

Leishmaniases in the European Union and Neighboring Countries

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Celine Gossner, a principal expert in emerging and vectorborne diseases at the European Centre for Disease Prevention and Control in Stockholm, Sweden. We'll be discussing animal and human leishmaniases in the European Union.

Welcome, Dr. Gossner.

[Celine Gossner] Hi Sarah. Nice talking to you today.

[Sarah Gregory] So you work for the ECDC. Is that actually part of the CDC in the United States? What activities do the ECDC do?

[Celine Gossner] Indeed, I work for the European Centre for Disease Prevention and Control (in short, it's ECDC). It is not part of the CDC in the U.S., but we consider there are some similarities in the mandate. The Centre is based in the lovely city of Stockholm in Sweden, and to give you an idea on the size we are about 300 staff members. So much smaller than the U.S. CDC. And to conduct our work, we therefore heavily rely on the national public health institutes of the 30 European countries that we are covering. And we also have some specialized networks of experts and laboratories.

So the aim of the Centre is to strengthen Europe's defense against infectious diseases. And to achieve that (or at least work in that direction), we perform surveillance of diseases, pathogens, and vectors; we have a lot of activities of epidemic intelligence; we provide support into most outbreak response; scientific advice; we provide also support in microbiology (even though we do not have a laboratory onsite); we do activities around preparedness; public health training; and actually we also have a scientific journal that is called *Eurosurveillance*. So while we are not part of the U.S. CDC, we closely collaborate with your CDC and we also work with other CDCs, such as Africa and China CDC. And of course we work very closely with the World Health Organization, and particularly their European office.

[Sarah Gregory] Okay. Well let's start with a little bit about your study. It was about leishmaniasis, as we said. What is leishmaniasis? And does it affect animals, people, or both?

[Celine Gossner] Leishmaniasis is a parasitic disease, and it's found in parts of Asia, Africa, Central and South America, Middle East, and also Southern Europe. And the parasite is called *Leishmania* and there are 20 *Leishmania* species that can cause disease in humans and we say that they are pathogenic to humans. So some people have a silent infection, meaning that they do not have symptoms or signs. But when people develop the disease, the most common forms are visceral leishmaniasis (also known as kala-azar), and then people would develop fever, they would lose weight, they would have an enlargement of the spleen and the liver. And without treatment, in most cases the person will die.

The second most common form is cutaneous leishmaniasis, and then people will have skin sores, papules that can develop to ulcers. And depending on the *Leishmania* species and the host immune response, people will develop one clinical form or the other. Leishmaniasis is not only a human disease, it is also an animal disease. So it affects both humans and animals. And dogs, for

instance, are the main reservoir of, and the most susceptible species, of *Leishmania infantum* and they can develop what is called canine leishmaniasis. Other animals can also be reservoirs, and we can cite wild canids, hares and rabbits, rodents, cats, and many more.

[Sarah Gregory] So how is it spread?

[Celine Gossner] The parasite is primarily transmitted via the bite of phlebotomine sandflies, which are very small insect vectors (2–3 mm long). In comparison, mosquitoes such as *Culex pipiens*—which is the main vector of West Nile virus in Europe and also actually in the U.S.—can be up to 10 mm long. So sandflies are very, very small. And they become infected by sucking blood from an infected animal or person and after some development of the parasite in the sandfly gut, the sandfly passes on the parasite to another person or animal during the following bloodmeal.

There are other types of transmission. Direct transmission of *Leishmania* parasite has been reported through contaminated needles (for example, exchange of needles among drug users), also through blood transfusion and organ transplant. And also congenital transmission from the pregnant woman, for example, to a baby has been reported.

[Sarah Gregory] Is it a big problem in those areas you mentioned?

[Celine Gossner] I would say that leishmaniasis is a global problem. The disease is found in 90 countries around the world, and it is difficult to precisely estimate the number of infections occurring globally as part of the cases remain asymptomatic and a small fraction of the cases are actually recorded. We only see the tip of the iceberg. And there are between 700,000 and 1.2 million estimated new human cases of cutaneous leishmaniasis every year globally, and between 50,000 and 90,000 estimated new human cases of visceral leishmaniasis every year. And over 90% of the cases of visceral leishmaniasis, the most severe form of the disease, occur in only 10 countries, and we can cite Brazil, India, Nepal. So these countries really carry a large part of the disease burden.

