Chagas disease in various Latin American countries, has estimated there are up to 346,000 cases among the Latin American-born population of the United States. Outside of blood donations, there has only been one large-scale screening study, undertaken by the Center of Excellence for Chagas Disease. This study found 1.24% prevalence among Latin American-born individuals in Los Angeles, and if we projected this figure to the entire Latin American-born population of the United States it would give us over 300,000 people with the disease. We do not have enough data to make the same kind of estimates for autochthonous, or locally transmitted Chagas disease in the U.S.-born population, but we do know that it takes place. Individuals who have never travelled to Latin America nor have any Latin American ancestry have tested positive after donating blood, suggesting the disease may be more common here than was previously thought.

Mr. Antonio Arce (Corporate Affairs & Communications Novartis): The key determinant is migratory movements. *T. cruzi* parasite can travel with population movements from endemic to non-endemic countries such as US, Europe, etc., looking for an improvement in term of employment and living conditions following a local economic crisis, displacements because of local civil wars, etc. Most estimations are based on legal immigration, but by considering non-legal migration, the final number is higher.

Dr. Cameron Durrant (CEO KaloBios): Most estimates seem to land in the 300,000 plus range. Immigration has been thought to be a driver for the majority of the people with Chagas disease in the United States, but it is unclear if there is a real increase for the same reasons, or whether there is a real increase at all. The vast majority of these people are likely to have contracted Chagas outside of the US and most living with

Chagas in the US don't know they have the disease. That said, there are likely significant cases of people with Chagas who have neither visited endemic areas of Latin America, nor are of Latin American descent. The level of knowledge about Chagas diseases in the healthcare professional community is relatively low, except for certain expert centers.

We also know that Chagas can be transmitted to the fetus during pregnancy, so women who have contracted Chagas can pass on the infection to a baby, although actual numbers are relatively low, both in terms of transmissibility and numbers of newborns with congenital Chagas. There may be between ~60-300 new congenital cases of Chagas disease annually in the US, according to Bern and Montgomery, though some people think it could be double that. While it is generally thought to be rare to become infected by the insect vector in the US, some fear this could change due to climate change and other factors. However, some people believe there are more and more new cases being contracted within the US. It may be that these have been previously under-reported or reflect a true rise in incidence. For certain populations, such as people who hunt outdoors regularly in some of the southern United States, the incidence may be much higher than expected, as there are multiple animal reservoirs of the parasite.

Dr. Monica Miranda Schaeubinger (Johns Hopkins Bloomberg School of Public Health): In the United States, there are at least eleven different species of triatomine bugs that are potential transmitters of the disease.¹ However, the real concern by virtue of the incidence of Chagas in the United States does not rely on the triatomine bugs. Except for a few studies, the actual burden of Chagas disease in the United States remains essentially unknown.^{2,3} Of the 55 million people in 2014 who identified themselves as of Hispanic or Latino origin in the US census, 35 percent (19.4 million) are immigrants.⁴ For example, over 50% of immigrants of Mexican origin, which comprise 63% of immigrants of Latino origin, come from Chagas endemic states.⁵ Moreover, with climate change, the triatomine bug that acts as a *T. cruzi* vector has expanded its range north into the United States, and it is increasingly present as far north as Pennsylvania.^{6,7} Furthermore, congenital *Trypanosoma cruzi* transmission is now estimated to account for 22% of new infections.⁸

Pr. Peter Hotez (National School of Tropical Medicine at Baylor College of Medicine, Dean; Sabin Vaccine Institute, President): We're not certain if there really is a rise or whether we just don't have the active surveillance data in place to know for sure. Recent CDC estimates indicate that there are just under 300,000

cases. In Texas where we are working, there is clearly transmission of human Chagas disease from kissing bugs underway. But it's unclear outside of Texas how much disease is due to active transmission within US borders versus immigration. Here in Texas, factors likely linked to Chagas disease transmission include poverty and climate change.

There is obviously a pressing need to raise awareness both in the affected populations - as an example, Latin American migrant workers living in the USA - and also the wider population. In your opinion what would be the most important blend of messages to send out?

Dr. Sheba Meymandi: One thing that keeps patient demand for screening low is that the disease is so poorly publicized at present, at least in the U.S., so getting any message at all out will be a good first step.

