PAHO/WHO Schistosomiasis Regional Meeting

Defining a road map toward verification of elimination of schistosomiasis transmission in Latin America and the Caribbean by 2020

Venue: Verdanza Hotel, 8020 Tartak Street
Isla Verde Carolina, PR 00979

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Abbreviations

MDA: Mass drug administration

AMR: Region of the Americas

COMBI: Communication for Behavioral Impact

COPT: Circumoval Precipitin Test

CWRU: Case Western Reserve University

NTD: Neglected Tropical Diseases

SCH: schistosomiasis

Epg: Eggs per gram of feces

LAC: Latin America and the Caribbean

LACEN: National and state central reference laboratory

IVM: Integrated Vector Management

WHO: World Health Organization

PAHO: Pan American Health Organization

POC-CCA: Point-Of-Care Circulating Cathodic Antigen

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses





Executive summary

The endemic and formerly endemic countries in the Region of the Americas (AMR) met with international experts to lay out a road map toward verification of the elimination of the transmission of the schistosomiasis (SCH) in this region, in San Juan, Puerto Rico, 21 and 22 October 2014. See the meeting agenda in **Annex 1** and list of participants in **Annex 2**. No regional meeting on SCH had been held since 2007.

In AMR the only species present is *Schistosoma mansoni*, which is associated with intestinal SCH. The principal risk factor for infection is exposure through domestic, labor, or recreational activities, to fresh water contaminated with human stools infected with the parasite. For transmission to be possible, a snail (intermediary host of the parasite) must be present in the contaminated water, which in this region is primarily *Biomphalaria*. Children and adolescents are at greater risk for infection with this parasite. If left untreated, the infection is chronic and can result in anemia, fibrosis of the intestinal and hepatic veins, splenomegaly; in serious cases it triggers kidney and neurological complications and death.

The interventions recommended by the Pan American Health Organization/World Health Organization (PAHO/WHO) primarily focus on improving sanitary conditions and access to safe water, environmental control, and mass drug administration (MDA). In highly endemic areas, praziquantel is administered to high-risk groups (school-age children, women of childbearing age, and workers in frequent contact with contaminated fresh water), based on prevalence. Treatment at regular intervals prevents the development and progression toward more serious forms of the disease.

During the regional meeting, eight of the ten health authorities from countries in the Americas with a history of SCH who were designated to participate in the meeting ratified the objective of SCH elimination established at the 65th World Health Assembly of the WHO (Resolution WHA65.21, May 2012) and Resolution CD49.R19 of PAHO (October 2009); the representatives of Montserrat and Guadeloupe were unable to attend. At this meeting, countries determined: (1) the epidemiological status of the countries on the road toward elimination of SCH (see **Annex 3**); (2) road maps toward verification of elimination of this disease for each country (to see **Annex 4**); and (3) the challenges and opportunities/recommendations for accelerating the elimination verification process (see page **38 of the report**).

The main conclusions and recommendations of this meeting were (for more detail see page **42 of the report**):

1. Update the epidemiological situation of SCH in the countries to guide the needed public health interventions. The countries are urged to use new geo-referencing technology, new diagnostic tools, and to integrate epidemiological surveys and sentinel surveillance with other neglected tropical diseases (NTDs), or other relevant diseases, in order to be cost-effective.





- 2. Encourage the ministries, partners, and allies channel more human and financial resources into fighting SCH and NTDs in general, including resources for both operating the programs and conducting research. It is recommended that PAHO promote and create the "Ciro de Cuadros Award for innovative and successful NTD control and elimination efforts," to encourage countries to move toward their goals and encourage them to learn about and share success stories. Acknowledging and publicizing the fact that subtle schistosomiasis infection has a significant social and economic impact can help to mobilize resources.
- 3. Define and publish the WHO criteria and procedures for the verification of elimination of the SCH transmission. Experts and working groups must be identified to help the countries meet these objectives, establish a prevalence cut-off point (or basic reproductive rate—Ro) below which transmission is not possible, and make available to the countries existing diagnostic tools useful for each stage: control, interruption, and elimination of schistosomiasis.
- 4. Promote integrated vector management and expertise in malacology.
- 5. Share information on SCH monitoring, evaluation, and surveillance programs at all levels (local, regional, national, and international) so as to help forecast needs and support decision-making. Countries are encouraged to measure data according to the same diagnostic techniques and to present them in the standard form recommended by WHO. Ideally data should be shared using standard WHO formats for this purpose.
- 6. Implement integrated inter-program and inter-sector strategies for the control and elimination of SCH and other NTDs. SCH control and elimination strategies should be addressed collaboratively among countries, universities, and the WHO Collaborating Center (WHOCC).





Background

Schistosomiasis (SCH) is a global health problem; 249 million people are infected in 78 countries, and more than 650 million live in endemic areas.

Schistosomiasis is a disease of the poor who live in conditions that favor transmission. It is also an insidious disease, poorly recognized at early ages but disabling to men and women during their most productive years. Rarely fatal, but strongly linked to diarrhea, pain, fatigue, anemia (hemoglobin deficit), under nutrition, and reduced exercise tolerance; schistosomiasis' effects are not negligible for those who are infected and live in endemic areas where recurring infections are possible.

Schistosomiasis is caused by schistosomes, which are parasitic trematode worms. Five of these species infect humans: *Schistosoma mansoni*, *Schistosoma japonicum*, *Schistosoma mekongi*, *Schistosoma intercalatum*, and *Schistosoma haematobium*. Schistosoma infection occurs through direct contact with fresh water that harbors free-swimming larval forms of the parasite, known as cercariae. These larvae are capable of penetrating human skin and causing infection. This parasite induces severe, acute and chronic morbidity among those infected. Acute SCH occurs 14-84 days after contact with contaminated water. The clinical presentation of acute SCH includes fever, headache, generalized myalgias, right-upper quadrant pain, and bloody diarrhea. Up to 70% of those infected with *S. mansoni* also report respiratory symptoms. Chronic SCH can present through gastrointestinal, liver, neurological, and/or genitourinary pathologies. Schistosomes can live in the host for years. SCH morbidity results from the host's immune response to the schistosoma eggs as their antigens trigger a granulomatous reaction. Granulomas destroy the ovules, but result in fibrotic depositions in the host tissues. Neural pathologies are also known to occur when schistosoma eggs accumulate in the central nervous system of the host. Higher prevalence of epilepsy and transverse myelitis or neuroschistosomiasis is observed in communities where SCH is highly endemic.

In the Region of the Americas (AMR), the only known species of the parasite is *S. mansoni*, which is associated with intestinal SCH. *S. mansoni* continues to be endemic in parts of Brazil, Venezuela, and the Caribbean. It is estimated that 1.6 million school-age children need preventive pharmacological treatment (with praziquantel), primarily in Brazil, and Venezuela. Suriname and Saint Lucia currently have low SCH transmission of SCH in some hot spot areas, and are very close to elimination of the transmission of the disease. In Puerto Rico, Dominican Republic, Antigua, Montserrat, Martinique, and Guadeloupe, available information indicates that transmission may have been interrupted. However, additional evaluation and compilation of evidence are needed to move toward verification of the elimination of SCH in AMR.

The control and elimination of SCH and other neglected tropical diseases (NTDs), is essential to ensure the promotion and protection of international human rights treaties and the "right to the highest attainable standard of physical and mental health." In 2001, the World Health Assembly of the World





Health Organization (WHO) adopted Resolution WHA54.19, urging all Member States in which SCH is endemic to achieve "a minimum target of regular administration of preventive chemotherapy to at least 75% ... of all school-age children at risk of morbidity by 2010." The WHO Global Plan to Combat Neglected Tropical Diseases, 2008-2015, includes SCH as one of the neglected diseases that will initially be targeted. In October 2009, the Directing Council of the Pan American Health Organization (PAHO) adopted Resolution CD49.R19, that expresses a commitment by PAHO Member States to eliminate or reduce the burden of the NTDs in the Region, including SCH, such that these diseases are no longer considered a public health problem by 2015, which would contribute to the attainment of several Millennium Development Goals. Recently, in May 2012, the World Health Assembly adopted Resolution WHA65.21 which urges Member States to eliminate SCH.

The most cost-effective intervention recommended by PAHO/WHO for the control of schistosomiasis is the large-scale distribution of the anti-parasitic drug (praziquantel) in endemic areas to high-risk target groups (communities or school-age children, women of childbearing age, and people in occupations that place them in frequent contact with contaminated fresh water). Treatment at regular intervals helps prevent the disease or its progression toward more serious forms. Furthermore, access to healthy water, improved basic sanitation, malacological control, and environmental enhancements are required to move toward elimination.

PAHO/WHO provides technical cooperation to the endemic countries and is helping obtain donated drugs and other inputs in order to interrupt transmission and eliminate the disease in Latin America and the Caribbean countries.

The endemic and formerly endemic countries within AMR met with international experts to lay out a road map toward verification of the elimination of SCH in the Region of the Americas, in San Juan, Puerto Rico, from 21 to 22 October 2014. The agenda of the meeting is detailed in **Annex 1** and the list of participants is in **Annex 2**.





General Objective

Establish a dialogue and consensus among schistosomiasis experts, partners, and the ministries of health of the endemic and formerly endemic countries in order to coordinate efforts toward verification of schistosomiasis elimination in the Region of the Americas by 2020.

Specific Objectives

- Identify and inventory existing schistosomiasis surveillance and control/elimination programs in the endemic and formerly endemic countries within AMR, and establish how to move from control measures to elimination strategies.
- Estimate the timeframe and resources needed to eliminate schistosomiasis within AMR.
- Compile data in addition to that which already exists, in order to map the current prevalence of SCH and praziquantel treatment coverage (WHO-recommended medication) in the endemic countries.
- Identify epidemiological and ecological data, and activities needed to plan for the elimination of SCH in AMR.
- Identify what information needs to be collected and/or additional evaluations need to be conducted before requesting verification of the elimination of SCH in those formerly endemic countries which may have eliminated transmission of the disease.
- Define AMR's road map toward verification of the elimination of SCH by 2020.





Summary of presentations

Background. Schistosomiasis: Moving from control strategies to elimination in the context of Neglected Tropical Diseases (Chair: Dr. King)

<u>PAHO Overview: Moving from control strategies to Schistosomiasis elimination in the context of Neglected Tropical Diseases (Dr. Catalá)</u>

Throughout the world there are 78 SCH endemic countries, of which 8% are in the Region of the Americas (AMR). Two hundred forty-nine million people require preventive pharmacological treatment, 1% of them in AMR.

In AMR, according to available epidemiological information, ten countries are historically endemic: two (Brazil and Venezuela) need to continue providing preventive pharmacological treatment in focalized areas; another two (Suriname and Saint Lucia) need to confirm interruption of transmission of the disease or to evaluate whether there is residual transmission in some foci and to intervene; and six countries should compile evidence of possible elimination of the disease and request verification of its elimination (Antigua and Barbuda, Martinique, Guadeloupe, Montserrat, the Dominican Republic, and Puerto Rico).

In the Americas there is only one species of *Schistosoma, Shistosoma mansoni*. The main intermediary host is *Biomphalaria glabrata*, and it is believed that there are numerous animal reservoirs, but that has not been sufficiently studied.

Regarding the global and regional framework for the prevention, control, and elimination of Neglected Tropical Diseases (NTDs), since 2008 several mandates, guidelines, strategic plans, and progress reports have been approved and published. In 2007 a worldwide consensus was reached that there were sufficient tools to control and eliminate 17 NTDs, and in 2008 the Global Plan to Combat Neglected Tropical Diseases 2008—2015, was launched. In 2010 and in 2012 progress reports on this global plan were published. In May 2012, the World Health Assembly adopted Resolution WHA65.21, in which Member States are urge to eliminate SCH.

