Multiplexed immunoassays: A new tool for better surveillance of vitamin and mineral deficiencies

BACKGROUND

Vitamins and minerals, collectively known as micronutrients (MNs), are essential for healthy growth and development, especially for children and women (pregnant, lactating, and those of childbearing age). MN deficiencies significantly contribute to morbidity, mortality, and a variety of disabling conditions:

- Iron deficiency is the most common nutritional disorder in the world; it causes irreversible physical and cognitive development in young children, contributes to a significant proportion of maternal deaths, and ultimately limits gross domestic product via a less productive workforce.[1]
- Iodine deficiency is the leading cause of preventable brain damage in childhood in the world. Extreme iodine deficiency can result in cretinism, a severe form of mental retardation accompanied by stunting. It can also result in stillbirth or spontaneous abortion.[2]
- Vitamin A deficiency is the main cause of preventable blindness in children, and it increases the risk of morbidity and mortality from infectious diseases. Nearly half of children who experience blindness from vitamin A deficiency die within 12 months of losing their sight.[3]
- Folate and vitamin B_{12} are essential for preventing neural tube defects during early fetal development (i.e., the brain, spine, and spinal cord). These defects are irreversible and can result in stillbirth, death, or permanent disability such as spina bifida.
- Vitamin D is necessary for bone development and strength throughout life; deficiency is also associated with elevated risk of cancer and/or infectious disease.

NEED

Micronutrient deficiencies affect an estimated 2 billion people worldwide, the majority of whom live in low- and middle-income countries (LMIC). However, tracking MN status is difficult, time consuming, invasive, and expensive. This leaves governments with very limited data from which to make decisions on how to most effectively implement nutrition programs and track progress.

Accurate population surveillance of MN status can provide a clear picture of the nutritional status of a country, region, or target group. While targeted nutrition-based interventions are commonly used to address MN deficiencies in a population (e.g., supplementation or fortification of common foods), there is a need to determine if these interventions have a marked impact on at-risk groups, such as young children and women of childbearing age.

GOAL

PATH and our partners sought to develop tools to enable improved population surveillance for MN status. A multiplexed assay approach permits rapid throughput as multiple MN biomarkers are simultaneously measured using a single sample and unified test method. A multiplexed panel for MN measurements can be used to determine the prevalence of nutritional deficiencies and offer a more accurate method by which to measure and track the effects of targeted nutritional interventions.

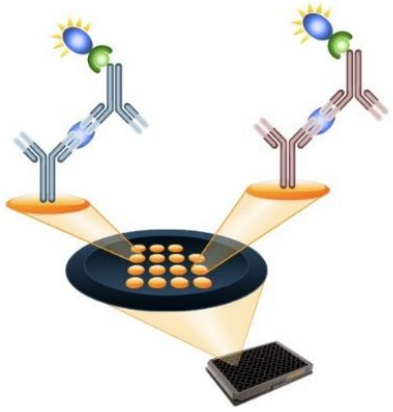

Illustration of the Quansys Q-Plex™ technology. Specific immunologic tests for individual MN biomarkers are printed as discrete spots in a geometric array to create multiple assays per test well. Image: Quansys.

APPROACH

Using an existing technology, the Q-Plex™, developed by private sector partner Quansys Biosciences, Inc. (Logan, UT, USA), PATH and the University of Washington have worked to identify, combine and validate further MN biomarkers, adding to the utility of the technology, improving upon the previously developed MN panel for vitamin A and iron deficiency.[4]

The product is the Q-Plex™ Human Micronutrient (7-Plex). This test kit quantifies vitamin A, iron, and iodine deficiency biomarkers in addition to biomarkers for inflammation and *Plasmodium falciparum* malaria, which can affect iron levels. The assay can be customized to specific subsets of the MN biomarkers as needed by users.[5]

The MN 7-Plex can use serum collected via finger-stick, greatly simplifying sample collection and preparation. Furthermore, a single sample enables surveillance of multiple MN in one test. These improvements address the key logistical obstacles to large-scale population surveillance by minimizing the complexity and cost of specimen collection, sample preparation, and testing. Initial verification on a cohort of pregnant women from Niger indicated the new assay is comparable to existing tests.[5]

As expanded population surveillance becomes simpler and more cost-effective with new tools such as the MN 7-Plex, countries and programs can make data-driven decisions for public health interventions and put limited resources to the most effective use.

CURRENT STATUS

PATH is further evaluating the MN 7-Plex assay against traditional enzyme-linked immunosorbent assays (ELISAs) and other analytic methods on other cohorts. PATH has ongoing collaborations with the University of California, Davis, and Johns Hopkins Bloomberg School of Public Health to validate the performance of the assays on key populations (e.g., young children) from high-risk settings. Independent evaluations of the MN 7-Plex are also being conducted by the US Centers for Disease Control and Prevention, GroundWorks, Craft Technologies Inc., and the Demographic and Health Surveys division of USAID.

The array is currently being expanded to include biomarkers for vitamin B_{12} and vitamin D and a further panel of biomarkers associated with childhood stunting and oral vaccine responsiveness. PATH and partners are also investigating dried blood spots as a sample type. This simple and minimally invasive sampling method will permit easier collection in the field than the current methods for the surveillance of MN status.

NEXT STEPS

PATH is looking to expand Q-Plex™ development to include vaccine and disease-related test panels. This would allow for combining programmatic MN surveillance testing with assessing vaccine seroconversion in young children or the prevalence of sexually transmitted infections in women of childbearing age. The flexibility of this platform to collect various population surveillance data from a single, small sample will be of significant value to ministries of health and national programs, enabling them to determine the efficacy of vaccine campaigns or the unreported actual burden of disease in addition to establishing MN status.

HOW TO ORDER THE TEST

PATH has licensed to Quansys the rights to manufacture and sell the MN 7-Plex. This array is offered as a 7-Plex or can be customized to a subset of MN biomarkers as supportive to the surveillance activity planned. Visit http://www.quansysbio.com/human-micronutrient/ for more information and to order. This product is available at preferential prices to NGOs, LMIC nutrition programs, and PATH affiliates.

FOR MORE INFORMATION

To learn more about PATH's work in MN assay developments, please contact David Boyle at dxinfo@path.org.

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