Towards a better surveillance in Public Health: Multiplex Bead Assay

Regional Initiative of PAHO, CDC, and participating countries

9th Global Health Conference
"Innovative Research, Global solutions"
May 8, 2019

Pan American Health Organization
World Health Organization
Regional Office for the Americas

PAHO

Contents

CONCEPTS

BACKGROUND STUDIES

REGIONAL INITIATIVE

PAHO/NID (Res. CD55.R9-2016)

Interrupt or eliminate:

1. Trachoma
2. Chagas disease
3. Rabies mediated by dogs
4. Leprosy
5. Taeniasis/cysticercosis
6. Lymphatic filariasis
7. Onchocerciasis
8. Schistosomiasis

Prevent, control and reduce the burden:

9. Cystic echinococcosis/hydatidosis
10. Fascioliasis
11. Human plague
12. Leishmaniasis
13. Soil-transmitted helminthiasis

Assess the regional epidemiological situation:

14. Brucellosis
15. Buruli ulcer
16. Ectoparasitic infections
17. Selected fungal infections
18. Myiasis
19. Strongyloidiasis
20. Venomous snake bite and arthropod bite poisonings
21. Yaws

PAHO/WHO

What is the Goal?

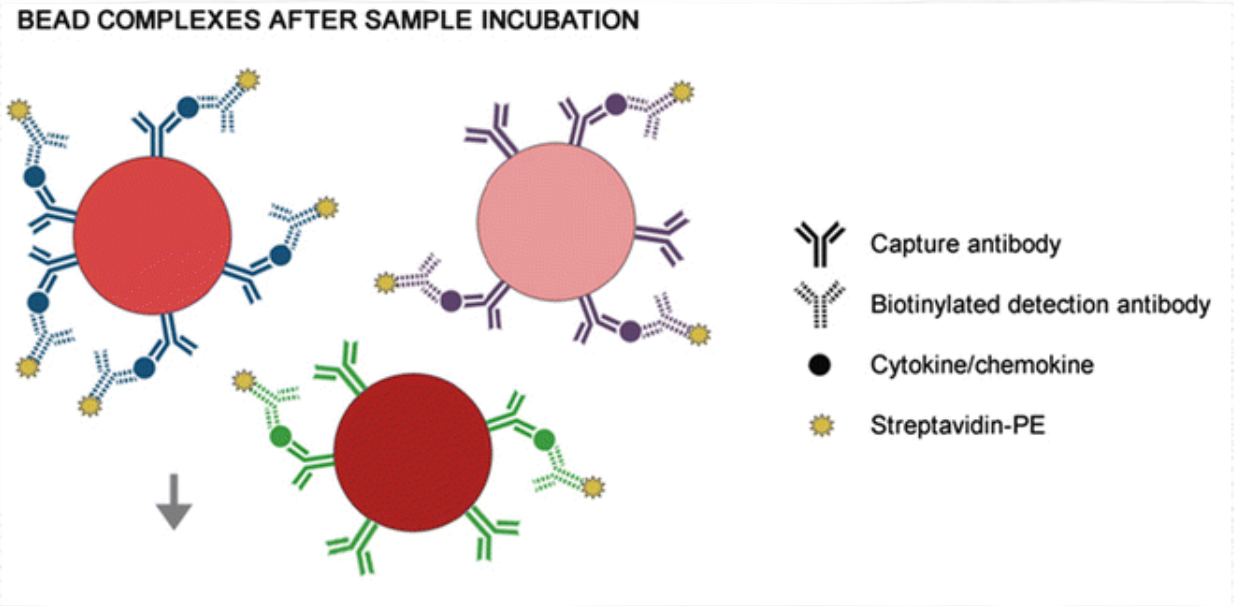
Develop a single, integrated sero-surveillance method for the measurement of

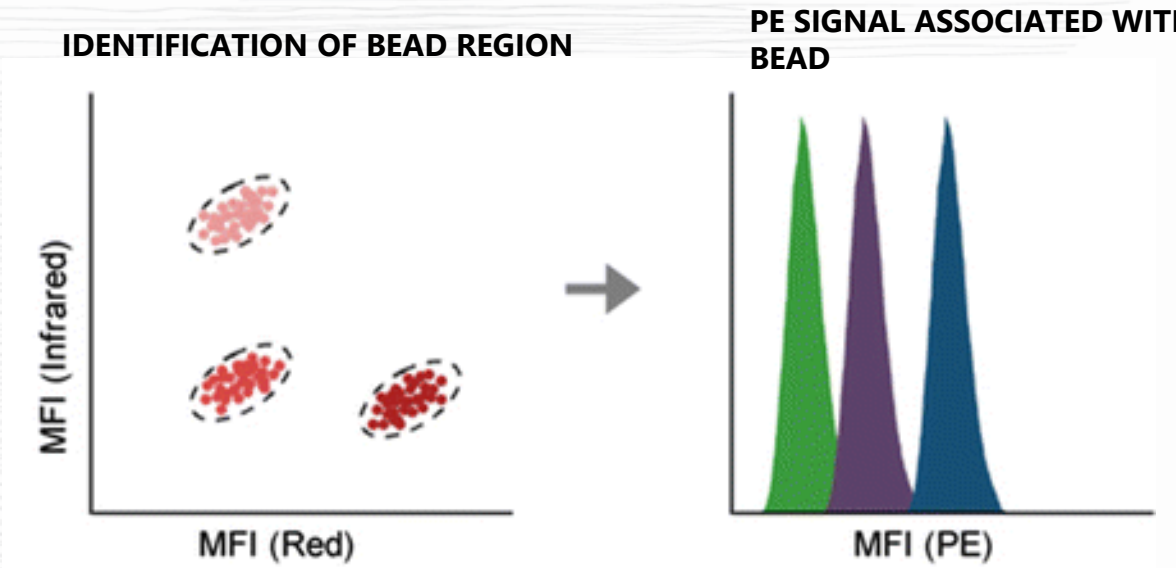
- **health impact across multiple programs or**
- **monitoring/documentation of situation**

