Reviewer's report

Title: Vaccine-derived poliovirus surveillance in China during 2001-2013: the potential challenge for maintaining polio free status

Version: 0 Date: 04 Feb 2017

Reviewer: Bruce Thorley

Reviewer's report:

Vaccine derived poliovirus (VDPV) evolves from long-term replication or transmission and is an important focus of the WHO global polio eradication initiative as it can give rise to outbreaks of paralytic polio. The paper describes 49 VDPVs detected in China between 2001 and 2013. The authors are requested to consider the following points. In particular to clarify the distinction between VDPV cases, which the authors classify as VDPVs isolated from polio-compatible cases, and the WHO virological definition of VDPVs based on VP1 sequence analysis. This distinction is most apparent with the seven VDPVs isolated in Guangxi province in 2006, which were not regarded by the authors as a circulating VDPV outbreak as only one case was considered polio-compatible.

The manuscript did not include pagination. The reviewer assigned the authors' title page as page 1 with the Abstract on page 3. Comments refer to the line numbering in the left hand margin of each page.

Background

Page 4, lines 1-4. The authors cite reference 1 to indicate polio was declared a global public health emergency but this paper notes the International Monitoring Board's conclusion of a public health emergency in Chad in 2011. Were the authors meaning to refer to the international spread of poliovirus as a IHR public health emergency of international concern declared by WHO in May 2014, which is still in place? If so a more recent reference would be appropriate.
Page 4, line 12 and throughout the paper. It is recommended to indicate the poliovirus serotype using standard (Arabic) numerals (1, 2, 3) rather than Roman numerals (I, II, III).

Page 4, line 12. Reference 3 should be updated as eradication of wild poliovirus type 2 was certified in 2015.

Page 4, lines 14-16. Reference 2 should be updated to list three countries endemic for wild polio after Nigeria reported cases again in 2016.

Page 4, line 41. Include an appropriate reference for the outbreak in the Xinjiang region of China in 2011.

Page 5, lines 4-9. The authors state the global switch from trivalent to bivalent oral polio vaccine (OPV) is planned in early 2016. Since this event was implemented in April 2016, the information should be updated with appropriate references.

Materials and Methods

Isolation and characterization of poliovirus isolates.
Page 6. The authors are requested to confirm the method of intratypic differentiation (ITD) used by the provincial polio laboratories and the National Polio Laboratory of China CDC during the study period. While the actual years of usage for particular techniques are not needed, it is important to convey the range of methods employed within the China polio laboratory network. The National Polio Laboratory and some provincial laboratories may have started to use real-time reverse transcription PCR before 2013. The abbreviation, PCR, should come after polymerase chain reaction in lines 23-25, whereas restriction fragment-length polymorphism (RFLP) is a separate methodology.

Case ascertainment and definition
Page 6, line 40. It would be useful to include the WHO definition for adequate stool specimens from AFP cases.
The authors state a VDPV case did not have wild poliovirus isolated and was determined to be polio-compatible by the provincial polio expert committee, in accordance with the WHO current recommendation. However, it is the reviewer's opinion that WHO consider VDPV as a virological definition, not phenotypic, based on nucleotide divergence in the VP1 region compared to prototype OPV strains. The delineation of the 49 VDPVs into three phenotypic categories (VDPV case, non-polio AFP case and healthy population) is an important element of the descriptive epidemiology but the VDPV case definition should not be attributed to a WHO recommendation unless the authors can provide an appropriate reference. Or is the VDPV case definition quoted by the authors a national guideline? The authors are requested to reword lines 44-54 to distinguish between the WHO virological classification of VDPVs based on VP1 divergence and the further assignment of a VDPV case as polio compatible by the provincial polio expert committee.

Results

Descriptive Epidemiology
Page 7, line 25. If known, it would be interesting to state the clinical diagnoses of the 15 non-polio AFP cases classified by the provincial polio expert committees; were they Guillain-Barré syndrome, transverse myelitis or other clinical presentations?

cVDPVs
Page 8, line 9. The authors are requested to state the % range of VP1 divergence of the 2004 VDPV outbreak in Guizhou province as was done for the other VDPV events.

Imported VDPV case
Page 10, line 1. It is suggested to finish the sentence with "...in Myanmar" to clarify the location. It would be useful to cite reference 27 at this point.

VDPV surveillance among healthy children

Page 10, lines 4-21. The authors' state VDPVs were isolated from seven contacts of one VDPV case in Guangxi province in 2006 but considered it to not be a circulating VDPV (cVPDV)
outbreak since only one VDPV case was detected. Reference 19 describes the 2006 Guangxi outbreak as a cVDPV outbreak involving one AFP case and six unimmunized healthy contacts, which supports the reviewer's earlier comment that VDPV is a virological definition. A cVDPV outbreak occurs in an area of low polio vaccine coverage with two or more poliovirus isolates determined to have genetically related divergence from prototype OPV strains. It is the reviewer's opinion that the Guangxi outbreak should be presented in this paper as a third cVDPV outbreak.

Discussion
Page 11, lines 25-28. The authors are requested to reword the sentence as it currently reads that the number of nucleotide substitutions in VP1 occurred in the children not the poliovirus genomes.

Page 12, line 13. The authors are requested to check reference 25. The reviewer's interpretation of the reference was that the period from infection to the onset of paralysis of the iVDPV case was most likely 6.9 years after receiving OPV rather than 9.3 years estimated from the rate of molecular evolution.

Page 12, line 29. The authors' state there was only one instance of VDPV importation in history. Do they mean worldwide or in China? The authors are requested to clarify the statement as there have been reports of other imported VDPVs; for example, Alexander JP et al. J Infect Dis (2009) 199(3):391-397.

Figure 3
Can the authors clarify in the legend whether the placement of the symbols for the geographical location of the VDPVs within each province was random or the approximate location of each case?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
I am able to assess the statistics

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