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the poliopipeline

A quarterly update of ongoing research in the Global Polio Eradication Initiative

Role of research in new Strategic Plan

In 2008, the World Health Assembly (WHA) recognized that the long-established polio eradication tactics that had eliminated poliovirus in all but four countries were not working in the remaining four endemic countries and called for a new strategy to eradicate the virus in these remaining reservoirs. In 2009, a special one-year Programme of Work was developed, introducing tactical innovations, new vaccine formulations and facilitating an independent evaluation of the major barriers to interrupting poliovirus transmission. These key initiatives informed the new Global Polio Eradication Initiative (GPEI) Strategic Plan 2010-2012, which was endorsed by the WHA in 2010, and publicly launched by stakeholders at a special meeting convened by World Health Organization Director-General Dr Margaret Chan and UNICEF Executive Director Anthony Lake on 18 June 2010.

To ensure international oversight of the new strategies, an Independent Monitoring Board (IMB) has been established. On a quarterly basis, the IMB will track tangible progress against the global milestones of the Strategic Plan and guide mid-course corrections, as needed. The IMB convened for the first time in December 2010.

This process will be underpinned by an expanded programme of research. Research will play a key role in evaluating the programmatic benefits of the new bivalent oral poliovirus vaccine (bivalent OPV) in improving population immunity; assess programme performance through measuring population immunity levels in key reservoir areas; better track the evolving epidemiology of transmission; assess and improve the quality of supplementary immunization activities (SIAs) and the related monitoring efforts; and, evaluate new tools and strategies to predict and stop outbreaks and limit new international spread of virus.

This issue of *Polio Pipeline* provides an in-depth look at the role research will play in helping to assess progress and to come up with new ways to further sensitize strategic approaches.

New Independent Monitoring Board to assess progress towards polio-free world

A new Independent Monitoring Board (IMB) has been established to assess progress towards the attainment of a polio-free world. The new IMB was established at the request of the Executive Board (EB) and the World Health Assembly (WHA), to independently monitor and guide the work of the new Global Polio Eradication Initiative (GPEI) Strategic Plan 2010-2012, providing advice on the status of Strategic Plan milestones and on corrective action plans.

The IMB, comprised of global experts from a variety of fields relevant to the work of the GPEI, will convene on a quarterly basis (beginning in December 2010) to independently evaluate progress towards each of the major 'milestones' of the GPEI Strategic Plan 2010-2012 as 'on track', 'at risk' or 'missed', on the basis of polio epidemiology, poliovirus virology, standard performance indicators and other programme data. Additionally, the IMB is expected to provide an assessment of the risks posed by existing funding gaps.

If, during its deliberations, the IMB should conclude any of the milestones or process indicators are 'at risk' or 'missed', the relevant national authorities and/or implementing/donor partners will be engaged to establish emergency corrective action plans. At subsequent meetings, the IMB will then evaluate the quality, implementation and impact of any corrective action plans.

Reports from the group's quarterly meetings will go directly to the heads of the spearheading partner agencies - the World Health Organization (WHO), Rotary International, the US Centers for Disease Control and Prevention (CDC) and UNICEF - and the Bill and Melinda Gates Foundation, and will be made public at www.polioeradication.org.

Polio Pipeline: to subscribe to this quarterly newsletter, please email: polioresearch@who.int.

Key expert groups convene in India to evaluate new research projects

The Polio Research Committee (PRC), which helps guide the Global Polio Eradication Initiative's (GPEI) research agenda, convened in Delhi, India, in December 2010 to discuss strategic research priorities. With the epidemiological opportunity which presents itself at the start of 2011, with key endemic reservoir areas reporting historic low levels of polio transmission, the PRC recommended research focus on further addressing critical operational gaps (see text box on PRC's call for proposals). At the same time, new outbreak response tactics should be evaluated, as well as additional measures to limit renewed international spread and minimise its consequences.

Following the PRC, also in Delhi, an Expert Meeting on Mucosal Immunity reviewed the current science and future research needs to better understand the role mucosal immunity plays in polio transmission and immunization. An increasing body of evidence, in particular since the increased per-dose efficacy of monovalent and bivalent OPVs has been established, suggests the importance of understanding both vaccine-induced mucosal immunity, in addition to humoral immunity. In particular, the meeting looked at risk factors of decreased mucosal immunity, possible interventions to boost mucosal immunity and surrogate measurements of mucosal immunity against poliovirus. For major knowledge gaps identified in epidemiology, immunology and possible interventions in this meeting, please see text box on PRC's call for proposals.