At the regional level, there have been several specific resolutions for some diseases such as onchocerciasis in 2008 and Chagas disease in 2010. But in 2009, Resolution CD49.R19 expressed the commitment of Pan American Health Organization (PAHO) Member States to eliminate or reduce the burden of disease of SCH, together with others NTDs in the Region to such a degree that these diseases would no longer be considered a public health problem by 2015. Another important document is the regional plan to control and eliminate 5 NTDs, including schistosomiasis. Several guidelines were developed to support the development of integrated plans of action and incorporate deworming





activities into existing health platforms in the countries. The last regional meeting on SCH was held in Grenada in 2007, and another sub-regional one was held in Paraguay in 2009. Of the ten historically endemic countries for schistosomiasis in AMR, all were represented at this meeting by a national authority, except for Guadeloupe and Montserrat that were not able to send a representative (October 21 and 22, San Juan, Puerto Rico, 2014).

Many countries are endemic for more than one NTD. For example, Brazil, Venezuela, and Suriname have co-endemicity for leprosy, trachoma, Leishmaniasis, malaria, Chagas disease, etc. It is very important to join forces and design joint approach strategies, and learn from the control and elimination programs that have succeeded against other diseases, such as the lymphatic filariasis elimination program which is combating soil-transmitted helminth infections through the co-administration of DEC+ALB in the Region.

WHO has identified six basic interventions to address NTD, always accompanied by interventions to improve the social determinants of health: (1) Preventive pharmacological treatment (mass, selective or focalized), which consists of distributing drugs to the population at risk of infection based on prevalence of the disease. This intervention is more cost-effective than performing diagnosis and treatment when prevalence rates of soil-transmitted helminth infection, SCH, trachoma, onchocerciasis, and filariasis are above the established limits. The advantage of this intervention is that there currently is a wide spectrum of drugs being donated, which are effective and easy to administer, and have excellent safety ratings and minimum adverse effects. (2) Innovative and intensified management of the diseases: this is a key intervention for such NTDs as leprosy and Buruli ulcer. (3) Vector control and pesticide management. (4) Veterinary public health services for zoonosis control: cysticercosis, echinococcosis, trematodiasis, Leishmaniasis, and rabies. (5) Safe water, sanitation, and hygiene; and (6) Capacity building.

Out of the 23 priority countries in the fight against NTDs in the Region, between 2009 and 2014 the number of countries with a multi-disease approach increased from 5 to 17. A majority of countries have active NTD programs supported by the Ministry of Health. Six countries have comprehensive NTD plans (Brazil, El Salvador, Honduras, Colombia, Guatemala, and Nicaragua).

When coverage with preventive pharmacological treatment in AMR is analyzed for type of disease during the 1995-2012 period, we see that the region recently achieved the levels recommended by WHO for both onchocerciasis and filariasis, in 2002 and 2011, respectively. For soil-transmitted helminth infection and SCH, we see that regional coverage in preschool and school-age children has been below 75% during that period. And for trachoma, regional coverage is also below the WHO recommended level (85%). It is important to expand interventions for these last three diseases, including SCH, and to improve information systems in order to better monitor and evaluate the efforts the countries of the region are making to combat NTDs.





As was discussed with the countries prior to the meeting, the gathering attempted to define where the countries in which SCH has historically been endemic are regarding the following four situations: (1) Country whose objective is to control morbidity (prevalence of severe intensity of infection less than 5% at all sentinel sites); (2) Country whose objective is to eliminate the disease as a public health problem (prevalence of severe intensity of infection less than 1% at all sentinel sites); (3) Country whose objective is to interrupt transmission (elimination, reduction of incidence of infection to zero); and (4) Country that has interrupted transmission (elimination, post-elimination surveillance). Finally, a road map will be laid out for elimination of this disease in the Americas.

WHO Overview: Moving from control strategies with a view to schistosomiasis elimination and the context of Neglected Tropical Diseases (Dr. Jiagang Guo)

A map of the geographical distribution of SCH shows that the areas with the highest rates of infection are in Africa. In the Region of the Americas, Brazil, and Venezuela are the only countries which, in principle, require preventive pharmacological treatment. Furthermore, Saint Lucia and Suriname need to update their information in order to plan and redefine their objectives with a view to elimination of the disease. Antigua, the Dominican Republic, Guadeloupe, Martinique, Montserrat, and Puerto Rico should confirm whether interruption of transmission has been achieved.

WHO envisions a world free of schistosomiasis. Its objective is to control morbidity from SCH by 2020. It also seeks to eliminate SCH as a public health problem by 2025 and interrupt transmission in AMR and the other continents by 2025. To this end, control and elimination activities must be stepped up in all the endemic countries, which include ensuring an adequate supply of praziquantel and other resources to meet demand.

The most important points of Resolution WHA65.21 (May 2012), which promotes the elimination of SCH, are: (1) Identify countries that have interrupted transmission; (2) Encourage Member States and the international community to provide sufficient resources, particularly interventions related to the administration of drugs, drinking water, and proper sanitation to intensify control programs, and to launch elimination campaigns, where appropriate; (3) Adopt other components to control the source of infection: malacological control, education, hygiene, agricultural practices, etc.; (4) Promote assessments of transmission interruption and give recommendations and guidelines for performing it; (5) Prepare a procedure to interrupt transmission with a view toward elimination; and (6) Support the country during the post-elimination stage (surveillance phase) in order to prevent reintroduction of the disease.

For SCH elimination, there is a need to develop and implement effective strategies to control reservoirs in animals (there are more than 40 different reservoirs), as well as the intermediary hosts—snails. Finally, pharmacological treatment is not 100% effective; a dose of 40mg/kg has a cure rate between





80% and 90%, and the eggs can continue to be eliminated for months after treatment. Furthermore, compliance with treatment has been seen to decline from one year to the next (low coverage).

The road from control to elimination is a long one. For example, in China it took 50 years. There was reservoir control (basically of water buffalos), malacological control, preventive pharmacological treatment, and later post-elimination surveillance to prevent reintroduction. To date (2014), surveillance is still conducted and although there are no cases of local infection, some snails (intermediary hosts) are still found.

The key strategies for each stage of SCH control and elimination programs have been determined. To control SCH morbidity, preventive pharmacological treatment, provision of safe drinking water and adequate sanitation, and hygiene education are the interventions needed. In order to eliminate SCH as a public health problem, the previous interventions (except for pharmacological treatment) are recommended; the latter should only be distributed in foci of transmission. The use of molluscicides in combination with environmental changes is also recommended, to limit the intermediary host (agricultural practices and construction of water works). In the interruption of transmission phase, it is important to reinforce surveillance. SCH is a disease that should be reported, in order to monitor and intervene rapidly in case the disease reappears.

In order to confirm elimination of this disease, a five-year surveillance period must be completed without any cases of people carrying the disease and with no infected domestic animals or infected snails (in China a ten-year period was established). The verification of elimination should be done through an independent panel of experts.

Finally, it is key to establish which diagnostic tests should be used at every phase of the process of control and elimination of SCH. For morbidity control the Kato-Katz technique can be used; filtering urine and urinary antigens is very easy to use and has adequate sensitivity and specificity. For the phase of elimination as a public health problem, the Kato-Katz technique can be used; emergence of the eggs and DNA detection tests of the parasite or of antigens can be used. In the interruption of transmission phase, currently available diagnostic methods are not very easy to use and the antibody detection tests are not very easy to interpret. However, the antibody detection tests can be used more than five years post-elimination and should be used on children up to age five. Tests to detect the DNA of the parasite can also be used on the intermediary hosts.

The challenges posed by verification of the elimination of SCH are to identify tests that are sufficiently sensitive and specific for the post-interruption of transmission phase, and determining the diagnostic criteria (case-finding, reservoirs, and infected snails). Finally, which indicators to use must also be determined (for example, in China it was the identification of snails, but that is very expensive).





DISCUSSION AND OBSERVATIONS

Moderator: We are proud of the many examples of SCH control in neighboring countries, such as Puerto Rico, which a few decades ago had levels of SCH infection similar to those of the African countries. He commented on the importance of the disease given its great morbidity: it causes congenital morbidity, and generates chronic inflammation from the ulcers made by the parasite when eliminated from the body through feces or urine.

It was stressed that in order to move toward elimination of the disease we should ask ourselves what resources and technical guidelines we need. We must create a monitoring, surveillance, and external audit program. The speaker mentioned that the establishment of a national program was essential for elimination of SCH in China. WHO has invited the experts to issue guidelines regarding how the verification of elimination should be conducted.

It was mentioned that Saint Kits should also have been invited, because historically cases have been identified in green monkeys. Transmission of SCH in rodents was described in Guadeloupe.

It was stressed that Antigua and Barbuda no longer has SCH because they diverted the water from where the snails were. It is easier to control SCH transmission on an island than in a large territory. To control snails, the environment must be modified and people capable of identifying this type of species are required. A list of people with experience in malacology is needed for the region of the Americas and there must be capacity building in this subject in the region.

Problems in the countries (Saint Lucia and Antigua): need to standardize tests among countries.

Brazil: Says it would be important to define goals for elimination at the national and sub-national level before talking about eradication criteria.





Topic 1.A. Epidemiological status of schistosomiasis in endemic and formerly endemic countries: Updates on SCH control/elimination programs and integration with other NTDs—Challenges and opportunities towards schistosomiasis elimination (Chair: Dr. Cook)

Brazil (Dr. Castalia and Dr. Scholte)

Demographic aspects: Brazil has a land area of 8 million km², with a total of 5,570 municipalities in 27 states. Its population is 201 million (85% urban), of which 85% have access to safe drinking water.

Historical framework: Five moments in time stand out within the chronology of SCH control strategies: (1) In 1975 the special SCH control program was established, with stool surveys, massive treatment based on prevalence, use of molluscicides, and basic sanitation projects. (2) In 1980 the federal government gave the municipalities human and financial resources for SCH control. Selective treatment of children aged 7-14 was started and massive treatment was done in areas with prevalence above 50%. (3) In 1990 the programs already established in the municipalities became decentralized. Treatment of cases, snail control, health education, and basic sanitation all continued, but some of the municipalities had trouble conducting the activities and sustaining the programs. (4) In 2011, Resolution WHA 65.21 (which was finally published in May 2012) set the goal of eliminating SCH as a public health problem. CGHDE (Coordenação Geral de Hanseníase e Doenças em Eliminação—General Coordinator for the Elimination of Leprosy and other Diseases) strengthening units were created, with an integrated approach based on PAHO Resolution CD49.R19 (published in October 2009). A study was conducted on distribution of the disease in the different municipalities, which determined that the northeastern part of the country was the most affected. In July 2012, the 2011-2015 comprehensive strategic plan of action was published, which summarized a political and institutional commitment to reduce the burden of disease of several NTDs. (5) In 2014, a revised manual on monitoring of schistosoma mansoni was published, which updated the epidemiological status of this disease in the country.

A recent map of SCH in Brazil showed that nine federal states are endemic (Maranhão, Alagoas, Bahia, Pernambuco, Paraíba, Rio Grande do Norte, Sergipe, Minas Gerais and Espírito Santo), while ten federal states have focal transmission (Pará, Piauí, Ceará, Rio de Janeiro, São Paulo, Paraná, Santa Catarina, Goiás, Federal District, and Rio Grande do Sul). Between 2004 and 2013 there was an average of 511 individuals with serious forms of the disease, and 500 deaths from it.

In 2013, the most affected states were Alagoas, Sergipe, Paraíba, and Pernambuco with 7.24%, 6.81%, 5.49%, and 4.19%, respectively, of people testing positive.





In endemic areas control strategies consist of case-finding through household parasitological surveys (biennial) and early treatment; health education; monitoring and control of intermediary hosts; and household and environmental sanitation.