But I think that message needs to emphasize two major points: 1) that you can feel perfectly fine and symptom-free for decades even though you are harboring a dangerous parasite, and 2) that early treatment is critical. If people wait until they are starting to feel the effects of chronic Chagas disease, our current treatment is much less likely to help them. On the other hand, early treatment can delay or prevent the onset of the complications of Chagas disease, which can include heart failure and sudden death.

Dr. Colin Forsyth: For people at risk of the disease, we should emphasize two things: 1) Chagas disease is asymptomatic for many years, so you could be unaware you have it and 2) early treatment is critical. Other public health campaigns, such as for breast or prostate cancer, have been able to get this type of message across effectively. The BENEFIT trial suggests treatment with benznidazole is not effective for people who have already begun to develop cardiomyopathy and other complications, but there is another body of evidence that suggests treatment can delay or avoid these symptoms if it is provided early enough, before these complications develop.

The general public needs to know Chagas is not some rare, exotic disease, nor is it being "brought" by immigrants. It has long existed within the U.S., it is not highly contagious from person to person (except through the blood and organ supply, which are monitored), and it is easily treatable if caught in time. These points are very important to convey to the public because some have blamed immigration for "bringing" the disease into the United States, and this is simply false.

Dr. Luis Filipe Delgado (Chief Scientific Officer Novartis Brazil): In the first step, the most important thing would be to raise awareness regarding the diagnostic process of the parasitic infection, and in case of having a positive diagnosis then proceed with respective antiparasitic drug therapy. Secondly, it is also important to raise awareness of pregnant women who have been detected as positive for *T. cruzi* (limiting the risk of mother-to-child transmission), or in blood/organ donors at risk of Chagas infection in order to reduce the risk of donor-donor transmission. Finally, once the cardiomyopathy and FH have developed, you should go to the respective doctor, be very compliant with both non-pharmacological and pharmacological therapy, ideally be educated in HF and rigorously follow the recommendations received.

Dr. Cameron Durrant: A large number of people in the US have a neglected tropical disease, like Chagas – and need help. Raising awareness is vitally important, not just in high-risk populations, but within the healthcare professional community. Unfortunately, raising awareness for testing for such a disease is only good if you have something practical to offer in terms of a solution. Clearly, our company is focused on developing and delivering on such a solution – but we are not there yet, and neither are any of our competitors. The availability of efficacious medicines for Chagas would intrinsically say two things: the US is aware of the need and making strides to take care of this neglected disease; and the policy incentives put in place to help vulnerable, neglected patients are working as intended. I also think there's an opportunity to make the US a model of care for Chagas. Some key things line up in our favor here. It appears the population is in densely populated areas which could make communication, outreach and treatment efforts targeted and effective. We have the healthcare infrastructure to take on a neglected tropical disease. Treating the disease early enough in its natural history with proven agents is vital and helps alleviate downstream morbidity, particularly potentially treatable cardiovascular complications, workplace and domestic impairment and costs, as well as higher costs on the healthcare system. And finally, some other countries may be able to utilize an FDA-approved product in their own markets, given the rigorous stipulations that would have been met for approval in the US.

Dr. Monica Miranda Schaeubinger: In terms of the Latin American migrant workers, an inclination towards a message that tries to be as objective as possible while trying to avoid stigma on one specific population (i.e. immigrants) could be beneficial. Much interest could come from talking about Chagas and its underlying economic burden. I would focus on how

increased attention to preventing, screening and treating Chagas would actually result in financial benefit. Chagas is a costlier disease than for example Lyme disease in the US and other diseases that get more attention and funding.⁹ Considering the high costs of Chagas cardiomyopathy, and the cost-effectiveness of prevention and screening, this would represent a smart investment.

A similar approach might help in endemic countries and to the wider population in general. Portraying Chagas as a disease in how it results in costly and deleterious consequences that could be avoided with screening and prevention could seem more appealing than portraying the disease as a silent disaster that only affects poor people. While I recognize that is the underlying bigger problem, we need to increase interest from different stakeholders that may otherwise not realize the importance of the disease.