- **Immune status of target populations for vaccine preventable diseases**
  - *Measles, Rubella, Tetanus, Diphtheria*
- **Efficacy of intervention programs (control, elimination, EPHP)**
  - ***Malaria***
  - *Water, sanitation, and hygiene (**WASH**) interventions*
  - ***Neglected Tropical Disease** (**DMA** programs):*
    - *LF, Schistosomiasis, Trachoma, Onchocerciasis, etc.*

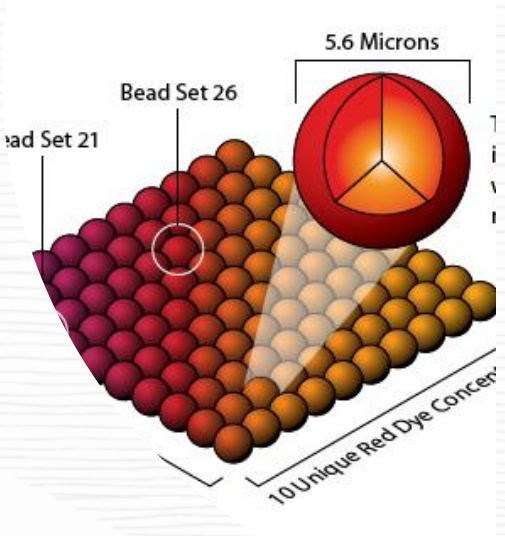
Pan American Health Organization / World Health Organization Americas PAHO

Luminex®-based multiplex bead assay (MBA)

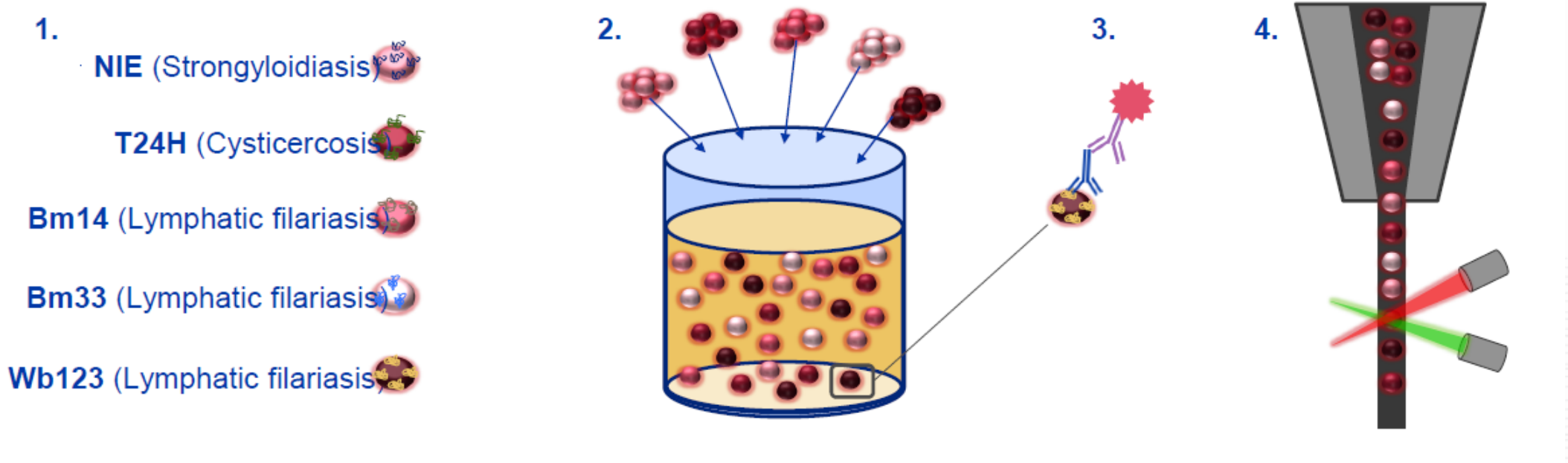




- ✓ **Can run up to 100 different bead-antigen sets in a single well**
- ✓ **Add beads of interest (relatively easy and fast)**
- ✓ **Single 1:400 sample dilution in duplicate**
- ✓ **Measure IgG from sample with fluorescent reporter**
- ✓ **Data reported in median fluorescent intensity (MFI)**