In Europe, leishmaniasis is less of a concern than in other regions. But the disease is nonetheless endemic in the southern part of the continent and the sandfly vectors are spreading northwards, increasing the areas at risk and relatively large outbreaks have occurred in Europe. A good example would be the outbreak of cutaneous and visceral leishmaniases (that was due to *Leishmania infantum*) that took place between 2009–2012 in the region of Madrid, right in the center of Spain. And there were more than 400 cases during these 4 years, and to date this outbreak is the largest outbreak of leishmaniasis recorded in Europe. And one interesting point about this outbreak is that it occurred in a residential area, near a park where there were hares and rabbits, which acted as the main animal reservoir.

[Sarah Gregory] Could you tell us the 10 worst countries and most endemic countries? You mentioned there were 10.

[Celine Gossner] Yes. So those are Brazil, India, Nepal, Ethiopia, Kenya, Eritrea, Iraq, Somalia, South Sudan, and Sudan.

[Sarah Gregory] Does the EU conduct surveillance for this disease?

[Celine Gossner] So for leishmaniasis, at the European level we exclusively conduct event-based surveillance, meaning that we have a mechanism to detect outbreaks or unusual events that could become public health threats. And for this we rely on different sources of information: media and

also the health authorities in the European countries. And then these authorities should report to us outbreaks of relevance. They can be autochthonous outbreaks, meaning that transmission occurs in their own countries, but also outbreaks among travelers returning from a particular place. And the role of ECDC is then to assess the situation and provide support to the affected countries.

[Sarah Gregory] And what was the goal of your study?

[Celine Gossner] The overall goal of the study was to describe and assess the epidemiological situation with regards to human and animal leishmaniasis in the European Union, but also in the neighboring countries. We also wanted to identify what were the challenges and how ECDC could support these countries in terms of disease prevention and control. And just to clarify, when I speak about neighboring countries, I refer to the countries surrounding the European Union, and they are the countries of Eastern Europe, Turkey and Caucasus, Middle East, and North Africa.

The study was divided in two projects. In the first project, we collected unpublished information through a questionnaire survey (which is what we published in EID). And in the second project, we conducted an extensive review of the literature. And the two projects complemented each other.

[Sarah Gregory] What specifically was the role of ECDC?

[Celine Gossner] ECDC was coordinating and financing this study. But the execution of the projects was done by Dr. Eduardo Berriatua from the University of Murcia in Spain and who is the first author of this paper. And I would like to take this opportunity to personally thank Eduardo for his great work. He's a true professional and it is obvious how passionate he is about leishmaniasis.

[Sarah Gregory] Glad to know that. Who were your international partners?

[Celine Gossner] So on this study we worked with the European Office of the World Health Organization, the European Food Safety Authority (in short, it's EFSA—this is another agency of the European Union that deals with food safety but also animal health), and the third partner was the World Organisation for Animal Health (it's also known as the Office International des Epizooties, or the OIE). So it was a real international and interorganizational work.

[Sarah Gregory] You conducted (as part of the main part of the study) a survey about human and animal leishmaniasis in different countries in and around the European Union over the last ten years. Who answered these surveys? And I don't suppose...you couldn't mail them to every capitol building. How did you do it?

[Celine Gossner] So we designed two online questionnaires: one to be answered by the public health authorities, and the other one to be answered by the animal health authorities. And we targeted 40 countries in Europe, Northern Africa, Middle East, Turkey, and Caucasus. And we selected these countries based on their epidemiological situation, so countries where the disease is known to be endemic plus the countries where there is evidence of presence of sandfly vectors. And we sent one email per country with the two questionnaires, and the email was addressed to the contact points of the four participating agencies or organizations. And these contact points are in national institutes and/or ministries in the targeted countries. So ECDC and WHO contact points are from the public health sector, while EFSA and OIE contact points are from the veterinary sector. So we reached out to at least four people per country, and we

specifically asked them to coordinate their replies so that we would get only one reply to the human questionnaire and one reply to the animal questionnaire. And we also specified that they could forward the questionnaire to the most suitable experts in their country.

[Sarah Gregory] Did you have a good response rate?

[Celine Gossner] So yes, the response rate was very good. We got 70% of countries replying to the animal questionnaire, and 60% of the countries replied to the human questionnaire. And so we were very pleased by these results, especially because the questionnaire was open just for a few weeks in October and November of last year, and we knew that a lot of people were really busy with COVID. So we were really pleased with the answers.