Pr. Peter Hotez: Because Chagas disease is mostly a neglected disease of poverty, it seldom commands the attention of other global health threats. So it's a disease of the voiceless poor. We need to get the word out that Chagas disease is one of the most common causes of heart disease among the poor living in the western hemisphere. According to the WHO, approximately 1.1 million people living with Chagas disease now have heart disease (Chagas cardiomyopathy). Sadly we know from the BENEFIT study reported in the New England Journal of Medicine in 2015, approximately 17-18% of those individuals will die over the next 5 years from their disease. We need to make more people aware and enlist the clergy, especially the Catholic Church, the celebrity community, and leaders of government more aware.

I'm particularly concerned that most people living with Chagas disease now live in the four wealthiest nations in the western hemisphere: Argentina, Brazil, Mexico and the USA. This means it's not a resource problem it's an awareness and advocacy problem!

Congenital Chagas has the potential to significantly raise the number of Chagas disease cases. How well are physicians equipped & educated to spot and diagnose this?

Dr. Sheba Meymandi: Currently, not very well. A survey done by Stimpert and Montgomery in 2010, which focused on Chagas disease awareness among different categories of physicians, found that OB/GYNs were the least aware, with 47% having never heard of Chagas disease before. No routine screening exists for women in prenatal care, or for their infants, or indeed for any population outside of

blood donors. Conditions which are much rarer and not as easily treatable do get screened, however. We know from the literature that congenital cases have occurred in the United States, but we currently have only a very limited idea of how extensive they are. Women who have the infection have a 2-5% chance of transmitting Chagas disease to their infants in a setting such as the United States.

Dr. Colin Forsyth: According to Bern and Montgomery, there may be between 63 and 315 new congenital cases of Chagas disease annually. In the U.S., congenital transmission was first documented in Virginia in 2012. However, most of these cases go unnoticed. Stimpert and Montgomery reported the results of a survey of physicians about Chagas disease awareness; roughly half of OB/GYN's had never heard of the disease. Because neither newborns nor their mothers are routinely screened for Chagas disease, it is likely we are missing a significant number of cases, which is a shame, because congenital Chagas can and should be treated.

Dr. Luis Filipe Delgado: As far as we know, Chagas is not on the radar of most primary care providers in the US. This may be changing in areas where there is a large recent-migrant Latin American population. However, certain clinics and clinicians in the immigrant communities are often aware and equipped to counsel a potential mother on testing and/or treatment to prevent congenital transmission. Obstetricians would need to have a level of awareness of the disease to test for it during routine ante-natal visits in women from Latin America. And we also hear that some patients actively seek testing due to family members infected or simply because they come from an endemic country.

Hopefully, through gatherings like ISNTD Chagas, we can find ways for stakeholders from across the spectrum to work together to improve primary care awareness and diagnosis. More hands to the wheel is a good thing. Getting all patients diagnosed is a significant issue beyond expectant or potential mothers.

Dr. Monica Miranda Schaeubinger: As of now, the awareness of Chagas disease amongst physicians is definitely not ideal, particularly in non-endemic settings. Preliminary studies conducted by the CDC found that the awareness deficit in the US was amongst obstetricians and gynecologists, a specialty that is key to screening and prevention this disease.¹⁰

Physicians in endemic areas might be aware that the disease exists and the consequences it brings, but might face a dead end when trying to find treatment

and the conditions to provide adequate follow up, especially in rural areas where this disease is most prevalent.

Awareness of Chagas disease needs to increase in the medical field. In primary care providers and in key specialties such as cardiology, obstetrics and gynecology and gastroenterology. Moreover, adequate screening and treatment protocols would help in treating the disease once detected. This topic goes back to the widely discussed problem on the difficulty for diagnosis, treatment, and surveillance of adverse effects during treatment.

Pr. Peter Hotez: Studis conducted by Susan Montgomery and her colleagues at CDC reveal that there is almost zero awareness by obstetricians regarding the high rate of maternal and congenital infection. This means that there is practically no awareness right now.

In light of the types of messages and call to action that you've highlighted, which types of stakeholder do you think will play an important role in this healthcare messaging or awareness raising phase?