The Polio Research Committee's call for proposals

The Polio Research Committee (PRC) is currently soliciting research proposals, particular focus on the following topics, to support the implementation and evaluation of the Global Polio Eradication Initiative (GPEI) Strategic Plan 2010-2012.

1. Operational research

A key aspect of the new GPEI Strategic Plan 2010-2012 is to continuously review the quality of surveillance and supplementary immunization activities (SIAs) and fill critical gaps in quality. With generous funding from Rotary International and the Bill and Melinda Gates Foundation, the GPEI is in a position to support research projects which can aid the process of identification of high-risk areas, and support and facilitate evidence-based solutions to improve programme operations.

Operational research priorities to be considered for funding include:

1. Identification of key issues in areas with persistent polio transmission and/or repeated importations resulting in re-established poliovirus transmission;
2. Social research to understand migratory populations and implications to the polio epidemiology in polio-infected countries (e.g., the size and pattern of migration and their knowledge, attitude and practice towards immunization and general healthcare seeking behaviour);
3. Effective models for the quality coverage of migratory populations during supplementary immunization activities;
4. Evaluation of initiatives to improve operations in areas with compromised security (e.g., short interval additional doses, alternative operational model to address security risks);
5. Evaluation of alternative supplementary immunization activity monitoring systems; and,
6. Improvement of acute flaccid paralysis surveillance (e.g., study on variation in definitions, guidelines, quality, indicators, data analysis and role of additional surveillance beyond indicators).

2. Improving mucosal immunity

An Expert Meeting on Mucosal Immunity reviewed and identified the following knowledge gaps:

1. Duration of mucosal immunity induced by OPV;
2. Evaluation of different IPV/OPV schedule/combinations to induce a longer-lasting mucosal immunity;
3. Evaluation of other interventions to enhanced OPV-induced mucosal immunity (e.g., vitamin A supplementation, probiotic use, antacid co-administration, deworming, Giardiasis treatment); and,
4. Development of new laboratory methods to measure intestinal mucosal immunity against poliovirus.

Research proposals are invited from GPEI staff (e.g., EPI managers) and independent institutions/investigators and private cooperation.

Procedure for submission of proposals: All research proposals should include the following information:

1. Research question/objectives (e.g., research questions, reference to published literature and cutting-edge science, description of how the results will be utilized);
2. Qualification of investigators and collaborators (e.g., track record of researchers, capability of laboratory, necessary contractual arrangements);
3. Budget request (e.g., appropriate for work anticipated); and,
4. Study design and methodology (e.g., detailed activities, timelines, deliverables, availability of necessary capacities, feasibility of methods, plans for ethical and government approvals).

The standard research proposal form is available at http://www.polioeradication.org/Research/Grantsandcollaboration/Howtoapply.aspx. Researchers are invited to submit proposals by 15 March 2011 to the Research and Product Development team, GPEI, WHO Geneva, by email to polioresearch@who.int.

Available and upcoming publications

- Progress report on global eradication of poliomyelitis. Progress report by the GPEI secretariat to the 128th Session of the Executive Board of the World Health Assembly (January 2011). Available at www.polioeradication.org.
- Sutter R et al. Immunogenicity of bivalent type 1 and 3 oral poliovirus vaccine: a randomised, double-blind, controlled trial. Lancet 2010;376:1682-88.
- Tebbens RD et al. The Economic analysis of the global polio eradication initiative. Vaccine 2010, doi:10.1016/j.vaccine.2010.10.25.
- Mohammed AJ et al. Fractional Doses of Inactivated Poliovirus Vaccine in Oman. N Engl J Med 2010;362:2351-9.
- Jenkins HE et al. Implications of a Circulating Vaccine-Derived Poliovirus in Nigeria. N Engl J Med 2010;362:2360-9.
- Resik S et al. Randomized Controlled Clinical Trial of Fractional Doses of Inactivated Poliovirus Vaccine Administered Intradermally by Needle-free Device in Cuba. The Journal of Infectious Diseases 2010: 201(9):1344-1352.
- Polio vaccines and polio immunization in the pre-eradiation era: WHO position paper. Weekly Epidemiological Record. No. 23, 2010, 85, 213-228.
- Outbreaks following importations of wild poliovirus into countries of the WHO African, European and South-East Asian Regions: January 2009 - September 2010. Weekly Epidemiological Record. Vol 85, 45 (pp 445-452).
- Health conditions for travellers to Saudi Arabia for the pilgrimage to Mecca (Hajj). Weekly Epidemiological Record. Vol 85, 43 (pp 425-436).
- Performance of acute flaccid paralysis (AFP) surveillance and incidence of poliomyelitis, 2010. Weekly Epidemiological Record. Vol 85, 37 (pp 357-364).
- Completion of national laboratory inventories of wild poliovirus containment: WHO Region of the Americas, March 2010. Weekly Epidemiological Record. Vol 85, 34 (pp 329-336).