[Sarah Gregory] What kind of questions did these surveys include?

[Celine Gossner] So both questionnaires were divided into the same four sections. The first section was on surveillance, and we asked whether leishmaniasis is mandatory notifiable, what type of surveillance is implemented, and who are the data providers. The second section was on prevention and control, and we asked what actions were taken for prevention and control, and what were the challenges. The third section was on diagnosis and treatment, and there we asked what was used for diagnostic methods and drugs for the treatment. And then disease emergence was the last section, and there we asked whether it was an emerging disease and what were the drivers of emergence.

[Sarah Gregory] And some countries ended up considering leishmaniasis to be an emerging disease and some didn't. What was the difference? Why is this?

[Celine Gossner] So, indeed. According to the questionnaire research, animal and human leishmaniasis are emerging in respectively 13 and 12 countries (or part of the country). So in some countries the disease is considered emergent in animals but not in humans and vice versa. So we should remember that we assessed the responses to questionnaires and therefore the perception of the respondents played a big role. And without solid surveillance data, it is complicated to assess the true emergence of a disease, especially for a complex disease like leishmaniasis. Also, the border between the disease being emergent or endemic can be sometimes difficult to define. But the emergence is a very interesting aspect that we are currently investigating further, and we are completing the literature review and we have collected incidence data in the 40 countries in the scope of the study. And we collected data at the regional level, and we are currently analyzing it to assess its true emergence. This is a work in progress.

[Sarah Gregory] In the article, you write that leishmaniasis is often considered to be a low-priority disease in the EU. Why is this?

[Celine Gossner] So in my personal opinion, it is a catch-22 situation. The disease is not notifiable at the European Union level, so we do not collect highly structured surveillance data (what we call indicators). And without such data, it is difficult to monitor and assess the epidemiological situation, without which it is more difficult to argue for prioritization of resources. Also, there are many other infectious diseases of concern for Europe, and it is a matter of prioritization of resources. So the list of notifiable diseases is regularly revised. The last time was in 2018, and we added Lyme neuroborreliosis. And this is why, through this study, we wanted to collect further information on leishmaniasis.

[Sarah Gregory] What made this survey important or different than previous studies?

[Celine Gossner] So there is quite a lot of publications describing the epidemiological situation in one country or part of a country. But this survey is different as it covers a large geographical area and addressed both human and animal leishmaniases. It therefore allows for some comparisons between countries, even if comparisons should be made with caution. And it also gives a general understanding of the situation in Europe and the neighboring countries. So this survey was just one part of the study, and the literature review should provide complementary information.

[Sarah Gregory] And ultimately what did you find? Was there anything unexpected in your study?

[Celine Gossner] So we were pleased to see that the mapping of the countries with autochthonous transmission matched pretty well previously published information. And this highlighted, to some extent, that the respondents were knowledgeable about leishmaniasis in their country. And we found that animal and human leishmaniases were notifiable in the majority of the countries of southern Europe despite it is not notifiable at the European Union level.

We were surprised to see that only one quarter of the countries conduct surveillance of animal leishmaniasis, which is indicative of its low priority among the animal health authorities. In comparison, surveillance of human leishmaniasis is conducted in 80% of the countries, including all of those with autochthonous infections except one, Serbia. And in terms of prevention and control, the main challenges were the lack of funds and the treatment costs for animal leishmaniasis and lack of funds and capacity constraints for human leishmaniasis. And this is, again, in line with the low level of priority of the disease.

[Sarah Gregory] Did you have any results that didn't agree with previous research and what did you do about that?

[Celine Gossner] So when the results did not match what was previously known, we contacted the respondents in the country to verify the information. And therefore, for instance, we had respondents mentioning that leishmaniasis due to *Leishmania donovani* was endemic in their country, and we could actually clarify that they referred to *Leishmania donovani* complex, which encompasses two *Leishmania* species: *Leishmania donovani* and *Leishmania infantum*, the latter being the only species endemic in Europe. And after analyzing, looking at the results, we provided a detailed report to all respondents to validate the information and our interpretation of the results.

[Sarah Gregory] So generally speaking, what are some risk factors for leishmaniasis?