Example of multiplex panel and assay



1. Panel of antigens is selected and antigens are chemically bound to beads.

2. Beads are mixed together in well and sample added.

3. Anti-human detection antibody with fluorescent tag binds antibody bound to antigen on bead

4. Sample is run through flow cytometer (Luminex or MagPix) and interrogated by laser.

Source: Presentation by Dr. Diana Martin, CDC

Current MBA Panels (IgG) at CDC

- Vaccine preventable diseases
  - **Measles, tetanus, rubella, diphtheria**
- Waterborne/foodborne diseases
  - ***Cryptosporidium, Giardia, Toxoplasma,* Salmonella LPS Group B and D, norovirus, *E. histolytica, Campylobacter,* ETEC/ cholera, *S. pyogenes***
- Neglected tropical diseases
  - **Filariasis, *Strongyloides*, trachoma, cysticercosis, onchocerciasis, schistosomiasis, yaws, taeniasis, toxocariasis, fascioliasis, *Ascaris***
- Vector-borne diseases
  - ***P. falciparum, P. vivax,* other *Plasmodium* spp., dengue, Rift Valley Fever Virus, Chikungunya virus, Zika, *Babesi microti***

For those highlighted in yellow, the CDC has serum panels with measured sensitivity and specificity for each antigen. For those in white, full characterization is incomplete, but coupled antigens are available and capable of binding antibodies.

Source: CDC

Contents lists available at SciVerse ScienceDirect

International Journal for Parasitology

journal homepage: www.elsevier.com/locate/ijpara

Current Opinion

Development of a new platform for neglected tropical disease surveillance

Patrick J. Lammie [a,*], Delynn M. Moss [b], E. Brook Goodhew [a], Katy Hamlin [a], Alejandro Krolewiecki [c], Sheila K. West [d], Jeffrey W. Priest [b]

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[c] Instituto de Investigaciones en Enfermedades Tropicales, Sede regional Orán, Universidad Nacional de Salta, San Ramón de la Nueva Orán, Argentina
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Table 1
Potential uses for multiplex tools for serosurveillance.

Uses for multiplex tools
• Mapping the geographic distribution of multiple infections in humans and animals
• Monitoring secular trends (e.g., improved access to water)
• Monitoring program impact
• Coverage assessments
• Post-MDA surveillance
• Outbreak investigations

