

Rapid diagnostics test for detecting Chagas disease - Breaking barriers to diagnosis access in remote areas

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Introduction

Chagas disease (CD) is a widespread zoonosis in Latin America caused by the flagellate protozoan *Trypanosoma cruzi* (*T. cruzi*). It is considered the main Neglected Tropical Disease in the region. The parasite infects 6–9 million people and cause more than 10 000 deaths per year [1]. The route of transmission is mainly vector borne through hematophagous triatomine insects (entomological route). Other routes of transmission of quantitatively lower public health significance are transfusion, connatal and digestive routes, and they are responsible for the urbanization and globalization of the disease [2]. For environmental and social reasons, the insect vector persists in the precarious dwellings of scattered and hard to reach rural populations where the prevalence of infection by this route is greater [3]. Entomological *T. cruzi* transmission persists in the Gran Chaco region, extends over sections of Argentina, Bolivia, and Paraguay, which is considered hyperendemic for CD. Rural populations and indigenous communities in this region have large prevalence rates of CD infection and very limited access to diagnosis and treatment [4–6].

The infection is often asymptomatic or oligosymptomatic in the acute period. The chronic stage is also silent until, after 20 years or more, cardiac and/or gastrointestinal pathologies appear and reduces life expectancy in approximately one third of the patients. The two drugs (nifurtimox and benznidazole) registered for treatment of CD since the late 1960s and early 1970s were shown to be especially effective in young age groups during the acute and early chronic phase regardless of transmission mode. Therefore, chemotherapeutic treatment of CD ideally should provide access to diagnosis as early as possible during the life course. However less than 1% of patients infected with *T. cruzi* have access to parasitocidal treatment due to lack of diagnosis [7].

During the chronic phase, the infection is confirmed by demonstrating the host antibodies against the parasite. World Health Organization recommends the simultaneous use of two serological tests with different principles or that detect antibodies against different specific antigens for the diagnosis of CD at the chronic stage. The results of the two tests must be coincidentally positive. In cases of discrepancy (a positive and a negative test), a third test should be conducted to confirm or rule out infection [8].

The most commonly used conventional serological tests (CST) are the enzyme-linked immunosorbent assay (ELISA) and indirect hemagglutination (IHA) and, in case of discrepancy, indirect immunofluorescence (IFI). There are currently various serological diagnostic techniques being evaluated, each of them using different principles [9]. However, conducting these tests requires equipped laboratories and human resources trained in biochemical analysis [10]. Fluorescence microscope and dark room are also needed for IFI

technique. The transmission occurs most often in populations far from urban centers, where access to health coverage is reduced and traveling to locations where more complex services are available is very difficult. It is also common in some areas in developing countries for births to occur without any control and, therefore, that children do not have access to laboratory testing for early detection of congenital transmission. Likewise, in unexpected situations in which an emergency transfusion is required, sometimes people must choose between the risk involved in the delay caused by the transfer of the patient and the risk of using blood unscreened for Chagas.

In response to the lack of availability in the field of laboratories with the necessary equipment to diagnose this infection, some authors have proposed, both by clinical interest and for population studies, several alternatives to perform CST in areas distant from health centers, such as collecting blood samples on filter paper [11], preserving blood in glycerin [12] and collecting oral mucosal trasudate specimens [13]. Although these studies yielded good results, they required transport of all the samples to the laboratory and the need to return to the field for venous blood sampling of positive patients, with the inherent expenses, loss of patient follow-up and delay in results.

Due to the difficulties described above, there is the need for techniques that can be used in the field, with no highly complex requirements such as specialized personnel and instruments, but that deliver results quickly and reliably.

Immunochromatographic tests with colloidal gold, commonly named rapid diagnostic tests (RDT), have been recently developed for diagnosis of physiological conditions (e.g. pregnancy tests) and infectious and noninfectious diseases. RDT have some advantages, including technical simplicity, conservation of the kits at room temperature, possibility of individual application, and rapid reading of results with no need for an equipped laboratory. These characteristics make them very useful as screening tests in distant sites; however, a positive result must be confirmed later in a laboratory by CST. The low sensitivity values obtained with RDT by different authors suggest that they would be useful only if used in parallel with a CST, rendering them less useful in the field [14–16]. Diagnosis sensitivity can be enhanced by performing tests simultaneously on a single sample. The simultaneous use of two different RDTs with the same sample allows the health

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professionals to obtain a complete diagnosis of CD in remote areas and without laboratory equipment, thereby complying with international recommendations. Given the short time involved in the whole process, including blood sampling, processing and RDT reading, the results can be returned almost immediately. Thus, only discordant samples, which represent a very low percentage, would have to be transported to a laboratory in a Health Center to be resolved using a third method (IHA, ELISA or IFI). On the other hand, in middle complexity laboratories where HAI and ELISA can be performed, RDT could be used to define discordant result in replace of IFI, due to the high specificity demonstrated by different authors [14-16]. Increasing access to high-quality serodiagnosis of marginalized rural populations, the RDTs will provide them the opportunity of treatment and prevent the associated pathologies.

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