Research evaluates progress

The Global Polio Eradication Initiative (GPEI) Strategic Plan 2010-2012 describes the usefulness of research in guiding the programme decisions in some of the endemic countries over the last years. The Strategic Plan recommends that the scope of research activities such as serosurveys, environmental surveillance, Lot Quality Assurance Sampling (LQAS) and better supplementary immunization activity (SIA) monitoring tools should be expanded to other key endemic areas.

Periodic serosurveys and adjusting programme decisions to achieve and maintain high population immunity have been recommended as a process indicator towards the achievement of milestones. To this end, a seroprevalence study was done in India in August 2010, one is ongoing in Pakistan and another being planned in Nigeria.

India seroprevalence 2010

India implemented a cross-sectional seroprevalence study in August 2010 in high-risk blocks of western Uttar Pradesh and central Bihar. Ten highest-risk blocks in each state were selected on the basis of highest polio rate and occurrence of polio cases in the last five years. Within these blocks, children aged 6-7 months were randomly selected from SIA microplans.

The implementation of this survey was a joint effort of the National and State Governments, National Polio Surveillance Project (NPSP) India, social mobilization network (SM net) of UNICEF and CORE, the World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC). Screening and selection of study participants was done in the identified field areas by the SM net and Surveillance Medical Officers (SMOs). The selected study children and parents were enrolled at the nearest health facility. In addition to the blood sample for serology, the study infants and their mothers were offered tests for anaemia and were given iron and folic-acid supplementation to help address nutritional anaemia.

The response and participation was high in these most challenging areas of Uttar Pradesh and Bihar. Transportation of study children in the difficult terrain of Kosi river area was a clear logistic challenge. It was heartening to see that the parents agreed to travel across long distances on foot and used boats, motorcycles, carts and other means of transportation to reach the health facilities.

Overall, 1200 serum samples were collected, 60 from each block. Samples have been sent for testing to the Enterovirus Research Centre (ERC) in Mumbai. Results of serology are expected in early 2011, and will provide key insight into the prevailing levels of seroprevalence in high-risk areas of India. At the same time, results will help in evaluating the impact of use of bivalent oral polio vaccine (bOPV) in these traditional strong holds of polio transmission.

Nigeria seroprevalence 2011

There is a dramatic decline in the number of polio cases in Nigeria in 2010 as compared to the last year. Though there has been an overall improvement in SIA operations, the percentage of zero-dose children remains high in some key northern Nigerian states.

To assess the immunity profile of young children in the highest risk Local Government Areas (LGAs - districts), the GPEI partners have agreed to conduct a health facility-based seroprevalence study in the city of Kano, in the northern state of Kano.

The study protocol has been drafted and is under technical and ethical review. The study is likely to be implemented in early 2011 and the serology results should be available in the first quarter of 2011, and should provide key insight into ongoing immunity gaps and operational programme efficacy in northern Nigeria.

The role of research to eradicate polio in Nigeria

Nigeria, at end-2010, reported a total of 18 wild poliovirus (WPV) cases with onset of paralysis in 2010, compared to 389 WPV cases at the same time in 2009. In 2003, though Nigeria had the highest number of polio cases in the world, planned polio supplementary immunization activities (SIAs) were suspended because of questions and concerns regarding the safety of oral polio vaccine (OPV) used in Nigeria. Consequently, the number of polio cases increased to 1,122 in 2006. The significant drop to 285 polio cases in 2007 was not sustained, as in 2008, the number of cases rose to 798. But this time, the downward trend from 2009 to 2010 appears to have been sustained.[1]

So how has Nigeria sustained, over the past 12 months, this very low transmission of WPV? Several factors contributed, including:

- improvements in SIA quality in high-risk Local Government Areas (LGAs);
- continued and sustained engagement of political, traditional and religious leadership; and,
- closing surveillance gaps for acute flaccid paralysis (AFP).

Importantly, these factors were catalysed by the application of new research tools combined with research into - and revised application of - existing and traditional social mobilization and communication practices.