In locations where prevalence is below 15%, only positive cases are treated. In locations where prevalence is 15-25%, positive cases are treated along with other members of the household. And in locations where prevalence is above 25%, MDA is done with preschool and school-age children.

In non-endemic areas passive surveillance is conducted through the primary health care system with diagnosis, treatment, and investigation of the case. SCH is a notifiable disease in Brazil (Ordinance Nº 1271-06/Jun/2014).

Brazil is currently among the countries whose objective is to control the disease as a public health problem. The available resources are: (1) Human resources from the Ministry of Health and from state and municipal health secretariats; (2) Infrastructure, including a national and state central reference laboratory (LACEN); and (3) Financial resources, including monthly budget allocations from Ministry of Health which set aside specific priority payments for each municipality.

Between 2011 and 2014, the national SCH and soil-transmitted helminth infection survey was conducted (Inquérito Nacional de Prevalência da Esquistossomose e Geo-helmintos, INPEG). The geographic distribution of intermediary snail hosts was mapped in the states of Paraná, Minas Gerais, Bahia, Pernambuco, and Rio Grande do Norte. Although the maps have still not been published, they show a reduction of SCH prevalence compared to the last survey conducted in 1975.

In conclusion, we note that the reduction in SCH has also been the result of: 1) major investments in basic sanitation and drinking water in Brazil; 2) an improvement in the population's income levels and quality of life; and 3) the availability and use of praziquantel (Brazil produces its own praziquantel at Farmanguinhos).

DISCUSSION AND OBSERVATIONS

Steven: He suggests that interventions in the states with low SCH prevalence be initiated and increased, to gradually reduce the number of states that have transmission of the disease.

It is suggested that the areas where there is new transmission may be the ones receiving large numbers of immigrants. The importance of analyzing migratory patterns is noted.





Venezuela (Dr. León)

Demographic aspects: Venezuela has a mainland and island land area of 916,445 km², with a population of almost 29 million according to the 2011 census (88.8% urban); 24.6% are poor (with 7% living in extreme poverty).

Historical Framework: In 1943 foci were identified in the North-Central Coastal area distributed over some 15,000 km² (1.6% of the national territory). Between 1943 and 1960 coprological prevalence exceeded 14% (M.S.A.S., 1986). In 1995 seroprevalence of 6.38% was reported, while coprological prevalence was at 0.31%. In the 1990s programs were decentralized, which dismantled the schistosomiasis program due to the emergence of dengue and the reemergence of malaria.

SCH transmission basically occurs around the Valencia basin. Venezuela has a "National Program for the Prevention and Control of Intestinal Parasitoses and Schistosomiasis," which leads these efforts and falls under the Ministry of People's Power for Health (MPPS). The objective of the program is to establish strategies for prevention, epidemiological surveillance, control, and pharmacotherapy of the main helminths, intestinal protozoans, and schistosomiasis, in order to reduce the prevalence of infection and morbidity-mortality in the Venezuelan population, such that these no longer constitute public health problems. The program includes the following activities: (1) monitoring and evaluation of the epidemiological status of parasites; (2) monthly registry of cases, reports, epidemiological situation analysis, databases-information systems; (3) supervision and advisory services to the program (visits-reports); (4) preparation, updating, and dissemination of standards and manuals (circulars-standards); (5) distribution of antiparasitic drugs and treatment guidelines; (6) training and updating in microscopic diagnosis; (7) pharmacological surveillance: Active product, resistance, efficacy, quality control; (8) control of reservoirs and intermediary hosts (Division of Vector Control for Reservoirs and Harmful Fauna); (9) promotion and communicating for health; (10) community participation and oversight; and (11) training and education.

The following goals have been proposed: (1) Reactivate the SCH program in the 9 states under surveillance; (2) Increase intestinal deworming activities at the national level in 75% of the school-age population; (3) Reclassify, update, and evaluate water samples from waterways and bodies of water in endemic areas where there is a risk of SCH; (4) Assess SCH in the population less than 20 years old in endemic and at-risk areas; (5) Establish a national computerized epidemiological surveillance system for intestinal parasitoses and SCH (risk maps, spatial distribution, satellite system (GPS)); (6) Include the program in the SPNS (National Public Health System of Venezuela); and (7) Make sure that SCH is a pathology for which reporting is mandatory.

The at-risk areas, by state and municipality, are the following: Aragua (Santos Michelena), Carabobo (Carlos Arvelo), Guarico (Juan Germán Roscio), Miranda (Guaicaipuro), Portuguesa (Monsignor José Vicente de Unda), Vargas (Naiguata).





In Carabobo in 2013, 9.7% tested positive with Kato-Katz, 34.5% with PPC, and of 0.0% with IEFA and Western-blot. The total number of seropositive people was 38. In Aragua 3.2% tested positive with Kato-Katz, 22.9% with PPCO, 34.5% with PPC, and of 0.0% with IEFA and Western-blot. The total number of seropositive people was two.

At present Venezuela is among the countries with the goal of interrupting SCH transmission—that is, to reduce incidence of the infection to zero.

Plan for the coming years: During 2014-2015 seven schools will be surveyed (people under 18) in the State of Carabobo (Carlos Arvelo Municipality and Guigue District). The results will determine whether MDA will be conducted, and in 2015-2016 the State Aragua will be evaluated (Municipality Santos Michelena).

The available resources are: (1) <u>Human resources</u>: At the central level there is one medical epidemiologist, four inspectors, one person with a degree in social work, one administrator, and one secretary. In each endemic and low-risk state there is a person in charge of the program—a physician or inspector—with a small team of collaborators. There are coprology laboratories, with professional and technical staff at the central level and in the states of Carabobo, Cojedes, Portuguesa, and Guárico; and there are a total of five bioanalysts and 10 microscopists. (2) <u>Material Resources</u>: There are three reference Laboratories (DGSA; UCV; UC) for serological and stool diagnosis, and there are malacology laboratories (snail strain and parasite). (3) <u>Financial Resources</u>: MPPS, research and infrastructure improvement projects.

Current challenges and difficulties include: lack of knowledge on the current epidemiological situation since periodic and timely evaluations have not been conducted; elimination of anti-biharzial engineering services since preventive construction projects were stopped; a lack of reports from the research projects that were conducted at the central and regional level; problems procuring reagents for laboratory tests; deficient malacological surveillance; and compulsory notification and SPNS.

There are several opportunities that favor SCH elimination: a legal framework to maintain operation of the program in each state under surveillance; public policies designed to improve the living conditions of the population are being developed (housing); there is interest in conducting activities within the SPNS and *Misión Barrio Adentro*; practical and effective diagnostic methods are available to investigate cases; single formats are being implemented for investigation of cases; there is inter-institutional collaboration among universities and research institutes for conducting activities; and there is a national deworming plan called "*Hijos de la Patria*" [children of the homeland] and "*La salud va a la escuela*" [health goes to school], which has distributed almost 3 million doses of tablets.

DISCUSSION AND OBSERVATIONS





Venezuela emphasizes that there is a lack of communication and coordination among the nine endemic states, and that it must promote the reporting of positive laboratory stool studies.

BRAZIL: Suggests that mapping delve more into the local level, beyond the municipal level.

Suriname (Dr. Malmberg) - Juanita Malmberg presented on behalf of Dr. Resida

Demographic aspects: Suriname has a total population of 541,638 (2012 census), with a growth rate of 9.9%, compared to the 2004 census. Its ethnic makeup includes 27.4% East Indian, 21.7% Maroons, 16.4% Creole, 13.6% Javanese, 13.3% mixed, 3.7 indigenous%, 1.5% Chinese, 0.3% white, and 1.3% others (2012 census).

It is divided into 10 districts which are in turn divided into 62 suburbs. With an average population density of 3.3/km² (ABS, 2010), the greatest density is in the Paramaribo capital district (1,323.8/km² (ABS, 2010) and lowest is in the district of Sipaliwini (0.3/km²). The coastal areas have 63 regional health clinics, with approximately 300 private physicians and five hospitals. There are 57 health clinics in the interior.

Historical framework: The first case of schistosomiasis was discovered in 1911. Since 1925 various periodic surveys were conducted that showed endemicity in different districts: Paramaribo (54.7%; 1949-1951), Coronie (34.0%; 1957), Saramacca (16.8%; 1974), Commewijne (2.7%; 1962-1963), and Marowijne and Nickerie (only one outbreak in 1967 and 1975, respectively). SCH is prevalent in the country's northern coast, where *B. glabrata* abounds in swamps and coastal channels. This area consists of coastal shell ridges, which provide an ideal environment for *Biomphalaria*. Shells are used in home and road construction and in agriculture. Not all settlements had adequate sanitation and drinking water services, which resulted in poor hygienic conditions. Control activities consisted of door-to-door surveys on treatment and occasional use of molluscicides, health promotion, and environmental inspection. Socioeconomic development—such as the installation of running water (1933), the enactment of a series of laws and environmental improvements (1960)—managed to continuously reduce SCH prevalence (with a range from 0.3 to 4.7%, 1997-2001).

The Office of Public Health of Suriname is responsible for epidemiology, vaccinations, diagnosis, treatment, health promotion and education, environmental inspection and intervention, vector control, and the planning of programs to control SCH among other NTDs (such as soil-transmitted helminth infections, SCH, filariasis, and Chagas disease). The SCH program activities are being planned with the support of PAHO and based on the PAHO/WHO directives. From the outset, SCH control efforts were integrated with efforts to control soil-transmitted helminth infections and filariasis, and a sentinel surveillance plan was developed for the three diseases. The Public Health Office has Parasitology, Entomology, and Helminthology Departments, as well as an Environmental Health Inspection





Department. And it is important to note that Suriname has experience in the elimination of several communicable diseases (such as filariasis).

Implementation of a strategy for SCH elimination in Suriname is hindered by the country's recent transition from a control strategy to one of elimination, and the switch from applying MDA to not doing so. Meeting participants were asked whether Suriname should conduct an epidemiological assessment or a representative survey and do an annual mapping of cases. The country is still debating which path to follow. The strategy and summary of activities to be carried out are included in the Comprehensive NTD Plan. Suriname is currently among the countries whose goal is to interrupt SCH transmission—that is, to reduce the incidence of infection to zero.

In 2009-2010 an SCH survey was conducted in seven of the ten districts (five historically endemic and two potentially endemic), at 132 schools with 1,700 6th grade students with an ELISA prevalence ranging from 3.4 to 11.8%. No cases tested positive with Kato-Katz. Other cases identified: clinical cases of SCH are identified annually (through routine stool analysis), primarily among adults and very few in schoolchildren (37 clinical cases 2008-2013). Occasional small-scale surveys might help identify 1 or 2 cases among 400-500 schoolchildren in areas in which there is a risk of transmission. SCH is not a notifiable disease in Suriname.

The available resources are: (1) Human resources are usually limited. Staff (particularly people with advanced degrees) is often "borrowed" from other departments when activities need to be conducted. In the Public Health Office the Chief of the Helminthology Department retired. There is a Director (Chief of the Parasitology Department), three Kato-Katz analysts, and young graduates who work in different departments. Personnel are borrowed from other departments or programs to conduct activities. Other professionals who support SCH control come from PAHO (one person), a university (one person), and there are some independent professionals who work as consultants (two to three people). (2) Financial Resources: Within the Ministry of Health NTD control is not given financial priority. Resources often come from PAHO/WHO and some of those funds are allocated for SCH. The Office of Public Health contributes financially for logistics (transportation/ fuel and lodging). (3) Material resources: drugs and diagnostic tests are donated, primarily by PAHO/WHO (Kato-Katz Kits, albendazole, mebendazole, praziquantel). But in short, the infrastructure for combating SCH is limited.