Dr. Sheba Meymandi: I feel the role of primary care providers and staff, especially nurses, will be critical to raising awareness. These are the people who provide day-to-day care for the population at risk and have more opportunities to share messages about Chagas and other diseases of concern. They can reach patients who are still in the asymptomatic phase and will benefit from early treatment. These centers are also located within communities where patients live and are more accessible. We are making efforts to introduce screening for Chagas disease into primary care centers in Los Angeles, and hope that one day screening for the disease will be routine in primary care throughout the country. The problem now is that we only screen blood donations, which does not even begin to capture the total population at risk of Chagas disease. Obviously, it would also be helpful if major public health institutions and media increase the dialogue for Chagas disease to the same levels we see, for instance, in Zika (which affects in the U.S. only a slight fraction of the number of people that Chagas disease impacts).

Dr. Colin Forsyth: The role of primary care physicians and staff is critical. They are on the front lines working with patients providing regular care, which is an opportunity to identify patients and risk and offer screening. Conversely, when physicians/staff at this level of care are unfamiliar with the disease or its treatability, we have found they can pose a significant

barrier to patients receiving timely treatment. Many patients have spent years looking for treatment and have spoken with multiple providers before getting the help they needed. Many more are likely to simply give up if they receive a negative response at their first or second point of contact with the medical system. It is essential to involve primary care providers if we ever hope to screen and treat significant numbers of people and eliminate the disease.

Mr. Antonio Arce: This ailment really requires for us to think more creatively and collaboratively, through Public-Private partnerships with Global Health institutions (WHO, World Bank, etc.), Regional institutions (PAHO, IMF, OECD, etc.) as well as Local (Local Ministries of Health, USAID, etc.). It's only through these collaborative efforts, that we will be able to make a substantial impact against this disease.

Dr. Cameron Durrant: I think there's an opportunity to apply the 'we're-all-in-this-together' approach from the rare disease playbook with Chagas in the US. This includes a symbiotic relationship between disease advocates, expert healthcare providers (perhaps in centers of excellence), industry – such as biopharmaceutical companies like KaloBios, the right mix of policy incentives as well as pharma-to-pharma company collaboration to help generate education, awareness and screening campaigns. We see this happen every day now in the rare disease setting. Organized and active patient-led disease advocacy organizations assertively prod and work with companies to help bring treatments faster, with experts in centers of excellence providing key scientific and practical treatment input, while enlightened policy such as the current Neglected Tropical Disease priority review voucher program provides a rational enticement for shareholders to invest in treating a disease that is otherwise "neglected" by industry due to numerous complexities. We have seen powerful results when these stakeholders join forces for a common goal.

Dr. Monica Miranda Schaeubinger: Universities, medical schools are of key importance. Chagas disease should be included in the medical school curriculum. Local institutions of each country in charge of disease surveillance should promote reporting at local and national levels. It is important to first have a better idea of the actual burden of the disease. Ministries of Health should reinforce Chagas programs at both national and regional levels, and should keep working in conjunction with PAHO to work with other countries in the region. Funding agencies could focus on Chagas disease to promote research.

Pr. Peter Hotez: The ignorance surrounding Chagas

disease is pervasive. We have mostly failed to get the word out, an issue which I hope we can address at the ISNTD summit.

We have come out of the BENEFIT and STOP clinical trials which highlighted important challenges such as the lack of animal models for the disease, difficulties in clinical trial design, lack of biomarkers for end-point measurement... In your opinion where does the R&D community have to now focus its efforts?

Dr. Sheba Meymandi: We need better and easier diagnostics for testing and a more reliable test of cure. We can gauge treatment failure much better than treatment success. It would also be helpful to have biomarkers to help us indicate which people are more likely to develop the chronic phase of Chagas disease, which affects 30-40% of those infected.

Dr. Colin Forsyth: Biomarkers to help us predict who will develop the complications of chronic Chagas disease would be very helpful. Right now we are obliged to treat everyone with *T. cruzi* infection, even though it is really 30-40% who actually develop these life-threatening complications. The BENEFIT trial indicated benznidazole was not effective in halting Chagas disease after the initial onset of cardiac damage. It would be ideal one day to have a medicine that can stop and even reverse cardiomyopathy in chronic Chagas disease. We still need a treatment option which produces fewer side effects. A study is currently underway to assess dosages of benznidazole, as well as combinations of benznidazole with another drug, in an effort to find a treatment regimen which will still be effective while minimizing adverse reactions. Recently there was also an interesting study by Fortes and colleagues which used bioluminescence to show where *T. cruzi* infection tended to persist at different stages following initiation of treatment. Research of this type is very promising for developing a definitive way to measure treatment effectiveness for human Chagas disease.