The introduction in 2006 of monovalent OPV type 1 (mOPV1) in Nigeria, was the beginning of a positive turn-around in the country's polio eradication efforts. Jenkins et al[2], reported that the mOPV1 was four times as efficacious than the traditionally-used trivalent OPV. The continued use of mOPV1 in frequent SIAs in Nigeria resulted in the progressive decline in the number of WPV type 1 (WPV1) cases – 724 in 2008, 75 in 2009 and seven WPV1 cases in 2010 (at end-2010). However, with an upsurge in WPV type 3 (WPV3) cases in 2009 (from 73 in 2008 to 313 in 2009), in 2010 the bivalent OPV containing both types 1 and 3 polio was introduced on the recommendation of the Advisory Committee of Poliomyelitis Eradication (ACPE) and the Nigeria Expert Review Committee on Polio Eradication and Routine Immunization (ERC).[3]

Equally important as the use of mOPV1 and bivalent OPV was the change in community perceptions towards vaccination, especially polio vaccination. This ensured that more susceptible children were reached with the potent and efficacious vaccines. Innovative social mobilization and communications efforts included a "re-search" into and a review of existing and traditional social mobilization and communication practices and their modification and re-application. This has contributed to correcting misconceptions about polio vaccines and led to renewed interest and acceptance of the vaccines. One such intervention is the "majigi". "Majigi" is a public awareness programme employing the use of open air cinemas in public places; in the past, it has been an effective and popular method of educating and informing citizens on government programmes and planned activities. The practice which was much used in the pre-independence (pre-1960) era had subsequently died out. With the traditional leaders in attendance, at the "majigi" shows, communities have become better informed, not only on polio eradication, but also on other health and community development issues. The direct involvement of traditional leaders in vaccination exercises and their engagement in mobilizing their networks has resulted in a more effective participation by the people at every level of vaccination activities and other health issues. Issues concerned with patterns of non-compliance and gender specific communication interventions require further detailed studies. For example, the "majigi" still reaches primarily men. There is a need to continue studies, in collaboration with women organizations, which will provide results that can be applied to ensure that women are reached and fully engaged in polio eradication programmes and other health interventions.

To further accelerate progress towards polio eradication, Nigeria must continue to apply the results of ongoing research and studies to enhance the quality of strategies. For example, the results of the ongoing seroprevalence studies would provide useful LGA-specific results and age-related immunity profiles that could be applied to enhance and further sensitise outreach tactics. At the same time, to adopt an aggressive mop-up strategy to respond rapidly and effectively to any remaining poliovirus transmission, the programme must take advantage of another research product, the real time reverse transcriptase PCR (rRT-PCR) technique, for the rapid and reliable identification of type and location of poliovirus isolates.

A traditional trumpeter announces the presence of a polio vaccination team in the streets of Kano, northern Nigeria.

1 Polio Statistics Nigeria 2006-2010.

2 Jenkins HE., Aylward RB, Gasasira A, Donnelly CA., Abanida EA., Koleosho-Adelekan T, Grassly NC. (2008) Effectiveness of Immunization against Paralytic Poliomyelitis in Nigeria N Engl J Med 2008; 359:1666-74.

3 Report of the 19th Meeting of the Expert Review Committee (ERC) on Polio Eradication and Routine Immunization in Nigeria, Minna, 22-24 March 2010.

Mobile phones help assess quality of polio campaigns

The Global Polio Eradication Initiative (GPEI) is actively evaluating ways to utilize mobile phone technology to collect and analyze data on immunization activities.

The use of mobile phones for data collection is already well-established and many products exist. *Episurveyor* is an open software which requires low-technical expertise to use and is designed for low-specification mobile phones (e.g., a key requirement, given the technical limitations of the field). *Episurveyor* software is specifically designed for the implementation of survey forms on mobile phones and aims to be technically-appropriate for developing regions. It consists of web-based software for designing forms and viewing data, and a Java-based mobile phone application for data collection (even without network coverage). Data is sent to a remote server, where it can be viewed and downloaded from any computer with internet access. The broad benefit of mobile phone applications is the real-time transfer of data and the removal of manual data entry.

The GPEI is now expanding this approach, utilizing the application of this software to collect Lot Quality Assurance Sampling (LQAS) data of polio campaigns to assess risks and guide improvements in both endemic and re-infected countries. LQAS is used to validate real-time independent monitoring data in areas of discordant epidemiologic and monitoring data. To date, an application has been developed and tested internally. The application will be further evaluated in the field before being subsequently rolled-out more broadly, with view of replacing paper forms currently used for data collection during LQAS.