Challenges include problems getting trained, dedicated, and continuously available human resources (i.e., it is hard to get stool samples analyzed). Authorities are discussing whether to provide individual treatment door-to-door (as has historically been done), or do MDA. A protocol of action for new cases must be prepared, and the Ministry of Health must commit resources for this purpose.

DISCUSSION AND OBSERVATIONS

As there is still interest in clinical cases, these are referred to the Public Health Department where they are treated with praziquantel.





It still needs to be determined when antibody analysis should be done, and at what ages an infection can be considered current.

Brazil suggests that people's personal networks be explored. That is, when a case is identified, to ask whether they know someone who has contact with the water where transmission is found; this will guide efforts.

Saint Lucia (Mr. Hewitt)

Epidemiology and current situation: Historical records show that the number of cases of the disease has declined, but compared to malaria, schistosomiasis is more prevalent in Saint Lucia. The southern part of the country, where a majority of the rivers are located, is the most affected. Socioeconomic and environmental conditions, as well as typical lifestyles, are the main factors contributing to infection: contact with water, mode of fecal disposal, and activities on the river (washing clothes, bathing, etc.).

Species *S. mansoni* is the parasite historically identified in the country. The incidence rate was six cases per 100,000 population in 2007. Cases reported in recent years were among patients at prenatal health care centers, and among food handlers who are routinely tested. Very few of these cases presented symptoms of the disease. Since 1995, 106 cases have been reported; in 2007 the first case in Babonneau was reported.





Topic 1.B. Epidemiological status of schistosomiasis in endemic and formerly endemic countries: situation analysis of countries that may have eliminated SCH transmission and could move toward verification of its elimination. Challenges and opportunities of verification (Chair: Dr. Hillyer)

Puerto Rico (Dr. Hillyer)

Where does *Schistosoma mansoni* come from? Some people believe that it originated as a rodent parasite which subsequently adapted to humans. Phylogenetic studies, backed by the fossil registry, suggest that the *Biomphalaria* probably originated in South America and then colonized Africa, in the last 5 million years. (DeJong, et al, 2001 Mol Biol Evol and, 18: 2225-2239). Subsequently *Schistosoma mansoni* arrived at the Americas with the African slave trade; but only the species that infect *Biomphalaria* could spread the infection. Hurricanes changed the ecosystem of the intermediary host, and very little is known about the current malacological distribution in the Region of the Americas.

Historical framework: Isaac González Martínez reported two cases in young Puerto Ricans from the Mayagüez region in a Puerto Rican Medical Association report called "Bilharziasis in Puerto Rico," on 3 April 1904 (Sir Patrick Manson reported a single case of an Englishman residing in the Caribbean who was diagnosed upon his return to London in 1902). In 1904, the first Puerto Rican Anemia Commission conducted the first stool survey among 4,482 anemic patients from Utuado, and detected 21 cases of intestinal bilharzia (0.4% prevalence); one of the positives was from the Dominican Republic. In 1913, the Institute of Tropical Medicine of Puerto Rico recorded 320 cases of bilharziasis among 10,149 patients (prevalence 3.16%). Schistosomiasis was prevalent along the island's coasts, along lowlands and valleys of the interior (where sugarcane is grown), in the banks of rivers, swamplands, lakes, reservoirs, and canals. It has been found in the north, east, south, west, and in the basins of large rivers. There were no endemic foci in the dry areas where coffee is cultivated, or in mountainous regions, except for Utuado. Between 1910 and 1930 different surveys were conducted and high endemicity areas were detected: Guayama, Arroyo, Patillas, Humacao, Caguas, Río Piedras, Aibonito, Barranquitas, Comercio, Utuado, Mayagüez, Añasco, Lajas, and Vieques. In 1950 a coprological survey (1 g of stool) was conducted on 11,690 schoolchildren between 5 and 18 years of age in 17 municipalities with a global prevalence of 10%. The highest prevalence (20-30%) was found in the municipalities of Jayuya, Ceiba, Río Piedras, Patillas, Guayama, and Caguas. An abundance of snails was directly related to prevalence of infection, and multi-parasitism was common. Between 1950 and 1960 acute and chronic SCH were defined, and important studies in immunology and clinical trials were conducted by professors at the new Medical School of the University of Puerto Rico. Biological and chemical control studies were conducted in Vieques and in Caguas, as were studies with high variability in skin test trials. Various projects were conducted in: CDC's San Juan laboratories and the Boquerón Project. In 1980 the Puerto





Rico Department of Health eliminated the SCH control program and transferred those resources to dengue control.

As regards diagnostic tests, when the burden of helminths and eggs declines, parasitological methods become insensitive. Antibody detection tests are useful for controlling SCH in low transmission areas that are moving toward elimination. Here, immunodiagnostic techniques such as ELISA, western blot, and COPT, are powerful due to their high yield, high sensitivity, and availability. The COPT (circumoval precipitin test) in low infection areas is simple, but tedious, laborious and subjective. It has 95% sensitivity, which varies—in areas with < 1 epg it is 80%; and with 10 epg it is 100%, and specificity is 96%. There can be cross reaction with another type of *Schistoma*. ELISA (96% sensitivity, 99% specificity) and Western Blot (99% sensitivity, 99% specificity) have high specificity and sensitivity but require technical experience.

A serological survey (ELISA + WB) conducted by the University of Puerto Rico in collaboration with the CDC, of 2,955 blood donors in 76 municipalities, yielded 10.6% positive (WB). In half of 17 municipalities (but only 18% of the population), only 10% were under 25 years of age, primarily in high prevalence municipalities. This suggests that transmission over the last 20 years was primarily in foci. Among the Puerto Rican patients (COP positive) treated with praziquantel, in all subsequent samples their levels of antibodies had dropped.

In Puerto Rico it is believed that transmission has been interrupted because no clinical cases or cases from coprological surveys (at all ages) or serological surveys (in children) have been detected in recent years.

At present, authorities must do serological monitoring and follow-up on all cases treated by serology. The concern is whether SCH may disappear on its own in the absence of control measures.

Dominican Republic (Dr. McDougall)

Demographic aspects: The Dominican Republic has a land area of 48,670.8 Km² with a total population of 10,385,697 and a growth rate of 1.1%. Population density is 213 people/Km². The country is divided into 31 provinces with 155 municipalities and 231 municipal districts. Some basic indicators (2012) are: maternal mortality 109.7/100,000, infant mortality 26.1/1000, life expectancy 72.04 years, illiteracy 9.9% and general poverty 40.9%.

Historical Framework: In 1918 a case was reported of a sailor who resided in endemic countries. In 1924 cases from the Lesser Antilles were detected. In 1942 Dr. Ponce de Pinedo identified the first autochthonous case in Hato Mayor. In 1951 the American Foundation of Tropical Medicine found infected snails (*Australorbis glabrata*). In 1952 a cooperation project between the U.S. and the





Dominican Republic applied molluscicides (Pentachloride sodium phenate) in the Paña-Paña and Las Guamas streams. In 1968 a Symposium on Bilharziasis was held in Santo Domingo where formation of a committee for eradication of schistosomiasis was recommended. In 1970, through Decree No. 2275, the Committee to Combat and Control Bilharzia, located in Hato Mayor, was created within the Ministry of Public Health and Social Welfare. The SCH control program had a national coordinator, a laboratory, and a supervisor in charge of fumigators, snail collectors, and health educators. Its activities ranged from community talks to biological control (with the introduction of competing snails, *Marisa cornuaretis* and *Thiara tuberculata*) and the application of molluscicides (Frescon and Bayluscide). Diagnosis was done with the Ritchie stool method. In 1980 the Bilharzia Institute was created at the UASD (Autonomous University of Santo Domingo) through Resolution 80-313 of the University Council. Numerous epidemiological and malacological studies were conducted and the institute became a Public Health Program as it continued its activities. In 1996 administrative changes led to the dissolution of the program.

The provinces with historical foci of endemicity are El Seibo, La Altagracia, and Hato Mayor, in which living conditions have improved substantially as described in various indicators from the 2010 census as compared to 2002. For example, the installation of sanitary latrines in Hato Mayor went from 81.2% to 86.5%.

At present the Dominican Republic is among those countries whose objective is to sustain interruption of transmission (post-elimination surveillance). In 2013 a survey on the prevalence and intensity of soil-transmitted helminth infection was used to survey SCH in provinces with a history of transmission of this disease: Hato Mayor, El Seibo, and Higüey. The Kato-Katz method was used to detect helminths and ELISA-SEA serology and MAMA-EITB (immunoblot) were used to detect *Schistosoma mansoni*. Of 612 samples collected, none was positive, which leads to the conclusion that SCH transmission is low or nonexistent since no case could be detected in the study sample. There is a need to update the map of the snail's location in order to update the map of *Biomphalaria* distribution.

Antigua and Barbuda (Dr. Beazer)

Demographic aspects: The island is in the Caribbean Sea (17° 03'N 61°48'W) with an approximate population of 89,000 (91% Afro-descendant). It has a democratic government. Per capita Gross Domestic Product (GDP) is 11,000 dollars per year. Annual spending on health as percentage of GDP is around 6.5%. There are 135 physicians per 100,000 population; there is one public hospital, Mount St. John Medical Center, a few small private institutions, four large clinics in the main population centers, and 17 more small clinics. There is universal access to potable water, sanitation, and health centers.





Situation analysis: The Ministry of Health would be in charge of elimination if any SCH is found. Antigua and Barbuda has only seasonal streams and no rivers. The intermediary host is present in swimming pools, channels, and reservoirs and could be infected with *S. mansoni*. In the past 20 years the health authorities have not reported any human cases in the areas previously infected with known foci (Sweet, Liberta, Bendals, and the area surrounding the John Hughes settlement).

Travel recommendations for visitors classify Antigua and Barbuda as at low-risk for SCH, but advise tourists to avoid streams and brooks while visiting, since the disease is known to still exist in specific areas.

Children are at the greatest risk since they still occasionally swim in streams, and hurricanes are a risk factor on the island.

There is a scarcity of data, thus estimates are based on empirical estimates. Definitive diagnosis has not been carried out. It is believed that SCH transmission has been eliminated from Antigua and Barbuda, however sufficient evidence of this has not been compiled.

The priority control strategies are: health education; provision of potable water; planning of adequate medical care, diagnosis, and treatment; environmental management; and control of the intermediary hosts (freshwater snails).

Martinique (Dr. Desbois)

Demographic aspects: Martinique is in the Caribbean Sea (14°30 northern latitude), with a land area of 1,128 km², and a tropical climate (25-28 °C and 80% humidity).

Historical framework: The first reported cases were in 1906 (Lahille), 1908 (Léger), and 1910 (NOC). In 1951 prevalence was estimated at 6.4% (Deschiens), and in 1961 at 8.4% (routine parasitological examinations by the Pasteur Institute of Martinique). In 1970 a parasitological and serological survey was conducted in schoolchildren (in 10 of Martinique's 34 communes). The results were 0.3% to 18% (stool) and 37% to 73% (immunological). In 1971 another large-scale serological survey was conducted in 5,000 people, primarily females from 5 to 20 years old in 20 communes, with a prevalence range from 5.3% to 73.5%.

Schistosomiasis was public health problem on the island of Martinique and in 1973 Decree No. 73-705 was passed to organize and finance epidemiological research on the subject. In 1978 the Department to Combat Intestinal Parasitoses was created (Department of Health and Social Affairs of Martinique).

A survey (INSERM) conducted by the National Institute of Health and Medical Research in 1977 and 1978 among 800 families for a total of 3,880 people, revealed an average prevalence (combination of parasitological data and serological results) of 12%. The results were heterogeneous: over 30% in Basse-





Pointe, St-Pierre, Morne-Rouge, Carbet, and Ducos; between 20% and 30% in Le Lorrain, Ste-Marie, Gros-Morne, St-Esprit, and Vauclin; between 10% and 20% in Case-Pilote, Morne-Vert, Fonds-St-Denis, Ajoupa-Bouillon, Marigot, Le Robert, Le Lamentin, Le Diamant, Ste-Luce, Rivière-Pilote, Le Marin, and Ste-Anne; while prevalence below 10% was found in 12 communes.