Mr. Antonio Arce: Science and medicine has interesting data in Chagas HF and many aspects as epidemiology and the general understanding of pathophysiology are areas where great advances are made but much more remains to be done. At Novartis, we believe that in Chagas HF we must join forces among all responsible actors like scientific associations, medical academy, non-governmental organizations, ministries of health, international organizations, pharma industry, etc. But the most important thing is that this effort should be coordinated to maximize the resources available through a great collaboration centered in Chagas HF patients.

Dr. Cameron Durrant: Delivering efficacy is vital. The focus I think should be in two buckets: immediate-term and long-term. In the immediate-term, we must focus on bringing efficacious medicines to as many Chagas patients as possible, as quickly and efficiently as possible. This includes drugs like benznidazole, which we are working to bring to US Chagas patients. Our view – and of course I am clearly biased here – is that our product candidate has been proven in other countries in which it has been approved as efficacious with well-understood safety and tolerability profiles. We hope to be successful in our effort to gain approval of benznidazole in the United States. In addition to offering domestic benefits, a new supplier of drugs like benznidazole could also benefit the Chagas fight in endemic areas, by introducing a new source of an essential medicine.

A significant issue in the US is that it's very difficult for Chagas patients to get medicine. As you know, there currently is no FDA-approved medicine available for Chagas. (Our company is working to address that.) Without a US-approved therapy, an affected person's physician must access drugs through an investigational protocol through Centers for Disease Control and Prevention. The uncertainty, time and administrative requirements in this process means patients are often lost to follow-up and walk away without getting any treatment at all. Approved medicines would open the door to a whole new dialogue about Chagas and building awareness to get people the help they need – and deserve.

Even if an approved medicine were readily available, tackling Chagas in the US also could be different in some ways. First, what is often seen as a rural disease in endemic areas, we've noticed that Chagas is likely more of an urban disease in the US and particularly a disease of the poor. Many immigrants from endemic countries have clustered in metropolitan areas here. Thus, the communities affected by Chagas are most likely in densely populated urban or metropolitan counties, not rural counties.

Second, identifying and treating Chagas patients is already challenging in any country, but it faces additional complexities in the US. For instance, care for this population could be complicated by the new presidential administration's attitude toward undocumented immigrants and immigration overall. We don't know what portion of US patients infected with Chagas might be undocumented immigrants. The reality is no-one really knows.

In the long-term, there is no question that the R&D

efforts should focus on delivering efficacy and tolerability beyond what we know existing drugs provide. We've seen some exciting new possibilities arise, such as Novartis' new early-stage targeted anti-parasitic compound, and we think those should continue to be pursued. Yet, the landscape in every disease is littered with potential new therapies which can take decades and cost a lot to bring through development and ultimately might not offer benefits compared with existing therapies.

So, until new approaches are proven, we must remember that patients need help now and there is no guarantee that new drugs will be more efficacious, or tolerable, than those we know that work. There may also be ways of using existing therapies in new ways. For example, lower doses, shorter duration in some patient groups, potential combination approaches and targeted therapy in high-risk groups. Patients with existing cardiomyopathy in the BENEFIT trial may not have necessarily received optimized therapy in terms of dose, duration and follow-up. Perhaps existing therapies optimized to such patients and in combination with effective therapies for cardiomyopathy, conduction defects and heart failure, provided the tolerability and side-effect profile of such combinations is acceptable, could still provide positive outcomes to such patients.

Thus, when we think about incentives for drugs, we should think about incentivizing relative efficacy – what actually works for patients – not just the seductive promise of novelty. Novelty in and of itself does not guarantee an improvement over existing treatments.

