Measles vaccines: WHO position paper – 28 April 2017
Grading of scientific evidence in support of key recommendations

Table IIa: Safety in HIV infected children

Population : HIV-infected children up to the age of 15 years
Intervention: Measles vaccination (any dose)
Comparison : HIV-negative children
Outcome : Serious adverse events following immunization

PICO Question: Are measles containing vaccines (MCVs) safe when administered to HIV-infected children up to the age of 15 years?				
			Rating	Adjustment to rating
Quality Assessment	No of studies/starting rating		19 observational studies[1]	2
	Factors decreasing confidence	Limitation in study design	Serious[2]	-1
		Inconsistency	None serious	0
		Indirectness	None serious	0
		Imprecision	None serious	0
		Publication bias	Not applicable	0
	Factors increasing confidence	Strength of association/ large effect	Not applicable	0
		Dose-response	Not applicable	0
		Antagonistic /mitigated bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**1**
Summary of Findings	**Statement on quality of evidence**			Evidence supports a very low level of confidence that the true effect lies close to that of the estimate of the effect on the health outcome.
	Conclusion			Measles immunization is not associated with an increased risk of serious adverse events (very low level of scientific evidence) and to date only one case of MCV associated death in an HIV infected patients has been noted.

[1] These tables are based on the systematic review and meta-analysis of the safety and immunogenicity of measles vaccine in HIV-infected children that was recently conducted by Scott P et al, 2011. This systematic review was updated by Nicky Mehtani based on articles published after the availability of HAART in 1996 through February 2015. Mehtani at al found no additional evidence of severe adverse events attributable to measles vaccine in HIV-infected children. For assessment of immunogenicity, 25 studies with comparison groups (involving 4519 vaccinated children) and 1 case report were found eligible for inclusion. For adverse event data, 13 studies without comparison groups (involving 690 vaccinated children) were also examined.
Most studies providing data on safety reported no serious adverse events. In prospective studies that allowed comparisons between HIV-infected and HIV-exposed, but uninfected or HIV-unexposed children, there did not appear to be an increased risk of serious adverse events in HIV-infected children.

[2] Relatively short follow-up period in the prospective studies.

Table IIb: Immunogenecity in HIV infected children

Population : HIV-infected children up to the age of 15 years
Intervention: Measles vaccination (any dose)
Comparison : HIV-negative children
Outcome : Immunogenicity conferred by measles vaccine

PICO Question: Are measles containing vaccines (MCVs) immunogenic when administered to HIV-infected children up to the age of 15 years?				
			Rating	Adjustment to rating
Quality Assessment	No of studies/starting rating		28 observational studies[3]	2
	Factors decreasing confidence	Limitation in study design	None serious	0
		Inconsistency	None serious	0
		Indirectness	None serious	0
		Imprecision	None serious	0
		Publication bias	Not applicable	0
	Factors increasing confidence	Strength of association/ large effect	Not applicable	0
		Dose-response	Not applicable	0
		Antagonistic /mitigated bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**2**
Summary of Findings	**Statement on quality of evidence**			Evidence supports a low level of confidence that the true effect lies close to that of the estimate of the effect on the health outcome.
	Conclusion			Measles immunization may be less immunogenic in HIV- positive as compared to children not infected with HIV (very low level of scientific evidence).

[3] Assessments of measles antibody levels suggested that measles vaccination at six months of age resulted in similar levels of protection in HIV-infected and HIV-unexposed (combined RR 1.05, 95% CI 0.83-1.34, heterogeneity I2 65.7%, P=0.06) or HIV-exposed but uninfected children (combined RR 0.91, 95% CI 0.80-1.04, heterogeneity I2 0.0%, P=0.46). By nine months of age, fewer HIV-infected children responded to measles vaccine than HIV-unexposed (combined RR 0.79, 95% CI 0.61-1.02, heterogeneity I2 81.5%, P=0.005) or HIV-exposed but uninfected children (combined RR 0.70 (95% CI 0.56-0.88) heterogeneity I2 79.6%, P<0.001). Two studies suggested that the antibody response in HIV-infected children waned faster than in HIV-uninfected children. Low measles seroprevalence at the time of starting antiretroviral treatment provides supportive evidence that antibody levels wane in HIV-infected children not receiving antiretroviral therapy. In the largest study, involving HIV-infected children aged 2 to 19 years receiving antiretroviral therapy in the United States, only 52% of 193 children had protective antibody concentrations at the time of starting antiretroviral therapy (Abzug 2012). Among 61 HIV-infected Zambian children 9 to 60 months of age starting antiretroviral therapy, only 23% were measles seropositive (Rainwater-Lovett 2013).

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