Based on this study, a control program was developed that included all the following areas: health promotion and education, patient detection and treatment, biological snail control of *B. glabrata* (with introduction of the competing snail *Melanoids tuberculata*), and the development of individual and collective sanitation.

The efficiency of programs to combat the parasite was evaluated through stool analysis and serological monitoring. Since 1984, no case of infection was observed in children under 10 years of age. In 1988 prevalence was 0.60%, and between 1994 and 1995 prevalence dropped to half—0.27%.

Until 1987 patients were treated through the Department to Combat Intestinal Parasitosis, which did screening and prescribed and provided antiparasitic drugs. Since 1987 treatment has been done on an individual basis (private practice). The drugs used were niridazole (1978), oxamniquine (1981), and praziquantel (1995).

Current situation: some symptoms of old infections (without eggs in the feces or rectal biopsy). Two active infections: One case detected in Pointe-Noire related to swimming at the Acomat waterfall (2000) and one imported case of a patient from St. Lucia (1999). Diagnosis is primarily done in non-hospital laboratories; there is no serological survey or detection of infected snails.

In conclusion, a decline in snails and parasite transmission was achieved, with a strong reduction in prevalence since 1977. At present there are a few cases corresponding to old infections. It is believed that transmission has been interrupted, but there are some doubts because there have been no studies of snails or prevalence in humans since 2000. In turn, the public health pressure regarding the ban on swimming in rivers has diminished.

DISCUSSION AND OBSERVATIONS

It is suggested that while education programs work, public health pressure regarding swimming in rivers has diminished. Response: It is very difficult to combat it only with good education programs.

SURINAME commented based on its filariasis experience. The representative said that repeating the same message over the course of years helps, but it takes years to get people to acquire certain habits.

Steven: There are no reported cases in hospitals, and there also is a snail competing with the intermediate host. While there have been vast improvements in living conditions, the challenge is to know what category this would fall into, and what should be done to verify elimination of the disease. He mentioned the political-administrative status of the country as an overseas French territory; therefore corroboration would need to be done with French Guiana and Guadeloupe (even Corsica). A plan to verify elimination of SCH should be launched in coordinated fashion, because verification is done by country—not by territory, department, or province.





<u>Topic 2: Systematic review of schistosomiasis prevalence and intensity of infection in the Region of the Americas (Dr. Zoni)</u>

Schistosomiasis is a public health challenge because it affects the most socioeconomically disadvantaged populations, which means that in order to be eliminated, there must be comprehensive interventions to address the social determinants of health.

The objective of this systematic review was to determine the prevalence and the intensity of *S. mansoni* infection in children (1 to 14 years) in the countries of Latin America and the Caribbean (LAC), at the second administrative level or lower, identifying critical geographical areas and areas without information.

A bibliographic search was done in different electronic databases: MEDLINE (PubMed), Embase, LILACS (SciELO), DARE (Database of Abstracts of Reviews of Effects), Database of systematic reviews of Cochrane, and institutional Web pages. The search terms used were: "schistosomiasis," "children," "epidemiology," and a combination of the names of all countries, capitals, and major cities in LAC.

This was conducted according to the criteria of the 2009 PRISMA guide for systematic reviews. The inclusion criteria were (1) Scope: studies conducted at the second administrative level (municipality) or lower administrative division (locality or neighborhood) in the countries of LAC. (2) Participants: children (from 1 to 14 years) infected with *Schistosoma mansoni* in LAC. (3) Results: prevalence and intensity of infection. (4) Types of studies: randomized clinical trials, systematic reviews and meta-analysis, cross-sectional studies and observational studies. Two independent reviewers applied these criteria. The discrepancies were resolved through discussion.

Included were 133 studies published between 1942 and 2014 in nine countries and additional territories of LAC (Brazil, Guadeloupe, Martinique, Montserrat, Puerto Rico, the Dominican Republic, Saint Lucia, Suriname, and Venezuela).

All the included studies reported SCH prevalence, and a total of 1,244 prevalence rates were recorded. A majority were from Brazil (92 articles; 727 records). Brazil was the only country that had conducted epidemiological surveys after 2001. When only this data was analyzed, several high prevalence hot spots (above 50%) were identified in the states of Minas Gerais and Pernambuco.

Intensity of infection was reported in 44 articles (199 registries), belonging to four countries (Brazil, the Dominican Republic, Saint Lucia, and Suriname). The way it was reported varied widely. For a majority it was done geometrically, and only three articles from Brazil reported on the intensity of SCH infection level according to the WHO categories. The importance of reporting this indicator was stressed, since it is the first one to decline when mass praziquantel administration is implemented.





The unequal distribution of publications per country and the lack of up-to-date information may reflect, in a worst case scenario, the difficulty countries have getting published in indexed journals, or the lack of human and economic resources to conduct epidemiological surveys. In a best case scenario, it may be indicative of interruption of transmission.

The most analyzed age group was schoolchildren (5-14 years old), but there was a great deal of variation in the ages of those surveyed and different ways to classify them. This may be due to the following factors: historically schoolchildren have had the highest rates in the region; it is difficult to survey preschool children; resolution WHA54.19 was aimed at minimum treatment for schoolchildren; and/or because praziquantel was not available in pediatric solutions. It was mentioned that new evidence in Africa reports rates in preschool children as high as those of schoolchildren.

In conclusion, heterogeneity was detected in the methodologies used and the way results were reported. Therefore, for future surveys that attempt to update the epidemiological status, it is recommended that the following methodological guidelines be followed: (1) Perform the analysis on children with a description of the results separate from the adult population; (2) Classify children based on school age—preschool (1-4 years) and schoolchildren (5 to 15 years); (3) report the sample size; (4) describe whether the survey was conducted in the entire locality, and if not, what type of sampling was used; (5) specify the diagnostic test used, and if possible use the one recommended by WHO (Kato-Katz stool examination with 2 tests per sample, or with 4 as the gold standard); (6) analyze intensity of infection by arithmetic mean; (7) report the percentage of children infected according to WHO's intensity of infection classification levels (mild: 1-99 epg; moderate: 100-499 epg; serious: 500 egpG or more).

This review identified some areas of Brazil that currently have high levels of transmission, which revealed a need to update the epidemiological status of some states in that country and others. For the rest of the countries, evidence must be compiled to see whether they really have interrupted SCH transmission, in order to verify SCH elimination in AMR.





Topic 3. Successful control and elimination programs globally – lessons learned to guide future verification of schistosomiasis elimination (Chair: Mr. Vlugman)

Saint Lucia's Project (Dr. Cook)

Historical milestones in Saint Lucia: In 1651 the island belonged to the French. In 1803 the island was controlled by the United Kingdom and France, until the French were finally defeated after several years of war. From 1842-1854 there were yellow fever and cholera epidemics. From 1914-1922 a campaign against hookworm was conducted with financing from the Rockefeller Foundation. In 1924 the first report on *S. mansoni* infection was issued. In 1957 malaria was eliminated. In 1961 schistosomiasis was found to be spread throughout the island, therefore, in 1965-1966 a research and control agreement was signed with the Rockefeller Foundation. In 1979 the island declared its independence. In 1981 investigation and control efforts continued through external departments.

In 1964 assistance from the Rockefeller Foundation was requested. The Foundation collaborated in part because the geography of Saint Lucia made it possible to isolate control methods in the different valleys and thus conduct comparative studies. The operational components of the control methods of the program were: (1) education for health/ behavior changes; (2) preventive chemotherapy; (3) safe drinking water supply and sanitation; and (4) snail control.

In order to determine the most effective way to control SCH, four different interventions were done in four different places: (1) In Cul de Sac Valley snail control was done with emulsifiable concentrate of niclosamide (Bayer 6076) in swamps, reservoirs, and drains on the banana plantation. (2) In Richefond clean drinking water was supplied out of Fordilla taps (education and health). There was one faucet for several houses. The drawback was that the water pressure was low and people broke the faucet to increase the flow, wasting several liters. Prevalence in 1971 was above 80% among children 15-19 years old, and by 1977 it had dropped to 20%. (3) In the Marquis Valley pharmacological treatment was administered (hycanthone and oxamniquine). This was the most efficient intervention. SCH prevalence fell by 90% in the high-prevalence villages and by 86% in the low-prevalence villages, while the cost per person was the lowest (0.88 dollars). (4) In Fond St Jacques snail treatment and control was done with molluscicide.

In conclusion, in Saint Lucia preventive pharmacological treatment was the most cost-effective method, which yielded a rapid decline in infection, disease, and potential transmission. Early treatment of children reverses the long-term damage. The molluscicides and clean water supply were also effective, but were slower and expensive. But it was stressed that all control modalities will be needed to eliminate transmission.

Thirty-three years after the program ended, we see that transmission continues at a very low level. In 2006 a stool survey was conducted in 554 children from 0 to 14 years old, and only 4 children were





positive. Between 1995 and 2007 106 cases were reported, and in 2007 the first case in Babboneau was reported. Molluscicides and the introduction of *Melanoides tuberculata* (*Thiara*) have had an impact on snail control, but *Biomphalaria glabrata* is still present.

The POC/CAC test may detect areas of SCH transmission and indicate what is to be done for elimination. An integrated program of treatment, sanitation, and snail control would make it possible to eliminate the *S. mansoni* and to reduce the burden of soil-transmitted helminths.

In 2013 PAHO/WHO and partners and allies working on SCH elimination visited the island to discuss NTD control; the recommendations of that qualitative evaluation are available.

<u>Success stories and lessons learned in schistosomiasis control and elimination in other regions (Dr. Jiagang Guo)</u>

Once the program was established in China and all levels of government got involved, considerable progress was made in SCH care, prevention, and control. Five of the country's provinces that were endemic for SCH have managed to interrupt transmission: Guangdong (1985), Shanghai (1985), Fujiang (1987), Guangxi (1989), and Zhejiang (1995).

The reason SCH is a priority in China and the government began to pay attention to it, is because *S. japonicum* has high morbidity and *Oncomelania hupensis* lives in swampy areas and is very difficult to control since its habitat expands easily with the annual floods. Eradication of this snail from the entire Yangtze River Valley is impossible. Furthermore, more than 40 types of mammals can be infected and act as reservoirs of *S. japonicum*. Therefore, it is difficult to control the source of the infection. Because of all this the government realized that SCH endangers the public health of the rural population, and that eliminating the disease is important for maintaining social stability.

Here is an overview of SCH control strategies in China: Between the 1950s and 1980s, SCH elimination methods focused on snail control, including through agricultural development and the construction of water works in such a way that would help eliminate snails. Between 1980 and 1990 there was no pharmacological treatment, only malacological control. Between 1990 and 2000, when praziquantel appeared, methods focused on controlling morbidity, such as mass or selective pharmacological treatment to reduce the infection. Ecological agriculture was combined with water services, in addition to MDA with praziquantel on an annual basis, yet every year there was reinfection. In 2003 elimination of the snail throughout the Yangtze River was impossible, so MDA was combined with control of multiple animal reservoirs. It was found that water buffalo and cattle acted as reservoirs. For this reason, in endemic areas water buffalo are no longer used in agriculture.





The strategies included preventing contamination through bovine species (replacing water buffalo with small tractors), stopping contamination of the environment with human feces containing eggs (MDA + sanitation), controlling snails with molluscicides and changing the environment, education for health, and supplying safe drinking water to the population.

The technical protocol in endemic areas considered the prevalence rate based on fecal examination: if the prevalence was: a) greater or equal to 10%, treatment was given to everyone; b) if it was between 5-10%, treatment was given to select individuals; and c) if it was between 1-5%, an epidemiological investigation was conducted and treatment was given in accordance with the assessment of risk of infection.

