Controlling neglected zoonotic parasitic infections

Meeting a global challenge?

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Introduction

The increase in both human migration and concomitant HIV infections are likely to cause important changes to the epidemiology of zoonotic parasitic infections. This article aims to explore the feasibility of strategies to prevent and control three neglected zoonotic parasitic infections. It emphasizes the urgency of the "One Health" philosophy, which is premised upon the inextricable connection between human and animal health and the need to safeguard both.

Trypanosoma brucei rhodesiense

Human African Trypanosomiasis (HAT), also known as sleeping sickness, is a vector-borne parasitic disease transmitted by the tsetse fly. There are two subspecies that infect humans. T.b rhodesiense occurs mainly in East Africa while T.b gambiense, arises mainly in West and Central Africa. Both infections are characterized by two similar stages. During an early stage, the preliminary haematolymphatic stage, trypanosomes are found circulating in the blood and lymph nodes, giving rise to hypergammaglobulinemia. The second stage is characterized by symptoms of meningo-encephalitis. Development of the infection in Rhodesian sleeping sickness is similar to that in Gambian, with a few important exceptions. T.b gambiense is chronic and there is little lymphadenopathy. Also, invasion of the central nervous system takes place early in the course of the Rhodesian infection. Finally, T.b rhodesiense has an animal reservoir, in contrast to T.b gambiense, which is mostly confined to a human-fly-human cycle and controlled with detection and treatment of cases.

Control methods:

The ability of the parasite to undergo antigenic variation dampens prospects of mounting an effective immune response as well as developing a trypanosome vaccine. This makes the discovery of alternative methods to control the disease necessary. These control methods have recently shifted from unsustainable, top-down, continent-wide spraying control campaigns, to local and individual control measures that are more feasible. In Uganda, livestock has driven the epidemiology, with a cow being five times

more likely to infect a tsetse fly than a human. This has had a profound impact on national level recommendations. It is now advocated that prophylactic trypanocidal drugs be administered to traded cattle on a regular basis to avoid the development of drug resistance, Unfortunately, until now, there has been a rather irregular use of prophylactic trypanocidal drugs, usually only in villages where cases occur and that have sufficient funds.

Insecticide regimen:

The tsetse fly transmission cycle will be broken when the sleeping sickness parasites are eradicated in cattle, in areas affected by t.b rhodesiense. This consideration led to controlling tsetse with insecticide-treated cattle. Since tsetse flies feed mostly on the legs and on the largest animals in the herd, the application of pour-on insecticides or sprays restricted to the legs, known as the "restricted application method" enables farmers to save up to 80% to 90% of insecticides. However, an insecticide treatment regime requires continuous entomological and veterinary monitoring to assess insecticide resistance and the need for reapplication. This may not be feasible when the sole responsibility for treating livestock lies upon individual farmers, who are often ill-equipped for control, diagnosis and treatment to distinguish among common endemic diseases.

Diagnosis:

Simple molecular tests are urgently needed for monitoring the effectiveness of the "restricted application method". Molecular tools, like PCR targeting the Serum resistance gene (SRA gene), have greatly facilitated the unequivocal identification of T.b. rhodesiense trypanosomes. However, a recent systematic review on diagnosis in first-line health services of endemic countries found that the lack of laboratory infrastructure hinders the integration of PCR and other and other available confirmation tests into the diagnostic algorithm.

Zoonotic Visceral Leishmaniasis (ZVL)

Another vector-borne parasite is the L infantum parasite, which is an obligate intra-macrophage protozoa. It is transmitted by phlebotomine sandflies causing ZVL in humans, and canine leishmaniosis (CanL), mainly in dogs. The emergence of cases of ZVL in new territories is usually preceded by an increase in the prevalence of CanL. A meta-analysis of dog studies confirms that infectiousness is higher in symptomatic cases. Infections in humans are generally subclinical. Most clinical cases occur among children and as opportunistic infections in HIV-infected patients. The endemicity of ZVL indicates that present control methods, consisting of human case detection and treatment, and direct and indirect CanL control methods to remove the source of infection, have been ineffective.

Direct control:

Direct control methods are aimed at infectious dogs. Although dog culling seems to have been effective in the reduction of infections among humans in China, in Brazil, ZVL has increased steadily during the past 10–20 years despite the spraying of 200.000 houses and the killing of 20.000 seropositive dogs per year. Clinical treatment of symptomatic dogs is currently the method used to reduce the infectiousness in countries where culling is considered unethical or not logistically feasible. Although treatment of infected dogs reduces or eliminates clinical signs, it is not usually parasitological curative and treated dogs may still be capable of transmitting the parasite. These direct methods partly rely on the immunofluorescence antibody tests, which are often used for mass screening of dogs.

However, sensitivity and specificity have been reported to be low, leading to many false-positive and false-negative results, the first mainly caused by serological cross-reactivity with other pathogens. There is a need for more reliable diagnostic tests.

Vaccine:
In some areas of Brazil, vaccination of healthy dogs has been used as a preventive tool in combination with regular culling of serologically positive dogs. Despite this promising tool, its use has been debated because healthy vaccinated dogs may present seroconversion, therefore being indistinguishable from infectious dogs.