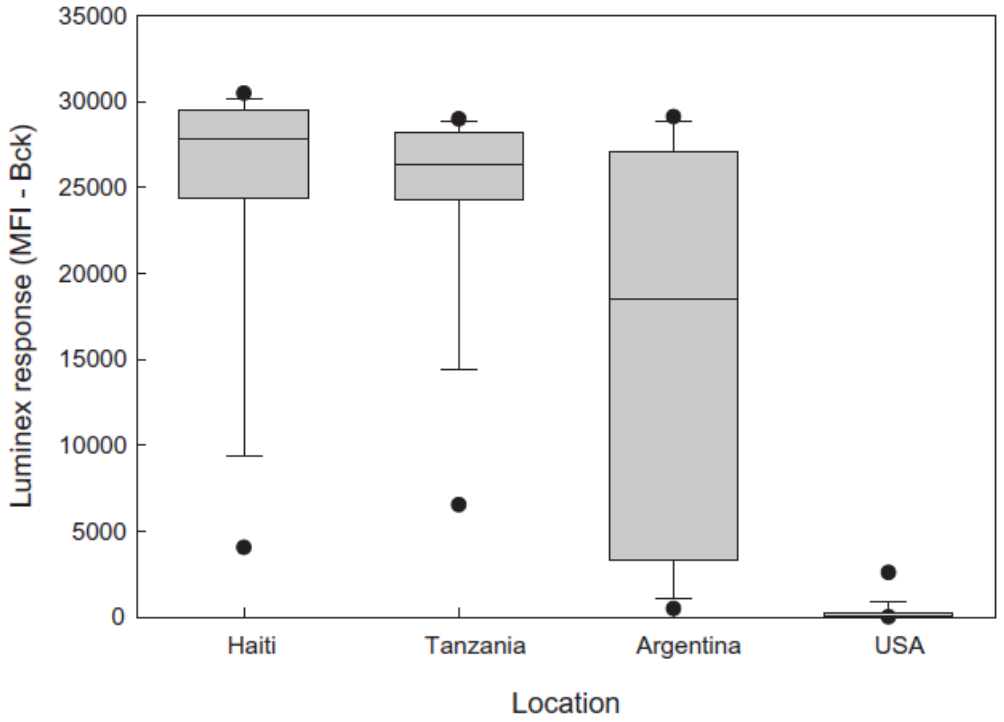


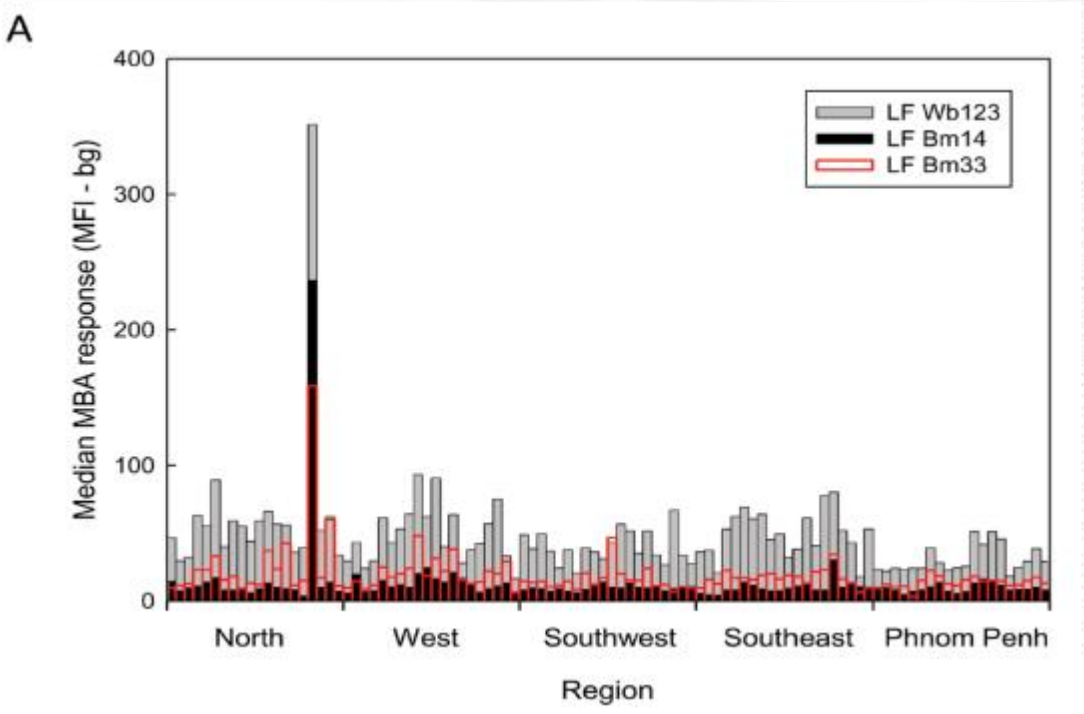
Fig. 2. Enterotoxigenic *Escherichia coli* (ETEC) responses among children <6 years old. A multiplex bead assay using a native *E. coli* heat labile toxin β subunit was performed as previously described (Moss et al., 2011) on sera from children from Haiti ($n = 115$), Tanzania ($n = 31$), Argentina ($n = 86$) and the US ($n = 107$). Samples were collected from children under 6 years of age in the course of studies approved by the relevent human subjects' protection offices. Boxes indicate the 25th and 75th percentiles, bars indicate the 10th and 90th percentiles, and dots indicate the 5th and 95th percentiles. Median values are indicated by a line within the box.