[Celine Gossner] So the epidemiological cycle of leishmaniasis is pretty complex. And factors affecting the host, the reservoir, the vector, and the environment may favor the emergence and the spread of the disease. For Europe, we can mention alterations in temperature/climate change that are facilitating the northwards spread of the vector; immunosuppression by HIV or organ transplant facilitate the occurrence of the disease; development of drug resistance, meaning that it's more difficult to treat cases but also more difficult to interrupt the transmission cycle of the parasite; increase in travelers and dog importation from endemic regions that can import the parasite into areas where competent vectors are present; and less applicable for Europe (but very relevant for other parts of the world), we can cite deforestation, changes in irrigation habits which change the habitat of the vectors and reservoir host; and in addition, war and poor socioeconomic status are also major contributors to the spread of the parasite.

[Sarah Gregory] How can countries help prevent or control this disease?

[Celine Gossner] To prevent and control this disease, countries need to implement—and this list is obviously not exhaustive—case detection and management, disease surveillance, control of the reservoir hosts (for example, the canine reservoir), integrated vector control (especially in domestic and peridomestic habitats), awareness campaigns among clinicians and also among the population so that they can apply personal protection, and also blood and organ safety measures.

[Sarah Gregory] Okay. So personal protection, how do individual people protect themselves and their pets?

[Celine Gossner] There is no human vaccine or preventive treatment. For humans, the prevention focuses on avoiding the bites of sandflies. And it is important to know that sandflies are most active in twilight, evening, and during the nighttime, so this means that people should be particularly vigilant during that time. And sandflies can bite indoors but also outdoors. So people should wear long-sleeved shirts, long pants, and apply insect repellent. In the home, people can install window screens, use fans and air conditioning. And if there is no window screens or air conditioning, it is advised to sleep under a bed net, particularly in areas where there are high incidence of human leishmaniasis. And it is important to remember that sandflies are smaller than mosquitoes so the screens and nets should be adapted. And there is one vaccine against canine leishmaniasis that is approved for use in the European Union, but it does not prevent infection and the efficacy in preventing diseases is only partial (60–70%). So the prevention focuses again on avoiding sandfly bites, and this can be done by applying insect repellents in the form of dog collars or topical pipettes, but also by keeping dogs inside the house when sandflies are most active.

[Sarah Gregory] Sounds very stressful to avoid them. So the insect repellent would be like the usual stuff with DEET or other things that we use for mosquitoes, yes?

[Celine Gossner] Exactly.

[Sarah Gregory] You mention the concept of One Health in your article. How does this apply to leishmaniasis?

[Celine Gossner] So we refer to One Health as being the collaboration between different sectors to reach a common goal, which in this case is to prevent and control animal and human leishmaniasis. So, leishmaniasis, it might be one of the best examples of disease that should be tackled with a One Health approach. And if we take again the example of the outbreak in Madrid, to control the outbreak, the different stakeholders should diagnose and treat clinical cases, control the hare and the rabbit population, investigate infection in dogs, clear potentially sandfly breeding sites, deliver information to citizens on protective measures, etc. And it is very clear that these actions should be performed by actors from different sectors, who should coordinate among themselves and share findings. And one actor alone will not be enough to control the outbreak.

[Sarah Gregory] In your opinion, what's the biggest challenge in controlling leishmaniasis?

[Celine Gossner] I would say that case detection and management is probably one of the biggest challenge, particularly for *Leishmania infantum*. In fact, a large proportion of the dogs remain asymptomatic (about 60%) and these asymptomatic animals can still contribute to the transmission cycle. Another big challenge is controlling sandfly populations because they breed in terrestrial environments. So they can more or less breed anywhere.

[Sarah Gregory] Well on that rather distressing note, are you looking forward to any plans this summer?

[Celine Gossner] Yes, orienteering. I would describe it as running through the forest with a map and a compass. It is a very popular sport in Sweden, and I plan to be out in the forest every day this summer.

[Sarah Gregory] Did you say running through the forest?

[Celine Gossner] Yes.

[Sarah Gregory] That's interesting. Sounds lovely. I was actually at one point planning a trip to the forests of Sweden this fall, can you imagine? But of course I had to cancel that. Maybe next year.

Well, thank you for taking the time to talk with me today, Dr. Gossner.

[Celine Gossner] Thank you very much, Sarah. It was a pleasure to speak with you.

[Sarah Gregory] And thanks for joining me out there. You can read the June 2021 article, *Leishmaniases in the European Union and Neighboring Countries*, online at [cdc.gov/eid](https://www.cdc.gov/eid).

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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