Dr. Monica Miranda Schaeubinger: As Dr. Caryn Bern says, it would be interesting to see the efficacy of adding a second drug while reducing dosage and adverse effects of benznidazole, or looking more into monotherapy with intermittent regimens or lower dose regimens.¹¹ It would also be interesting to focus drug research on different age groups and different stages of cardiac disease. How does treatment benefit patients with no signs of cardiac nor gastrointestinal symptoms?

Pr. Peter Hotez: in my opinion based on the scary results of the BENEFIT study showing 17-18% of people with Chagasic cardiomyopathy will die from their disease, we urgently need better drugs, diagnostics, and/or therapeutic vaccines, in addition to more basic research.

What kind of partnerships and collaborations between endemic countries and the USA would be use-

ful in tackling Chagas?

Dr. Sheba Meymandi: In our population in Los Angeles, we have noted a higher number of cases among Salvadorans. We think it would be very helpful to develop bilateral partnerships with health ministries and other stakeholders in El Salvador, Mexico, and other endemic countries so that we can increase sharing of resources and knowledge, and more effectively reach people in need. For instance, we have seen many of our Salvadoran cases come from a particular part of the country, and this information could be of value to Salvadoran officials looking to create treatment programs. On the other hand, local programs in Latin America often have developed social marketing materials that would more effectively impact Spanish-speaking patients in the United States, and Latin America is currently where much of the cutting edge research on Chagas disease occurs. My center is very involved in the Chagas Platform, which is a community of international researchers, and we regularly attend international meetings to stay in tune with the latest developments. Diseases are not confined by national boundaries, and our R&D efforts should not be, either.

Dr. Colin Forsyth: Binational efforts will be extremely important if we are to eradicate Chagas disease. First, the U.S. is not strictly a nonendemic country, but rather we simply have a lower transmission rate than is found in Latin America, partly due to differences in housing construction, and partly because some of the vectors here behave differently. However, some species of the vector are naturally found on both sides of the border, such as *Triatoma protracta*. The U.S. has the potential to set an example for the rest of the Americas by developing an aggressive program to screen and treat Chagas disease. Unfortunately, we are only setting an example now in terms of our neglect. Clinical and epidemiological research in Latin America and Europe are much more advanced, which is why, for example, we have an idea about disease prevalence in Latin American countries but not for autochthonous cases in the U.S. Major studies on Chagas disease, such as the BENEFIT trial, have all taken place outside the U.S. Thus, there is a missed opportunity to be involved in research which could ultimately benefit people living here.

Further, collaboration with ministries of health in Mexico and Central America could be highly fruitful for developing programs to screen and treat people with the disease. This can help us develop programs to more effectively reach all the people living with Chagas disease. We can use the expertise of our southern neighbours to help us design more linguisti-

cally and culturally appropriate interventions. Many families are split between both sides of the border, and many U.S. workers or tourists may end up being exposed to the vector while in Latin America. It makes sense to have treatment wherever people with the disease reside, not only for moral reasons, but to avoid the calamitous expenses of heart failure and other complications from Chagas disease, and to enable people to continue to live active, productive lives.

Antonio Arce: We consider that we first need to have all the stakeholders at the table, understand their needs and identify critical path forward to tackle Chagas. The partnerships and collaborative efforts may vary in the country and based on the needs.

Dr. Cameron Durrant: The US should benefit from on-the-ground experience in endemic countries and partnerships ranging from providers to advocacy groups to public health experts. But the immigration component in the US Chagas landscape makes it a different dynamic than endemic countries. For instance, some patients might not want to step forward due to their family's immigration status. One of the keys to tackling US Chagas now and in the future will be sorting out this unusual distribution, or market, dynamic.

So, I envision great potential for a novel commercial

approach in Chagas, whereby a collaboration between patient groups, non-governmental, or non-profit organizations, health providers and industry can drive the distribution of and access to an approved therapy for Chagas in the US. This undoubtedly would benefit from expertise and resources of groups from endemic countries, as well as those in the US. Overall, I see this as a great way to explore novel commercial models using collaboration among stakeholders to ensure we cut through the complexities of Chagas, identify and treat the right people and achieve the maximum public health benefit as quickly as possible.