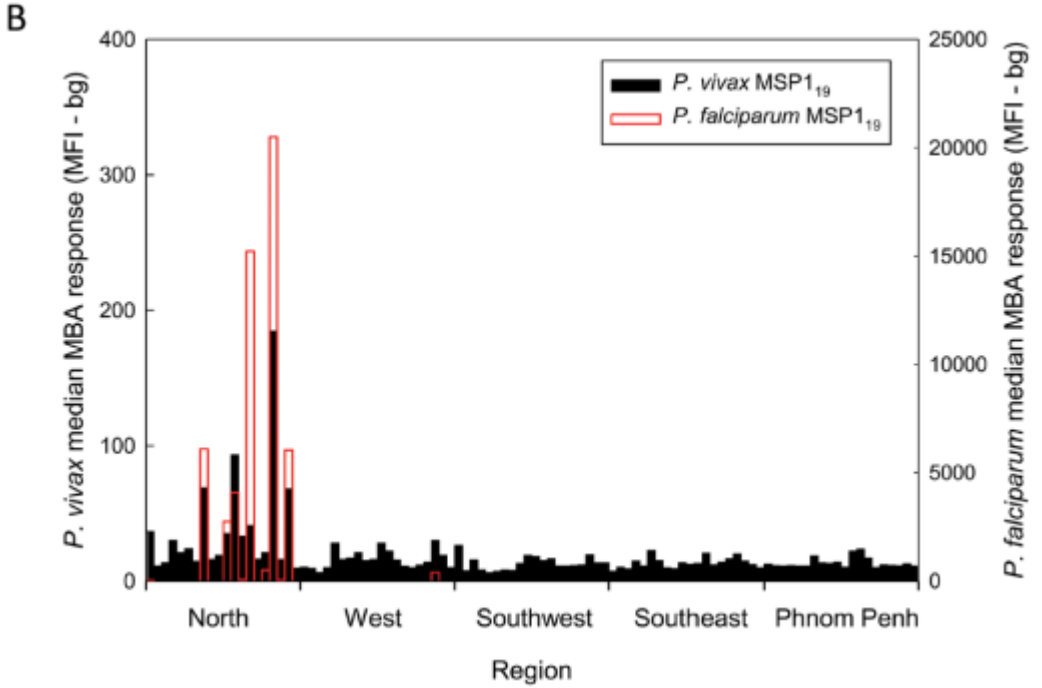
2012

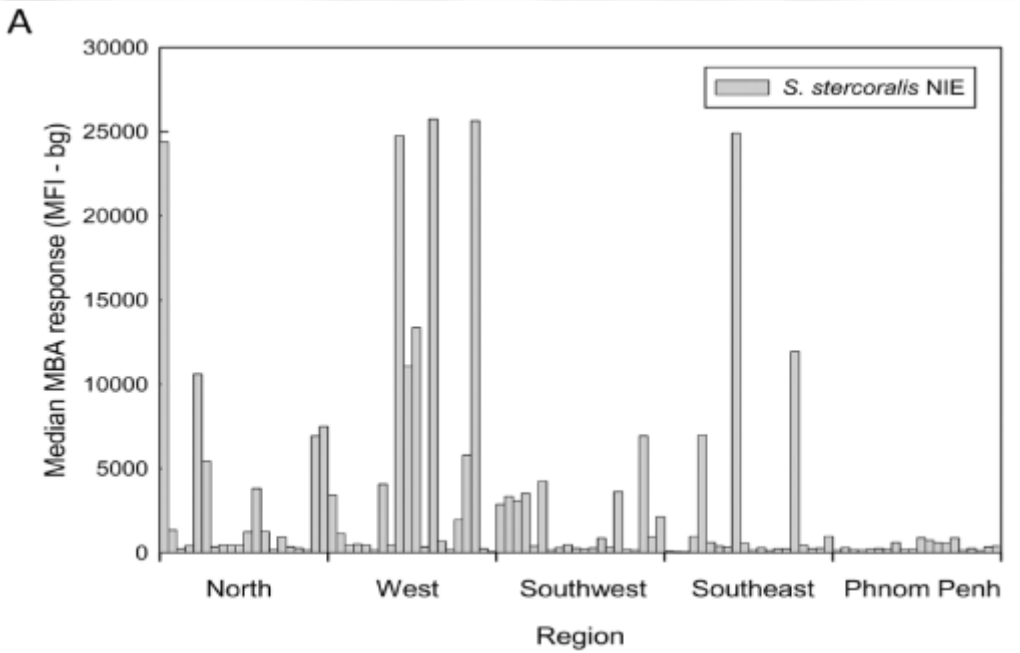
RESEARCH ARTICLE

Integration of Multiplex Bead Assays for Parasitic Diseases into a National, Population-Based Serosurvey of Women 15-39 Years of Age in Cambodia

Jeffrey W. Priest[1]*, M. Harley Jenks[2], Delynn M. Moss[1], Bunsoth Mao[3], Sokhal Buth[4], Kathleen Wannemuehler[5], Sann Chan Soeung[6], Naomi W. Lucchi[2], Venkatachalam Udhayakumar[2], Christopher J. Gregory[5], Rekol Huy[7], Sinuon Muth[7], Patrick J. Lammie[2]







2016

RESEARCH ARTICLE

The impact of school water, sanitation, and hygiene improvements on infectious disease using serum antibody detection

Anna N. Chard[1]*, Victoria Trinies[1], Delynn M. Moss[2], Howard H. Chang[3], Seydou Doumbia[4], Patrick J. Lammie[5], Matthew C. Freeman[1]

Abril 2018

Table 4. Linear regression model results of the association between the school WASH intervention and antibody responses.

	β	95% CI	*p*
Campylobacter jejuni (P18 Antigen)	0.02	-0.20, 0.24	0.88
Campylobacter jejuni (P39 Antigen)	-0.12	-0.31, 0.06	0.18
Cryptosporidium parvum (17 KdA Antigen)	0.29	0.09, 0.49	0.01
Cryptosporidium parvum (27 KdA Antigen)	0.09	-0.11, 0.28	0.41
Dengue 2	0.09	-0.21, 0.39	0.55
Dengue 3	0.29	0.04, 0.54	0.02
Entamoeba histolytica	-0.06	-0.31, 0.20	0.65
Escherichia coli	-0.18	-0.40, 0.05	0.12
Giardia intestinalis (VSP 3)	-0.02	-0.20, 0.16	0.84
Giardia intestinalis (VSP 5)	-0.19	-0.37, -0.01	0.04
Norovirus (Norwalk strain)	-0.01	-0.24, 0.22	0.92
Norovirus (St. Cloud strain)	-0.02	-0.25, 0.22	0.88
Norovirus (Sydney strain)	0.12	-0.28, 0.04	0.14
Plasmodium falciparum (MSP_{19})	0.07	-0.13, 0.27	0.51
Plasmodium falciparum (MSP_{42})	0.16	-0.13, 0.46	0.29
Plasmodium falciparum (AMA_1)	0.16	-0.20, 0.52	0.38
Plasmodium vivax (MSP_{19})	0.14	-0.06, 0.34	0.16
Salmonella enteritidis	0.10	-0.05, 0.25	0.20
Salmonella typhimurium	0.06	-0.11, 0.23	0.50
Schistosoma mansoni	0.22	-0.02, 0.45	0.07
Chlamydia trachomatis (CT-694)	0.39	0.20, 0.58	<0.001
Chlamydia trachomatis (Pgp3)	0.15	-0.03, 0.33	0.10
Vibrio cholerae	-0.07	-0.27, 0.13	0.49