The criteria for determining infection control in China are as follows: (1) The prevalence rate among residents should be below 5%. (2) The prevalence rate in domestic animals should be below 5%. (3) Outbreaks of acute SCH should not occur: less than 10 cases of acute SCH, including clinical or parasitological confirmed cases, occurring within two weeks in one village, or less than 5 cases of acute SCH within one week in the same place when the infection was caused by contact with water. (4) Data and files should be available in the administrative villages showing changes in infections and in the examinations of snails.

The criteria for determining transmission control are as follows: (1) The prevalence rate among residents should be below 1%. (2) The prevalence rate in domestic animals should be below 1%. (3) There should be no cases of acute SCH with local infection. (4) Infected *Oncomelania* snails should not be found in two successive years. (5) Data and files should be available in the administrative villages showing changes in infections and in the examinations of snails.

The criteria for determining the interruption of transmission are as follows: (1) No case of local infection of SCH in humans should be found for five consecutive years; (2) No case of local infection of SCH in domestic animals should be found for five consecutive years; (3) No *Oncomelania* snails should be infected for five successive years. Every year samples must be collected at sentinel and verification sites. (4) Data and files should be available in the administrative villages showing changes in infections and in the examinations of snails, along with the surveillance plans and measures that were implemented. (5) To verify SCH elimination, no new infections should be found in either humans or domestic animals for five years after achieving the criteria of interrupted transmission. This must be checked because there is mobility.

Today, in China, everyone is familiar with the disease and has received health education about it. This means, for example, that everyone recognizes the disease and if they have been fishing or been exposed to water that is likely to be contaminated, they know it is very easy to get treatment free of charge at the local clinics.





After 30 years, in provinces where the disease has already been eliminated, a team goes out each year to verify that the disease has not reappeared.

These achievements contributed to the original goal of eliminating the disease from all endemic areas where it was feasible to do so through integrated approaches, including preventive treatment, snail elimination, environmental changes, health education, and better sanitation and water supply services. The sustained commitment of the national and local governments and the technical support they provided, as well as collaboration between the health sector and other government sectors (particularly agriculture and water and forest conservation), were all key to the success of this effort. China was able to achieve this through political will and a national SCH control program, and with a team comprised of people in various ministries, not only health teams.

DISCUSSION AND OBSERVATIONS

Brazil: Who does the snail control? Response: local people (farmers) who are contracted to collect them; then technical personnel do the infection study.

What types of malacological control measures are used? Niclosamide in oil is placed in the infected water, because most of the schistosoma are on the surface. Also in dry areas, when water comes in, it is released slowly.

Venezuela: What are the doses used in humans, and in animals? Answer: 40 mg/kg is used in humans.

In animals it is different from the dose for humans.

Brazil and Venezuela said they are afraid to treat people with praziquantel in areas that have schistosomiasis—cysticercosis coendemicity. They stressed a need to study this interaction.

Adrianus Vlugman: In conclusion, the government of China is very committed to the elimination of SCH. MDA is the most efficient control measure, but it alone does not suffice to achieve elimination; it must be complemented with other control methods.





Topic 4: Surveillance: Surveillance systems, new tools for mapping and surveillance in low endemicity areas (Chair: Dr. Teixeira)

<u>Updates on integrated surveillance tools for schistosomiasis and other neglected diseases (Dr. Secor)</u>

Moving from schistosomiasis control to interruption of transmission can be done through MDA and stool examination. However, to move from interruption of transmission to verification of elimination, other more sensitive and specific diagnostic methods must be used, since Kato-Katz is not highly sensitive. Antibodies can be used based on age and in low-intensity areas.

Challenges arise when countries come close to SCH elimination because the cost per diagnosed/treated infection becomes much higher, while its relative importance for public health diminishes. Therefore, funds from the SCH control/elimination program may be needed for other higher priority health problems. Moreover, economic development is largely responsible for the suspected interruption of transmission (vis-à-vis the programs). However, elimination still must be verified.

The presence of intermediate snail hosts is associated with a risk for reappearance of the infection. The Kato-Katz technique is not sensitive enough to identify SCH infection in areas of low prevalence and intensity of infection (however it is useful for measuring soil-transmitted helminth infection). Antigen detection methods currently available (CCA cassette) may not be specific enough (giving rise to false positives). The antibodies are not useful in distinguishing current infections from old ones. However, the absence of antibodies in small children may be useful to verify interruption of transmission.

The multiple antibodies approach (Luminex-based serological assays) may be used to integrate the programs and share the cost of collecting samples, which can be analyzed to identify antibodies for various diseases. Additionally, if samples need to be shipped, it is much cheaper to ship filter papers at room temperature than to ship frozen sera. Currently, one hundred different microspheres are available, each with its own fluorescent imprint, and the antigens are of a higher quality, which minimizes non-specific reactions. Panels are available to identify various NTDs: schistosomiasis, lymphatic filariasis, *Strongyloides*, onchocerciasis, trachoma, cysticercosis, yaws, *Ascaris*, *Plasmodium*, dengue, Chikungunya, and Rift Valley fever.

Multiplex assays, as a surveillance platform, make the following possible: a) an instant snapshot of the epidemiological context, helping to define which interventions are necessary and where; b) measure changes and trends over time; c) associate between groups to collect multi-program data; d) address cross-cutting issues, such as the effects of co-infection and interactions around vaccination and infection. The disadvantage of multiplex assays is that they are not as easy to establish as ELISA, making them more appropriate for regional laboratories. Alternatively, MAGPIX, the portable version of this technology, has easily transportable discs and a larger dynamic range than ELISA, and can distinguish





between current and past infections. Multiplex PCR is also available, and is based on a stool exam to diagnose SCH and soil-transmitted helminth infection.

Some examples of programs that could benefit from this type of tool are: vaccination programs against measles, tetanus, and rotavirus which need coverage surveys; and programs that do sanitation interventions, such as for neglected tropical diseases, with MDA campaigns, where the effectiveness surveys are needed to monitor the progress or help determine the end points of the program.

In conclusion, integrated serological surveys are feasible, will generate useful data, and could potentially save money and human resources. Surveys conducted among children generate valuable information regarding recent transmission. And efforts are needed to validate additional antigens and standardize assays to ensure that data can be compared between laboratories.

DISCUSSION AND OBSERVATIONS

Steven Ault: Do these technologies come from more than one company? Answer: The biggest limitation is that we are the only ones conjugating these antigens with pearls, and some of the antigens only are available at CDC.

What kind of mapping and surveillance tools should be used in low schistosomiasis transmission areas? Is there enough evidence to make recommendations? (Dr. Colley)

We have many cut-off points between control of the disease and elimination, based on the goals we want to reach and baseline prevalence: (1) Control when prevalence is between 25 and 100%; (2) Sustained control when prevalence is between 10 and 24%; (3) Elimination of the disease as a public health problem when prevalence is between 1 and 5%; (4) Elimination when prevalence is at 0% transmission; (5) Post-elimination surveillance.

Regardless of a country's status, there are questions regarding the administrative level that analyzed prevalence (national, district, municipality, village), and which diagnostic methods should be used to determine that prevalence.

Cure rates measured with Kato-Katz (a method that has less sensitivity in low prevalence areas) may be overestimated. This is a problem for analyzing elimination and post-elimination phases.

Therefore, as a group we must discuss which tools to use in the SCH elimination phase in low transmission areas.

What should be achieved with a diagnostic tool? (1) Mapping to start a program to gain control; (2) Monitor the impact of a "gain or maintain control" program; (3) Determine whether it is time to change





the strategy; (4) Specifically in the Americas, determine whether it is time to start an elimination program.

As a country passes through these stages, increasingly sensitive and specific diagnostic tests are needed. The post-elimination phase requires a test with excellent sensitivity and excellent specificity based on exposure or infection.

We propose using the POC-CCA (Point-of-Care Circulating Cathodic Antigen) test. The first question is whether the POC-CCA urine test is as good as the Kato-Katz for mapping the prevalence of *S. mansoni*. The answer is yes, based on a study of 4,305 children at 63 schools in five countries with very different prevalence levels.

But there is no gold standard test by which to compare; so the debate continues. The POC-CCA test is being tried in many large-scale countries (in some cases even at the national level: Burundi and Rwanda). Even though the POC-CCA assay is being used, it should continually be studied to determine its possible shortcomings and ease of application. Four different POC-CCA assessments were done between 2013 and 2014 in Kisumu, Kenya by Pauline Mwinzi, Nupur Kittur, Elizabeth Ochola, Phillip Cooper, Daniel G. Colley, and Charles H. King:

- 1- They studied cassette batch variation, which showed no real variation.
- 2- Intra-reader reliability showed insignificant variation (2% variation).
- 3- Day to day variability between CCA and Kato-Katz, measured in 73 participants over 3 days, showed that both tests had a certain degree of variability, but this was greater with the Kato-Katz stool technique. This means that if only one test is done per day, even in high prevalence areas, CCA should be used. In addition, specificity was studied in areas endemic for soil-transmitted helminths, which were never endemic for SCH, such as Ethiopia (100 participants) and Ecuador (74 participants), and the specificity was 99-100%.

There is a correlation between a moderate-high egg count according to Kato-Katz and a positive POC-CCA test, which means that semi-quantitative intensity data can be obtained from the POC-CCA test. Among 10 participants with moderate infections according to Kato-Katz (104-452 EPG), all POC-CCA results were positive (Intensity 1, 2 or 3); that is, all subjects with a moderate or high egg count per gram of stool yielded a clearly positive POC-CCA result. Their POC-CCA scores correlated well with egg counts from the Spearman test.

4- POC-CCA evaluation after treatment with praziquantel, studied in 149 children at a school in an area with 10-15% prevalence, gave a cure rate of 48% after the first cycle of treatment, and 34% after the second. In the scientific literature, a cure rate is normally described between 70% and 90%, but these results were measured with Kato-Katz, a test known to have low sensitivity in areas with low





intensity of infection. Therefore, when a more sensitive test is used, many of the Kato-Katz negatives/POC-CCA positives are real; that is, the patients are still infected with some worms and are not totally cured. As a result, standard cure rates are overestimated when based on a low sensitivity test.

Based on the data from the POC-CCA trials that were shown, and data that many other groups have published, the speaker concluded that POC-CCA is not a perfect test. However, it is better than the Kato-Katz test for conducting surveys when Kato-Kats shows a prevalence of *S. mansoni* below or equal to 5%. The data indicate that most, if not all, Kato-Katz negatives/POC-CCA positives in a single person from a previously endemic area, probably constitutes a "low level infection" worthy of monitoring to ensure elimination.

Going back to the question of which tools should be used for each phase from control of morbidity through elimination, the answer can be summarized as follows:

- For maintaining morbidity control, the POC-CCA test has good sensitivity below 60-80 epg
 measured through multiple Kato-Katz depositions, and reasonable specificity. Furthermore, it is
 easy to use and collect the sample.
- In order to move toward a strategy of elimination and interruption of transmission, the POC-CCA test (perhaps if the reader receives more training) has high sensitivity below 20-50 epg measured through multiple Kato-Katz depositions, and reasonable specificity. Furthermore, it is easy to use and collect the sample.
- To achieve elimination, UCP-CAA (test of nucleic acids in urine) has very high sensitivity and high specificity; also, the sample is easy to obtain and has a high yield.
- To conduct surveillance after achieving elimination, multiplex antibody assays have very high sensitivity and very high specificity; it is easy to obtain the sample, and it is possible to group surveillance for several diseases and thus obtain a high yield.