Dr. Monica Miranda Schaeubinger: It is challenging to study Chagas due to spatial heterogeneity, temporal trends, and considerable variability in risk of acquiring the disease in region of origin.¹² Therefore, it would be helpful to have multicenter prospective studies that include regions with as many strains of the parasite as possible. Ministries of Health could strengthen national Chagas programs and work with PAHO in order to combine efforts and strategies.

Pr. Peter Hotez: So far the donor community committed to global health has mostly ignored Chagas disease. We need to get Chagas disease on the radar screen of the major governments and private philanthropies focused on the world's poor.

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DR. SHEBA MEYMANDI

Director of the Center of Excellence for Chagas Disease at Olive View-UCLA Medical Center

Dr Meymandi is the director of the Center of Excellence for Chagas Disease at Olive View-UCLA Medical Center, in Sylmar, CA, which opened in 2007 as the first US clinic for the diagnosis and treatment of Chagas disease. The Center has since diagnosed and treated over 50 patients and conducts free comprehensive mobile medical evaluations in a grassroots effort to educate about the disease and to detect cases early. It also performs important clinical research into rates of prevalence, conduction abnormalities, pregnant women, and congenital transmission. Such research aims in part to identify potential markers for those at risk of sudden death due to Chagas. Dr Meymandi is a Clinical Professor of Medicine at UCLA's David Geffen School of Medicine, the Associate Program Director of the UCLA Cardiovascular Disease Fellowship Program, and the Director of Cardiovascular Research and Invasive Cardiology at Olive View-UCLA Medical Center. She graduated from George Washington University School of Medicine and has a Bachelor's in Psychobiology from the University of Southern California. She completed her Internal Medicine residency at the UCLA-San Fernando Valley Program.



DR. COLIN FORSYTH

Chagas Epidemiologist, DNDi North America

Colin is an epidemiologist and medical anthropologist who lived in Bolivia in the 1990s and became acquainted with the devastating impact of Chagas disease while there. His dissertation focused on the sociocultural dimensions of Chagas disease in Bolivia. He conducted research in 2013 at a nonprofit clinic in Bolivia where more than half of the patient population was infected with *T. cruzi*. He investigated the beliefs, experiences, and treatment strategies of patients affected by Chagas disease, and identified key barriers that hampered access to healthcare. His research won a prize from the Society for Applied Anthropology and has been published in *Social Science and Medicine*. Previously, Colin participated in epidemiological research on access to recommended treatment for heart disease in Florida hospitals. In 2009, he was involved in a project at the Florida Mental Health Institute which documented mental health practices designed for Latinos in different areas of the U.S. He completed an M.P.H in Epidemiology in 2011, and a Ph.D. in Applied Anthropology in 2014, at the University of South Florida, Tampa.



MR. ANTONIO ARCE

Corporate Affairs & Communications Regional Head for Latin America and Canada (LACan)

Antonio Arce is an international business executive with a career of over 15 years of outstanding achievements in key multinational companies. He has worked across an extensive range of markets and cultures such as US, EU, Singapore, Peru and most recently Mexico.

Antonio has a solid background in obtaining results through a focus on win-win collaborative initiatives where he always places his partner at the forefront of any negotiation. He has also focused on major improvements in productivity and cost-effectiveness in his regional positions and in the operations of the countries of which he oversaw. This successful track record makes him a key contributor for the Novartis Group. He is currently responsible for the Regional Corporate Affairs and Communications strategies for Novartis Pharmaceuticals in Latin America and Canada; he oversees the corporate external engagement of the company with other economic, political and social agents that are active in driving better health outcomes.

Previous to his current role, Antonio was the Corporate Affairs Head for Novartis Mexico. Antonio joined Novartis in 2009 in the area of Supply Chain and Logistics for Latin America. He holds a Bachelor Degree in Economics, Marketing and Management Information Systems from Florida International University, and also holds a certificate in International Trade and Logistics from California State University.



DR. LUIS FILIPE DELGADO

Chief Scientific Officer. Novartis Brazil

Luis Filipe is a senior executive with a proven success in business and healthcare sectors (Medical Practice, Medical Education, Consultancy and Pharma segments). He has deep knowledge of the Pharma and Healthcare market from the physician and industry perspective with more than 20 years' experience leading and managing cross-functional, multi-cultural matrix and non-matrix teams in all aspects of Clinical Development and Medical Affairs at country, region and global level.