PAHO

Regional Initiative for Integrated Surveillance of Communicable Diseases

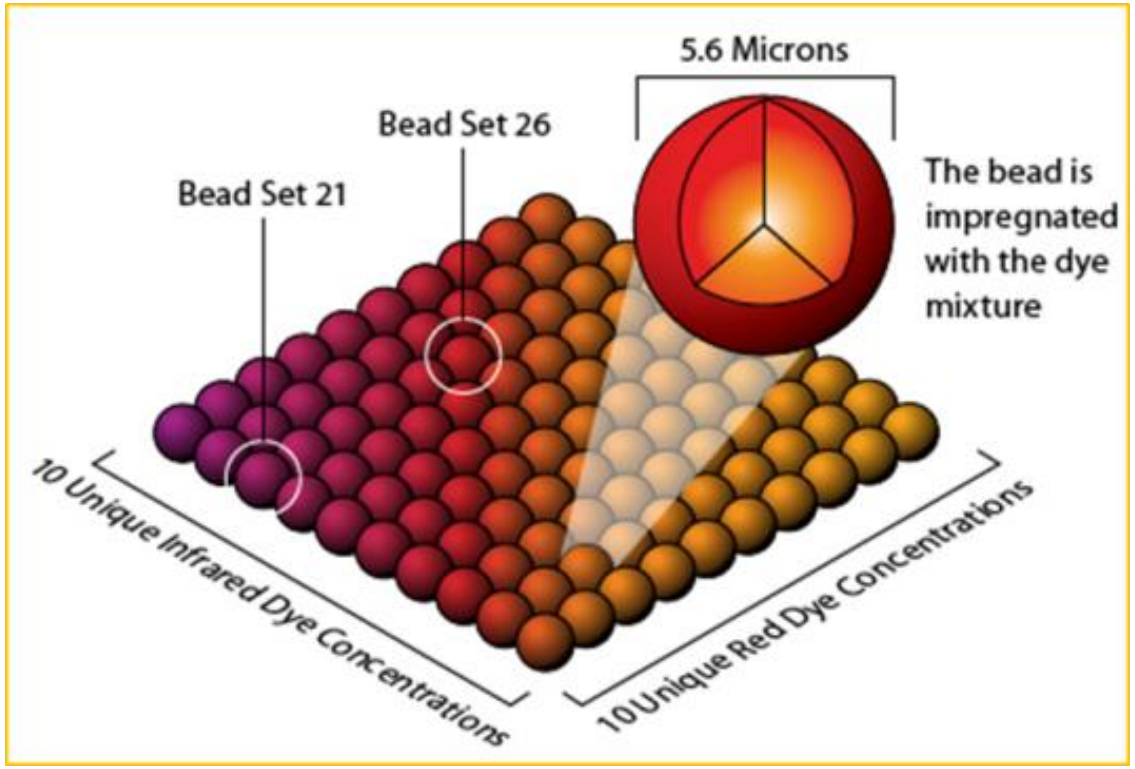
PAHO: health workers collecting samples of the LF and other communicable diseases survey in Guyana, 2019

Regional Initiative for the Americas

- Multiplex Bead Assay (MBA) developed by CDC based on Luminex
- 2016 started collaboration CDC and PAHO (*NTD and Immunization programs*)

Use serology for *integrated surveillance of communicable diseases*:

- Transfer MBA capacities to countries-*pilot project*
- Expand use of serology in surveys planned for communicable diseases: NTDs, VPDs, WBDs, FBDs, etc.



Source: CDC

Integrating serology-based surveillance into national surveillance systems – pilot project

Mexico:

- Serologic survey for NIDs, VPDs = *15 antigens* (malaria, trachoma, taeniasis/cysticercosis, measles, rubella, diphtheria, and tetanus).
- **Currently:** Analysing results (from 6 municipalities and school age children)

Paraguay:

- Serologic survey for NIDs, VPDs, WFBDs = *14 antigens* (trachoma, taeniasis/cysticercosis, Toxoplasma, Strongyloides, Giardia, Cryptosporidium, measles, rubella, diphtheria, and tetanus)
- **Currently:** Field work started in March 2019 in El Chaco Region – school age children

Brazil:

- Serologic survey for NIDs, VPDs, WFBDs = *22 antigens* (LF, malaria, trachoma, taeniasis/cysticercosis, Strongyloides, Giardia, Cryptosporidium, Toxoplasma, measles, rubella, diphtheria, and tetanus)
- Working on protocol – sample from serum bank –children under 15 years old.