The GPEI is also planning to scale-up application of this technology to other operational areas. Indeed, this approach has already been successfully employed in Kenya. Following the importation of polio into Turkana, Kenya in 2009, the Kenyan Ministry of Public Health and Sanitation implemented Short-Interval Additional Dose (SIAD) campaigns in August and October 2009 to rapidly stop the outbreak. With the SIAD approach, campaign managers needed even faster turn-around of information to monitor campaign performance and take corrective action where necessary. Standard, paper-based surveying methods of monitoring the campaign would have been prohibitive. That is why independent campaign monitors used *EpiSurveyor* software downloaded onto basic Java-enabled mobile phones, while field supervisors were able to deliver reports to the national level within hours of finishing the campaign thanks to the automatic report feature of the software. Health officials collected the information on the phone and then transmitted the data to the central servers. National and sub-national level managers had a constant snapshot of the campaign in the 12 target districts in real-time and could monitor the progress on the website. In addition, a GPS-enabled mobile phone allows to record and transmit GPS coordinates of each sampling site so that any geographic gap in monitoring can be identified. Any weaknesses observed were acted upon nearly immediately. Such interventions included the re-distribution of the vaccines where field stocks were running out, dispatching supervisors for problem-solving, staff and transport re-deployment, immediate investigation of suspected cases, as well as re-enforcement of radio messages for communities. The use of *EpiSurveyor* and mobile phones thus enabled managers to make real-time evidence-based decisions, thereby improving the efficacy of the campaign.

The Polio Research Committee (PRC) is currently soliciting operational proposals on a wide range of topics, to improve the implementation and evaluation of polio eradication strategies (see page 2).

Mobile phone technology is helping to assess quality of polio campaigns in key areas.

Research helps optimize outbreak response

In 2010, high-profile and devastating outbreaks occurred in a number of previously polio-free countries, including new outbreaks in the Republic of Congo and Tajikistan. These outbreaks resulted in significant tragic humanitarian consequences, and have been associated with a high level of disease burden and - in particular in the case of the Republic of Congo - with an apparent unusually high case fatality rate (upwards of 40%). These two outbreaks are a real reminder of how dangerous this disease is, and underscores the urgent need to rapidly interrupt wild poliovirus transmission everywhere. With most of the world polio-free, there is a very real danger of new groups of susceptible population cohorts emerging, and should they be exposed to re-infection, would result in a higher likelihood of devastating consequences. To minimise the risk of outbreaks from importations, countries should maintain high population immunity levels, however the only way to truly address this is by removing the risk of importations from occurring by successfully interrupting the remaining chains of transmission.

These outbreaks also provide critical new insight into the importance of ensuring appropriate strategies are in place for the post-eradication era, and of the need to further optimise outbreak response activities. International outbreak response standards endorsed by the World Health Assembly (WHA) in 2006 (Resolution WHA59.1) significantly reduced the consequences (duration, geographic extent and associated cases) of new outbreaks since then, but focus must be on optimising outbreak response, be it associated with wild polioviruses or circulating vaccine-derived polioviruses (cVDPVs). Research is playing a critical role in this.

To help predict high-risk areas for outbreaks, mathematical modelling is aiding to classify areas at risk of both an importation and subsequent outbreaks, to help prioritise resources to highest-risk countries. New outbreak response tactics that have already shown promising field results will be clinically evaluated. A planned clinical trial will help determine the degree to which population immunity in outbreak settings may be more rapidly enhanced through application of the Short Interval Additional Dose (SIAD) strategy. This strategy exploits the availability of monovalent OPVs to shorten the interval between large-scale supplementary immunization activities (SIAs) in selected high-risk or infected areas, more rapidly building immunity. Serologic surveys can help determine impact of outbreak response and validate programme performance indicators. This tactic is providing crucial evidence on population immunity achieved as a result of outbreak response activities in Tajikistan last year. Further monitoring of outbreak response activities include the newly-evaluated Lot Quality Assurance Sampling (LQAS), to more definitively ascertain the level of vaccination coverage that is being achieved.

At the same time, ongoing transmission of the 2009 outbreak in Kenya detected in 2010 in Uganda underscores the urgent need to fill sub-national surveillance gaps for acute flaccid paralysis (AFP). Targeted surveillance reviews will now more readily identify any sub-national gaps, to enable operational teams to fill any identified gaps.

These activities will provide invaluable insight into optimizing outbreak response, and may potentially lead to a revision of internationally-agreed outbreak response guidelines. The newly-formed Independent Monitoring Board (IMB - see page 1) will monitor whether ongoing and any eventual new outbreaks are on track to being stopped in an epidemiologically-appropriate timeframe.

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