He currently leads the Medical organization in Brazil with the highest standards of quality and compliance. He is a Member of the Pharma Executive Committee (PEC) Luis Filipe joined Novartis in 2013. Previously, he worked for Eli Lilly, Bristol Myers Squibb, Public and Private Hospitals He has a Medical Degree from Rio de Janeiro State University, Internal Medicine from Rio de Janeiro Federal University and holds an MBA from Warwick University.



DR. CAMERON DURRANT

CEO KaloBios

Dr. Cameron Durrant is the Chairman and Chief Executive Officer of KaloBios, since March 1, 2016. He was elevated to that position after serving on the board of directors starting January 7, 2016. Dr. Durrant's expertise and business career has revolved around transformations, whether for brands, business units, or small companies.

He has particular therapeutic experience in infectious diseases, pediatrics and oncology – coupled with experience as a practicing physician. He has served as board chairman, lead independent director and as CEO for several specialty pharma or biotech companies in both the private and public sector. He has been involved in several exits and has raised significant funding from a variety of sources. His career has been built on extensive experience – including commercial, P&L, US and global responsibilities – as an operating executive at blue-chip pharmaceutical companies. Dr. Durrant has been President and CEO of PediaMed Pharmaceuticals, a company focused on bring important medicines to children in the US; and held senior executive positions at Johnson & Johnson and Pharmacia. He also had earlier roles at GlaxoSmithKline and Merck. He is a prior regional winner of the Ernst and Young 'Entrepreneur of the Year' award.

Dr. Durrant earned his MD from the Welsh National School of Medicine, Cardiff, UK, his DRCOG from the Royal College of Obstetricians and Gynecologists, London, UK, and his MRCP from the Royal College of General Practitioners, London, UK. He practiced medicine for eight years in the UK and Australia. He also earned his MBA from Henley Management College, Oxford, UK.



DR. MONICA MIRANDA SCHAEUBINGER

Johns Hopkins Bloomberg School of Public Health

Mónica Miranda Schaeubinger coordinates a research project on Chagas disease as part of Dr. Robert Gilman's team, at the International Health Department of the Johns Hopkins School of Public Health, where she recently completed a MSPH.

She is a physician from the National Autonomous University of Mexico and her research interests include pediatrics, infectious disease and underserved populations. More specifically, her current work seeks to ascertain the seroprevalence of Chagas disease in pregnant women of Latino origin in Baltimore to elucidate the subsequent effects of Chagas on pregnancy.



DR. PETER HOTEZ

National School of Tropical Medicine at Baylor College of Medicine, Dean; Sabin Vaccine Institute, President; Texas Children's Hospital Endowed Chair of Tropical Pediatrics

Dr. Hotez is an internationally-recognized physician-scientist in neglected tropical diseases and vaccine development. He leads the only product development partnership for developing new vaccines for hookworm infection, schistosomiasis, and Chagas disease, and SARS/MERS, diseases affecting hundreds of millions of children and adults worldwide. In 2006 at the Clinton Global Initiative he co-founded the Global Network for Neglected Tropical Diseases to provide access to essential medicines for hundreds of millions of people. He obtained his undergraduate degree in molecular biophysics from Yale University in 1980 (phi beta kappa), followed by a Ph.D. degree in biochemistry from Rockefeller University in 1986, and an M.D. from Weil Cornell Medical College in 1987. Dr. Hotez has authored more than 400 original papers and is the author of the acclaimed *Forgotten People, Forgotten Diseases* (ASM Press) and the recently released *Blue Marble Health: An Innovative Plan to Fight Diseases of the Poor amid Wealth* (Johns Hopkins University Press). Dr. Hotez served previously as President of the American Society of Tropical Medicine and Hygiene and he is founding Editor-in-Chief of *PLoS Neglected Tropical Diseases*. He is an elected member of the National Academy of Medicine (formerly the Institute of Medicine – IOM), and in 2011 he was awarded the Abraham Horwitz Award for Excellence in Leadership in Inter-American Health by the Pan American Health Organization of the WHO. In 2014 the White House and U.S. State Department selected Dr. Hotez as its United States Science Envoy.