- National public health labs with capacities to use MBA: CDC providing beads coupled with Ags.
- Lab professionals trained at CDC – supervised by CDC
- Samples collected and analyzed in each country – seed funds from CDC and PAHO
- *National teams working together*: epidemiological surveillance, programs, and nat. labs + PAHO + CDC

INTEGRATED COMMUNICABLE DISEASES SURVEYS
Opportunities for Expanding MBA

Guyana:

- LF Remapping, NTDs and VPDs = *19 antigens*: (LF, malaria, strongyloidiasis, trachoma, yaws, cysticercosis/taeniasis, measles, rubella, diphtheria and tetanus).
- FTS and DBS; *Tropical Data Platform*
- CDC will analyse DBS
- Collecting samples from school-age children – survey will end by mid-2019

Guatemala:

- STH national survey, NTDs, VPDs = *20 antigens* (malaria, onchocerciasis, strongyloidiasis, trachoma, Giardia, cysticercosis/taeniasis, measles, rubella, diphtheria and tetanus).
- Kato-Katz and DBS
- CDC will analyse DBS
- Working on protocol – school age children

Integrating serologic surveys into NID surveys already planned/funded-

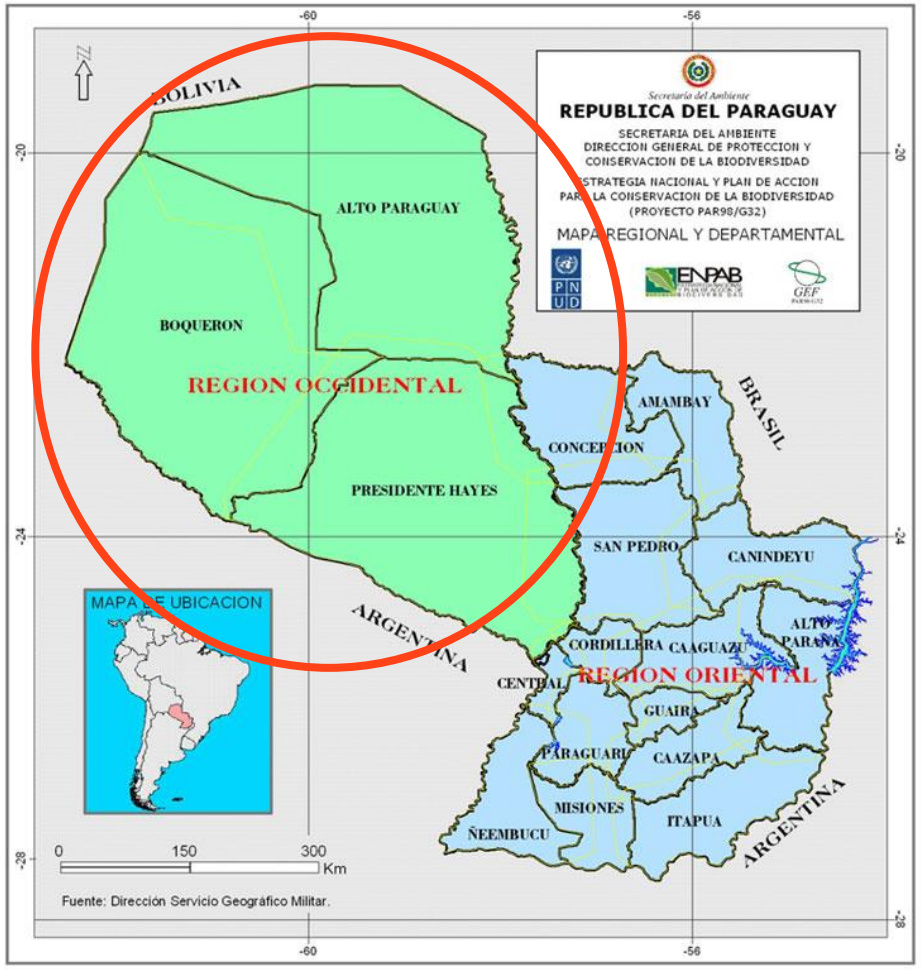
cost saving

Transferring capacities for MBA - Costing MBA at country level

Example of Paraguay – *survey for 14 antigens*...

- ~1,300 samples in 35 schools in the Chaco Region
- Building capacity:
  - National epidemiological surveillance system to incorporate serologic surveillance
  - National public health laboratory to use MBA platform

Item	Cost
Protocol	$5,000
Supplies: sample collection and reagents for lab (not including the machine and labor hours)	$15,000
Sample collection – pre field work coordination, and field work (only operational costs)	$50,000
Training of Nat. lab staff at CDC (only travel costs, not including labor hours at CDC and supplies)	$15,000
Approx. Total cost	*$85,000*



Chaco Region in Paraguay

Our vision of integrated serology-based surveillance in the Americas

- Countries using MBA as a complementary tool to monitor the elimination of CDs, monitoring impact of interventions
- Contribute with evidence to fill gaps derived from using MBA.
- Countries producing panels of beads customized for public health needs and for other countries
- To establish a regional network of labs with MBA capacities – South to South cooperation

PAHO: health workers collecting FTS, DBS, and survey data with *Tropical Data platform*, Guyana 2019.