Indirect methods:
In contrast, indirect methods consist of targeting vectors themselves. Similar to malaria control, which uses deltamethrin impregnated mosquito nets, deltamethrin impregnated dog collars are used for ZVL control. However, despite their potential use in control, the effectiveness of collars on domestic dogs, like direct control methods, will be restricted in areas where wild canines or other mammals constitute a significant reservoir. The failure of dog culling to reduce human cases in Brazil can also indicate the existence of other reservoirs. Both identification of the existence of other reservoirs, as well as accurate and early diagnosis of CanL are required to reduce ZVL. But unless field molecular tools are developed for ZVL, these few available control weapons may be in jeopardy.

Toxoplasmosis

Toxoplasmosis, one of the Center for Disease Control and Prevention's five neglected parasitic diseases, is an important food-borne zoonotic disease caused by infection with Toxoplasma gondii, an obligate intracellular parasite. Toxoplasmosis has been found in nearly all warm-blooded animals. The sexual cycle occurs only in cats, the definitive host. The majority of human infections with Toxoplasma are benign. When symptoms do occur, they are mild and mimic infectious mononucleosis, with chills, fever, headache, myalgia, lymphadenitis and extreme fatigue

Transmission:
Infection can occur by ingestion of sporulated oocysts, following the handling of contaminated soil, cat litter, or through the consumption of contaminated water or meat. Transmission of tachyzoites to a human fetus can occur via the placenta following a primary maternal infection. Such an acute infection in pregnancy may lead to fetal infection and subsequent fetal loss, or birth of a manifestly or latently infected infant. Fetuses, newborns, and the immunologically impaired are at risk for life- threatening toxoplasmosis. The seroprevalence of T gondii antibodies in the human population varies geographically, with prevalence rates approaching 93% in Parisian women who consume undercooked or raw meat and usually exceeding 50% in African countries. While, in industrialized countries, improved hand hygiene has resulted in undercooked meat becoming the most significant cause of T gondii infection, in resource-poor settings, contact with oocyst-contaminated soil is the major means by which intermediate hosts, including humans are exposed.

Congenital transmission prevention:
The major toxoplasmosis-induced public health issue in Europe is congenital toxoplasmosis. Congenital toxoplasmosis may manifest as a mild or severe neonatal disease. Symptoms may include fetal death, stillbirths, or long-term

disabling ophthalmologic and neurologic sequelae, which can be present even when the congenital infection is asymptomatic. Prevention is through primary health education, by secondary serological prenatal or neonatal screening to identify and treat early gestational toxoplasmosis when still asymptomatic, and/or tertiary prevention by administering antimicrobial treatment of infected newborns, to prevent further clinical damage. France, a country with a high incidence of infection, has successfully instituted secondary prevention programs through universal maternal serum screening. The United Kingdom, which has a low incidence of T gondii, has no universal serologic screening program but a nation-wide health education for pregnant women.

In Africa, where the infection rates are likely to be underestimated, a cost effective national screening program is unlikely to be feasible. Pyrimethamine and sulfadiazine are currently recommended in the treatment of toxoplasmosis. These drugs act primarily against the tachyzoite form of T gondii, when visceral disease is clinically severe, following a positive fetal diagnosis. This treatment is often unavailable and may, therefore, not justify a national screening program.

Opportunistic infection

The significance of Toxoplasmiosis as an opportunistic infection has been recognized after the worldwide increase in immunosuppressed individuals. Central nervous system (CNS) toxoplasmosis is almost always caused by a reactivation of CNS lesions, or by the hematogenous spread of a previously acquired infection. Symptoms may include confusion, ataxia, hemiparesis and retinochoroiditis. It occurs during advanced HIV infection when CD4+ counts are below 200 cells/μL. Without adequate prophylaxis or restoration of immune function, patients with CD4 counts below 100 cells/μL who are T gondii IgG-antibody positive have a 30% risk of eventually developing reactivation of disease. In industrialized countries, the incidence rate of Toxoplasmosis as an opportunistic infection has decreased due to the availability of HAART treatment and primary anti-T gondii prophylaxis, trimethoprim-sulfamethoxazole, which is administered to all HIV-infected patients with CD4 counts of <100 cells/μL who are seropositive for Toxoplasma. However, in Africa, approximately 25 million people have an HIV infection, and co-infection with T. gondii frequently remains undetected and thus untreated. Given the public health impact of Toxoplasmiosis in Africa, Africans would benefit the most from the development of a vaccine.

Conclusion

Controlling neglected, vector borne, zoonotic, parasitic diseases entails many challenges.

Affordable and sensitive field molecular diagnostics are needed urgently. Unless a balance is struck between government and community involvement for control initiatives, zoonotic, vector-borne, disease control community-based programs may meet with limited success. Also, there is a dearth of contextualized, evidence-based control methods for controlling the spread of sporulated oocysts in resource-limited settings, which in turn may be hampered by the lack of baseline data. Neglected zoonotic parasitic disease control begs for a One Health approach, uniting human and veterinary medicine, an approach which is also integrated within national HIV prevention strategies.

About the author

Sonia Menon is a PhD student at Ghent University.