DISCUSSION AND OBSERVATIONS

WHO guidelines are required regarding which tools should be used in each phase from control to elimination of schistosomiasis. There is no "gold standard" test, not even to compare with the Kato-Katz technique, which is the only one recommended by WHO for the control stages. WHO needs to define feasible criteria for adding tests. The countries cannot use new tests if they have not been validated by WHO.

How can more tests be included in the WHO guidelines? WHO is now trying to assemble a committee of experts but the process is slow. WHO should work on identifying the basic reproductive rate of the disease, below which will transmission will not be possible.





Topic 5. Morbidity Control (Chair: Dr. Colley)

Morbidity control in areas of high versus low endemicity (Dr. Cook)

Two hundred and forty million people are currently infected, of which 100 million are asymptomatic. Why control morbidity? Because the tools to treat people with the most intense infections (5-14 years old) are currently available, and it is easy to reach this age group through schools. Furthermore, early diagnosis and treatment improves chances for reversing clinical signs of the disease. Additionally, this reduces the percentage of schistosome eggs in the environment, and prevents the reintroduction of infection into communities. Initially there was a reluctance to treat communities because of the high cost of praziquantel and concerns about treating communities without a definitive diagnosis. However, this has now changed thanks to donated drugs and the WHO guidelines.

It is important to remember that among the ten leading causes of years of life lost to disability and premature death, calculated with WHO data, are the NTDs, including schistosomiasis.

Periodic treatment of endemic communities with praziquantel has an almost immediate impact on intensity of infection and prolonged treatment has an impact on prevalence of infection. Treatment of infection causes a reduction or regression of morbidity. However, the impact will depend on levels of transmission. There may be high rates of reinfection with low intensity of infection and no apparent effect on prevalence. The reinfection rate will be higher among those who had higher initial rates of infection.

Morbidity control strategies include preventive chemotherapy treatment for the population in highly endemic areas; and diagnosis and treatment of infected people in low prevalence areas. To control transmission and move toward elimination of morbidity, as was mentioned during the meeting, additional interventions are needed, such as access to safe drinking water, sanitation services, environmental changes, and snail control. Therefore, applying all the operational components will translate into reduced levels of infection and less disease. The strategy to be implemented will depend on the epidemiologic status of the country and available resources. However, it must be stressed that the most important factor in reducing morbidity, was a reduction in the cost of treatment and its expanded use.

Experiences in morbidity control at WHO Collaborating Centers (Dr. King)

The purpose of this presentation was to review multidisciplinary research conducted at the Case Western Reserve University (CWRU)-WHO Collaborating Center on Schistosomiasis. The speaker described the change in approach marked by this research in the area of morbidity control associated





with *Schistosoma*, and explained the evolution of current thinking regarding morbidity prevention by reducing and eliminating transmission.

The Center was founded in 1980 by Dr. Adel Mahmoud, Director of the Division of Geographic Medicine at Case-Western Reserve University. The initial objectives were: (1) to study the immunology and immunopathology of *schistosoma* infection; (2) to study the populations at risk for infection with the disease; (3) to conduct medical trials on school-age children for the control and prevention of advanced pathology from *S. mansoni* and *S. haematobium*. Recent studies have focused on viewing *schistosoma* infection as a chronic inflammatory disorder. What is the spectrum of disease caused by the infection? Why does transmission persist despite mass treatment campaigns? Why does transmission continue to be highly focal?

The many collaborating Centers, agencies, institutions, and donors who are working on this agenda bear mention:

- Local—CWRU Departments of Medicine, Pediatrics, Epidemiology and Biostatistics, Pathological Anatomy, Biology, Applied Mathematics, Anthropology.
- The U.S.—University of Illinois, Emory University, University of Michigan, University of Georgia/SCORE, NASA, Stanford University.
- International—FIOCRUZ Salvador, Belo Horizonte/ UFMG, Brazil; Hebrew University of Jerusalem/ Al
 Quds University; School of Hygiene and Tropical Medicine of London, School of Tropical Medicine of
 Liverpool; Swiss Tropical and Public Health Institute.
- Funding partners—WHO TDR, Rockefeller Foundation, the National Institutes of Health, the National Science Foundation, Thrasher Research Fund, and the Bill and Melinda Gates Foundation.

The principal findings from research conducted by these centers are that *Schistosoma* infection has an enormous and long-lasting impact on health, producing inflammation and systemic damage that goes far beyond the organ-specific disease described in textbooks. In children it causes anemia and decreases physical and cognitive development, creating problems with fluency and memory and increasing school absenteeism. Urogenital SCH in women causes fertility problems and increases the likelihood of contracting HIV. And the remission of symptoms in infected people is not observed for some time after treatment.

Despite preventive pharmacological treatment, *Schistosoma* transmission is robust. The problem is reinfection six months after treatment. Thus it is important to control infection. The median time for reinfection ranges from 2 to more than eight years, depending on the community and its level of endemicity.

It is possible to break the cycle of transmission thanks to the development of more sensitive techniques to measure infection in snails, and thanks to water contact studies and geo-referencing which make it





possible to identify focal areas of transmission and intervene appropriately. Communities are increasing their infrastructure (safe water alternatives, environmental changes, and modifying habits), which will most likely help them succeed in eliminating the disease.

Final messages: With a multidisciplinary approach which takes a wide view of things, we can fully address the problem. Better diagnosis of the infection (and the disease) now allows us to know where there continues to be a problem—in reinfection—which is why morbidity persists or recurs at a subclinical level. Additional efforts should be made to completely interrupt *Schistosoma* transmission in order to eliminate schistosomiasis.

DISCUSSION AND OBSERVATIONS

Subtle morbidity is real. So how important is the morbidity cut-off when a person feels less intelligent due to anemia/fatigue produced by the infection? What is the socioeconomic impact of subtle SCH infection?

The importance of publicizing the social and economic impact of SCH was stressed, even if infection is subtle, in order to plan the required public health interventions. For example, national authorities in Suriname were encouraged to allocate funds to find foci where the disease persists and so they can intervene.





Discussion of priorities and next steps toward schistosomiasis elimination in the Region of the Americas by 2020—Defining a road map for the region (Dr. Catalá)

Challenges and opportunities for accelerating the process toward verification of elimination

- The epidemiological situation of schistosomiasis must be updated in some countries. Annexes 3 and 4 show tables summarizing the epidemiological status of each country in the Americas on the road toward elimination, including a timetable.
 - The countries are urged to do the following: (a) use new geo-referencing technologies (GPS and mapping); (b) use new diagnostic tools, useful even in low prevalence areas because of their increased sensitivity and specificity, to map prevalence; (c) integrate SCH surveys with those of more publicly visible diseases (dengue, chikungunya, malaria, etc.); (d) integrate SCH surveillance with that of other diseases through sentinel or randomized sites, to optimize the use of both human and financial resources; and (e) continuously monitor the evolution of programs so as to implement corrective measures if needed (instead of waiting for the next epidemiological survey to assess the impact of interventions).
- There is a shared concern that SCH, together with others NTDs, is considered a low priority on the public health agendas of the ministries of health of the region. In most countries there are insufficient human and financial resources to support control of SCH and parasitic diseases in general, especially those that have low transmission rates. It was stressed that since 2008, public and private entities have made a commitment to control and eliminate NTDs, including SCH, and several drugs needed to treat these diseases are being donated through PAHO/WHO, including praziquantel. Additionally, PAHO is offering Kato-Katz kits. Furthermore, the time has come to identify potential donors who could support SCH elimination in the region (PAHEF, BMGF, Sabin Institute, TDR, Esai). Countries should be encouraged to invest human and financial resources in the control and elimination of these diseases.
- It is recommended that PAHO promote and create the "Ciro de Cuadros Award for innovative and successful NTD control and elimination efforts," to encourage countries to move toward their goals and encourage them to learn about and share success stories. An approach that integrates SCH control and elimination with that of other more publicly visible NTDs (dengue, chikungunya, even malaria) can also bring the issue to a higher priority level at ministries of health and the ministries of education, agriculture, and environment, thus tapping into more resources.
- The criteria and procedures toward verification of SCH elimination are not clear and require
 precise indications regarding what should be included in the country dossier before asking
 PAHO/WHO to verify SCH elimination. WHO has prepared a draft procedure and criteria to request
 verification of elimination, and this was shared and reviewed by the countries. It was stressed that





some countries, such as Montserrat, Antigua and Barbuda, and St. Kitts and Nevis, are probably unable to verify SCH elimination due to a lack of human and/or financial resources, or because these countries have not reported a single case in several years. Therefore, it will be difficult to prioritize this issue on the public health agendas of those countries, which raises the question of whether they should be removed from the list of endemic countries if there is enough evidence that the disease has been eliminated. This will require the following: (a) identify groups of experts and working groups to define the criteria and post-treatment surveillance procedures to verify elimination and support the countries in that process; (b) define the prevalence cut-off point (or basic reproductive rate) below which transmission of the disease is not sustainable (such as those established for filariasis or onchocerciasis); (c) make recommendations available to countries regarding the use of diagnostic tools that can be used in low endemicity areas. Aside from the Kato-Katz technique which is very specific to highly endemic areas—there are no clear WHO recommendations on the other diagnostic tools and their usefulness in low endemicity areas. Some new tools are being developed that may facilitate mapping, monitoring, evaluation, and post-elimination surveillance of the programs (i.e. multiplex, CCA, etc.). It is recommended that PAHO hold an expert consultation to review available tools, and determine which ones are useful for verifying SCH elimination and can be recommended to countries. Essentially, highly sensitive and specific tools are needed for the later stages of elimination programs.

- There are few malacological experts in the Region of the Americas knowledgeable about the intermediary snail hosts of *S. mansoni* and other trematodes. As a result, few biological control interventions are attempted, due to lack of expertise, and insufficient resources are channeled into this activity. With the support of the Regional Advisor on Integrated Vector Management, Dr. Haroldo Bezerra, a regional workshop should be organized for 2015, for the purpose of strengthening malocological expertise in the region (cascade-style training), and integrated vector management to promote cost-effective interventions. A list of malocological experts in the Region of the Americas should be prepared and made available to the countries upon request.
- It was stressed that monitoring, evaluation, and surveillance of SCH programs—and the data they
 provide—is generally insufficient for decision-making toward elimination of the disease. Information
 systems should be enhanced, and there should be better monitoring, evaluation, and surveillance of
 the programs, optimizing resources through multi-disease sentinel sites and surveys integrating
 several diseases.
- The regional NTD program conducted a systematic review, with the support of consultant Ana Clara Zoni (M.D., MPH, and PhD), on SCH prevalence and intensity of infection. It demonstrated that the scant data published are not presented in standardized fashion, nor are they measured with the same diagnostic techniques. This makes it hard to compare data over time, between regions, and to assess progress made by the programs. Brazil is the only country that has published articles on this subject since 2001, and it has three articles that report on intensity of infection according to the





WHO criteria. The countries are urged to use the WHO criteria (described in the 2011 program managers' guide) when presenting data on SCH prevalence and intensity of infection, and to use the standard tools WHO has developed (i.e. JAP—Joint Application Package—or the NTD databank), for the compilation and reporting of program data. Information systems must be developed that make it possible to report data on schistosomiasis in a standard way, but also allow certain flexibility so that it can be easily adjusted as SCH control and elimination programs evolve. Countries are encouraged to publish their recent surveys in an indexed scientific journal (Suriname, Brazil, and the Dominican Republic).