PAHO

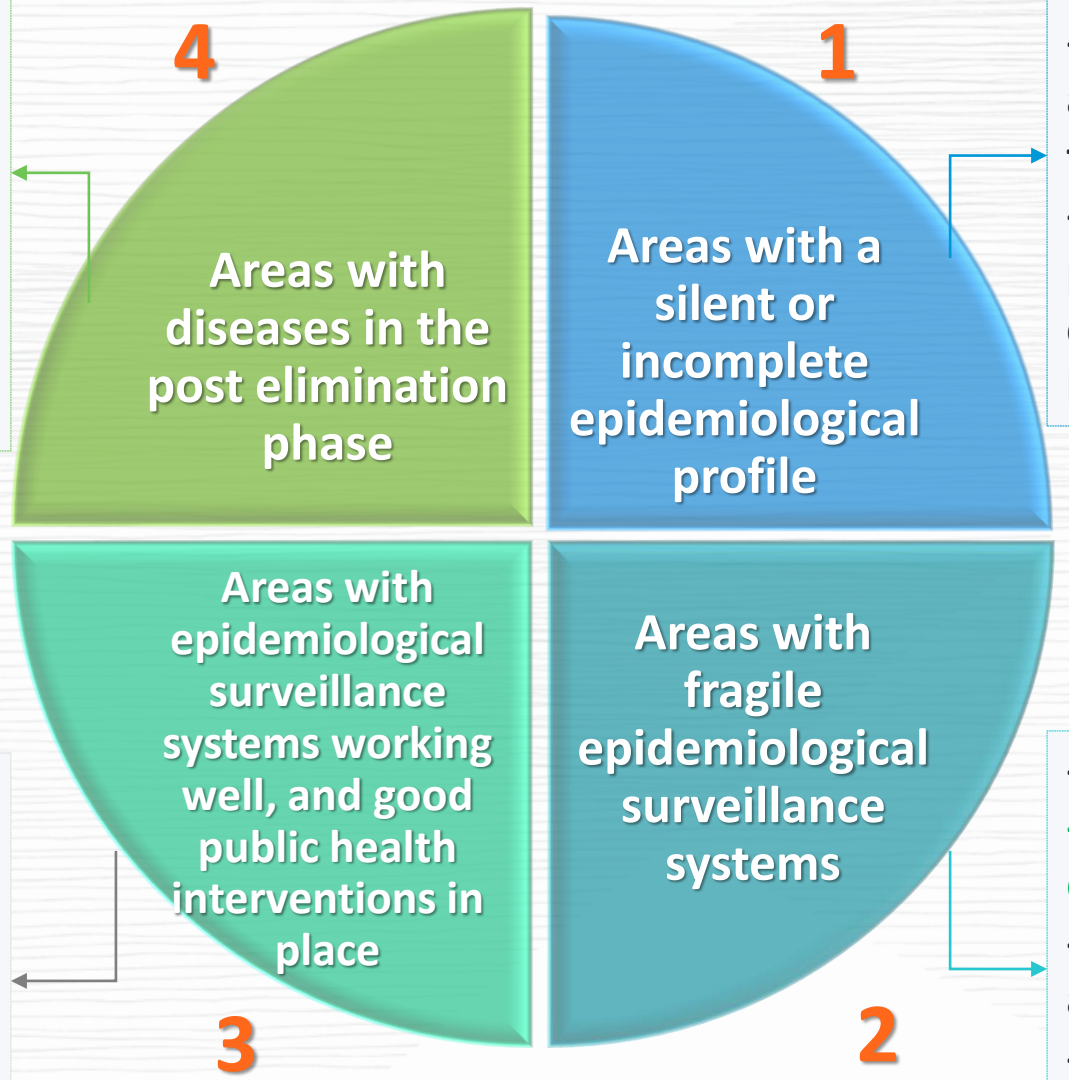
Challenges to overcome

- **Multidisciplinary group work** – different expectations, needs, interests, etc.
- **Multi-disease survey protocols** - different programs, epidemiological status of each disease is different, multi-objective survey, sample size calculation for several diseases, etc.
- **Analysis and interpretation of results** – Consensus/understanding of the use of MBA for different groups of diseases: VPDs *vs* NID.
- **Decision-making process** based on the results – understanding the application/utility of results

PAHO: health workers collecting DBS, Paraguay, 2019.

Scenarios for Integrated Immunological Surveillance - Opportunities

-To detect re-introduction or re-establishment of a disease; to support surveillance of other events and interventions
-To anticipate risks and implement actions accordingly
-Example: in the Americas: Oncho, Trachoma, LF, Schisto, Malaria, VPD, VBD, WBD, etc.



-To establish epidemiological situation (baselines)
-And further design and implement actions and interventions according to the profile
-Example: hard to reach areas and populations living in vulnerable conditions (deficient access to health services)

-To evaluate impact of interventions
-And make decisions based on results
-Example: Prevention, control and elimination of NID, VBD, VPD, etc.

-To improve quality of data
-Monitor/assess the epidemiological situation
-And further improve surveillance and implement interventions
-Countries with priority infectious diseases overlapping in geographic areas (NID, VBD, WBD, VPD)

The Pan American Health Organization
Department of Communicable Diseases and Environmental Determinants of Health
Washington, DC

PAHO: school age children participating in the LF and other communicable diseases survey in Guyana, 2019