- It is striking that not enough resources are invested in SCH research in the region. Multidisciplinary research capacities and attitudes must be created, to promote a comprehensive approach that can resolve SCH/public health operational issues, particularly for interface among the different disciplines (biomedicine, epidemiology, sociology, etc.). Additionally, among the priority research questions to be addressed in the Region of the Americas are the following:
 - Development of a pediatric formula for SCH treatment. It is noteworthy that DNDi,
 Farmanginhos, and the Liverpool School of Tropical Medicine are working (separately) to develop such a formula.
 - Conduct a systematic review or more studies on the effects of MDA (praziquantel) in combating SCH in areas of co-endemicity with neuro-cysticercosis, and possible adverse effects. It was mentioned that the Bill and Melinda Gates Foundation is currently financing a study on this subject.
 - Ascertain the impact of climate change and natural disasters, such as hurricanes, on the life cycle of the intermediary snail hosts and their distribution.
 - Demonstrate the basic reproductive rate—minimum prevalence—below which it is not
 possible for SCH transmission to continue in communities.
 - Identify affordable measures to control transmission in the definitive host. China's experience in this area was discussed, including its elimination of *Schistoma hematobium* in 5 provinces; the case of Guadeloupe was also mentioned.
- The need to increase and sustain management of SCH morbidity, even in areas of low endemicity, was discussed, because of the social and economic impact of chronic latent infections, even though their prevalence and level of intensity are low. There is a need to ensure that evidence on the impact of SCH infection translates into policies and actions. Therefore, continuing medical education sessions and training on the diagnosis and treatment of morbidity caused by infection should be encouraged, through both in-person and distance education. The countries said it is crucial to integrate care at existing health services, and to encourage the reporting of the disease.





• It is a challenge to implement SCH control and elimination strategies in tandem with efforts for other NTDs, because this requires coordination and agreements with other programs and even other ministries. However, participants stressed the need to integrate these programs, and to improve water, sanitation, health and hygiene education, and environmental control to accelerate the process of elimination of schistosomiasis and other NTDs. Six countries in the region have launched integrated plans of action to combat NTDs, some of which include Schistosomiasis because it is endemic in the country; at least two other countries are planning to do so soon.

Changing the behavior of communities is one of the biggest challenges. Information, education, and communications materials and campaigns that have been successful in some countries may be used in others. Furthermore, the region has some experts trained in the COMBI methodology (Communication for Behavioral Impact—Linda Lloyd) that can advise the countries on changing people's behavior in order to reduce infection.





Main recommendations for the PAHO/WHO Regional Program on Neglected Tropical Diseases and representatives from the ten invited countries and Saint Kitts and Nevis:

- 1. Follow up on the points raised at the meeting which were mentioned in the previous section. Give technical support (and mobilize human and financial resources if necessary) to countries to update their epidemiological status and plan the strategies recommended for that status (sustain and/or expand MDA, implement IVM, strengthen diagnosis and case management). Also, support countries that may have eliminated SCH to compile the evidence needed to verify elimination, even though the WHO verification procedures and criteria have not yet been launched. Countries must compile information on their programs and former programs before the historical memory is lost.
- 2. Encourage the coordination of actions and technical cooperation among countries and partners interested in the control and elimination of SCH and other NTDs.
- 3. Encourage the WHO to organize a consultation of experts to identify new diagnostic tools with high sensitivity and specificity, so that they can be offered to countries to use during the final stages of SCH elimination.
- 4. Ask WHO to launch a guide with the criteria and procedures for verification of SCH elimination, including the minimum information that must be included in the dossier. Even though these guides are not yet available, countries can continue to move toward the goal of elimination.
- 5. Improve the monitoring and evaluation of SCH control/elimination programs and SCH information systems, and disseminate data from the monitoring and evaluation of programs, to make SCH more visible and mobilize resources through the ministries of health and interested partners and donors.
- 6. Strengthen the following capacities: integrated vector management with special emphasis on expanding malacological expertise, laboratory diagnosis, and management of morbidity in the Region of the Americas. There is a proposal to hold a workshop on integrated vector management, with special emphasis on malacological control, in 2015, prioritizing the participation of representatives from countries that are endemic for SCH and other vector-transmitted NTDs, and to foster cascade-style training. It was stressed that distance courses should be developed to improve and promote IVM, and strengthen malacological capacity and the diagnosis and management of SCH morbidity in the region, as an optimal way to build capacity in the countries.
- 7. With the support of universities and WHO Collaborating Centers, promote the research that SCH control and elimination programs need (see list above).
- 8. Disseminate the report on the meeting so that countries can follow up on the conclusions and recommendations. Also disseminate and create forums for identifying best practices and success stories in the region toward elimination of schistosomiasis and other NTDs (such as creating the "Ciro de Cuadros Award for innovative and successful NTD control and elimination efforts").





ANNEXES

Annex 1. Agenda

8:00-8:15 a.m.	Registration in the lobby						
8:30-8:45 a.m.	Opening remarks						
	Assistant Secretary of Environmental Health. Representative of the Puerto Rico Department of Health (Dr. Carlos Carazo, 5 minutes)						
	PAHO Representative in Puerto Rico (Dr. Raúl Castellanos, 5 minutes)						
	PAHO/WHO Regional Advisor on Neglected Infectious Diseases (Mr. Steven Ault, 5 minutes)						
8:45-9:00 a.m.	Introduction of the participants and review of the agenda (Dr. Laura Catalá)						
9:00-10:00 a.m.	 Background. Schistosomiasis: moving from strategies of control to elimination in the context of Neglected Infectious Diseases (Chair: Dr. Charles King, 60 minutes) WHO Overview—from control toward verification of the elimination of schistosomiasis in the context of Neglected Infectious Diseases (Dr. Jiagang Guo, 25 minutes) PAHO overview—from control toward the elimination of schistosomiasis in the context of Neglected Infectious Diseases (Dr. Laura Catalá) Discussion and wrap up (Chair: Dr. Charles King, 20 minutes) 						
10:00-10:15 a.m.	Coffee break (15 minutes)						

10:15-12:30 p.m. **Topic 1 A. Epidemiological status of schistosomiasis in endemic and formerly endemic countries:** Updates on SCH control/elimination programs and integration with others NIDs—challenges and opportunities towards elimination of schistosomiasis (Chair: Dr. Joseph Cook, 135 minutes)

- Brazil (Dr. Rosa Castalia and Dr. Ronaldo Scholte, 30 minutes)
- Venezuela (Dr. Luisa León, 25 minutes)
- Suriname (Dr. Juanita Malmberg, 25 minutes)
- Saint Lucia (Mr. Reynold Hewitt, 25 minutes)





Discussion and wrap up (Chair: Dr. Joseph Cook, 30 minutes)

	Discussion and Wap ap (chair. 51. 363cpir 666k) 36 minutes)				
12:30-1:30 p.m.	Lunch (60 minutes)				
1:30-4:00 p.m.	Topic 1 B. Epidemiological status of schistosomiasis in endemic and formerly endemic countries: situation analysis of countries that may have eliminated schistosomiasis transmission and could move forward toward verification of elimination - challenges and opportunities toward verification (Chair: Dr. George Hillyer, 60 minutes)				
	 Puerto Rico (Dr. George Hillyer, 15 minutes) Dominican Republic (Dr. Lourdes Mc Dougall, 15 minutes) Antigua and Barbuda (Dr. Cleofoster Vivian Beazer, 15 minutes) Martinique (Dr. Nicole Desbois, 15 minutes) Monserrat (absent) Guadeloupe (absent) Discussion and wrap up (Chair: Dr. George Hillyer, 15 minutes) 				
4:00-4:15 p.m.	Coffee break (15 minutes)				
4:15-5:00 p.m.	Topic 2. Systematic review of schistosomiasis prevalence and intensity of infection in the Region of the Americas (Dr. Ana Clara Zoni, 30 minutes)				

4:15-5:00 p.m. Topic 2. Systematic review of schistosomiasis prevalence and intensity of infection in the Region of the Americas (Dr. Ana Clara Zoni, 30 minutes) Discussion and wrap up (Chair: Dr. Laura Catalá, 15 minutes) 5:00-6:00 p.m. WG1- Working group by country/organization and partners: SWOT analysis-Discussion of specific strengths and needs toward the elimination of schistosomiasis in the Region of the Americas (Dr. Laura Catalá, 60 minutes)

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Topic 3. Successful control and elimination programs globally—lessons learned to guide future verification of the elimination of schistosomiasis (Chair: Mr. Adrianus Vlugman)

8:30-9:30 a.m.

- Saint Lucia's Project (Dr. Joseph Cook, 20 minutes)
- Success stories and lessons learned on schistosomiasis control and elimination in other regions (Dr. Jiagang Guo, 20 minutes)

Discussion and wrap up (Chair: Mr. Adrianus Vlugman, 20 minutes)

Topic 4. Surveillance: Surveillance systems, new tools for mapping and surveillance in low endemicity areas (Chair: Dr. Carlos Teixeira)

9:30-11:15 a.m.

- Updates on integrated surveillance tools for schistosomiasis and other neglected infectious diseases (Dr. Evan Secor, 15 minutes)
- What kinds of mapping and surveillance tools should be used in low schistosomiasis transmission areas? Is there enough evidence to make recommendations? (Dr. Daniel Colley, 15 minutes)

Discussion and wrap up (Chair: Dr. Carlos Teixeira, 15 minutes)

11:15-11:30 a.m. Coffee break

Topic 5. Morbidity control (Chair: Dr. Daniel Colley)

 Experiences on morbidity control at WHO Collaborating Centers (Dr. King, 20 minutes)

11:30-12:30 p.m.

 Morbidity control in areas with high versus low endemicity for schistosomiasis (Dr. Joseph Cook, 20 minutes)

Discussion and wrap up (Chair: Dr. Daniel Colley, -20 minutes)

12:30-1:30 p.m.	Lunch (60 minutes)
1:30-3:00 p.m.	WG2. Working group 2 by country/organization: Plan of Action toward verification of schistosomiasis elimination. Identify gaps in data, activities, tools and resources toward the elimination of schistosomiasis in the countries of Latin America and the Caribbean by 2020 (Dr. Laura Catalá, 90 minutes)
3:00-3:15 p.m.	Coffee break





WG2. Presentations by country/organization: Plan of Action towards verification of schistosomiasis elimination. Identification of gaps in data, activities, tools and resources toward the elimination of schistosomiasis in the countries of Latin America and the Caribbean by 2020

3:15-5:20 p.m.

Discussion of priorities and next steps toward schistosomiasis elimination in the Region of the Americas by 2020: Defining the road map for the region (Dr. Laura Catalá, 125 minutes)

5:20-5:30 p.m.

Closing remarks (Mr. Steven Ault, 10 minutes)





Annex 2. List of participants

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Annex 3. Draft of status toward verification of schistosomiasis elimination in AMR, 2014.

Morbidity control	Improve morbidity control	Interruption of transmission	Post-elimination surveillance or compile evidence toward verification	Verification
	2	2	6	
	only in 2 municipalities; in the rest diagnosis	- Saint Lucia (or perhaps transmission has already been interrupted and epidemiological status needs to be evaluated)	 Puerto Rico Dominican Republic Guadeloupe Martinique (need to coordinate with Guadeloupe/Corsica/French Guiana) Montserrat * Antigua and Barbuda * 	

^{*} There is a need to assess whether Antigua, Montserrat, and Saint Kitts and Nevis can be removed from the list of endemic countries.





Annex 4. Summarized regional timetable for the elimination of schistosomiasis as defined with the countries.

	2014	2015	2016	2017	2018	2019	2020	2021
Brazil	Improv	e morbid	ity contr	ol			Interruption of transmission	
Venezuela								
Suriname	Interruption of transmission Interruption of transmission			Post-elimination surveillance or compile evidence toward verification				
Saint Lucia								
Guadeloupe								
Martinique (DEA)								
(DFA)								
Dominican Republic							Verification of	
Puerto Rico	Post-elimination surveillance or compile evidence toward verification						ion	
Antigua and Barbuda *								
Dai Nuuu								
Montserrat *								

^{*} There is a need to assess whether Antigua, Montserrat, and Saint Kitts and Nevis can be removed from the list of endemic countries.