

WHO Position Paper on Rabies Vaccine - 6 August 2010

Grading of scientific evidence

Table II: Duration of immunity following pre- or post-exposure immunization with cell-culture-based rabies vaccines

Settings: Global

Question: What is the scientific evidence that pre- or post-exposure immunization using cell-culture based rabies vaccines* (by intramuscular or intradermal administration) provide long-term (≥ 10 years) immunity against rabies?

Conclusion: Moderate scientific evidence that using cell-culture-derived rabies vaccines induces ≥ 10 years of immunity against rabies.

*Include cell culture-derived rabies vaccines based on human diploid cells (HDCV), Vero cells (PVRV), chick embryo cells (PCECV), hamster kidney cells (PHKCV) and duck embryo cells (PDEV)

Quality assessment						Summary of findings
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Quality
4	Observational ¹	No serious	No serious	No serious	No serious	Moderate

¹ Normally, observational studies achieve only low quality of evidence in the currently used grading system. However, all of these 4 long-term studies showed immunity lasting for ≥ 10 years. This is also in line with most studies with observation periods of < 10 years that do not suggest waning of immunity/immunological memory with time. Besides, immunity appears to persist even when antibodies are no longer detectable (*Gherardin AW et al 2001*). Therefore, the scientific evidence that cell-culture derived rabies vaccines induce ≥ 10 years of immunity is upgraded from low to moderate.

Thraenhart O et al (1994) demonstrated neutralizing antibodies and elicited anamnestic responses in all of the 18 vaccinees 2 -14 years after immunization; the anti-rabies T and B cell response showed no time-dependent pattern. *Suwansrinon K et al (2006)* carried out a prospective study on 118 vaccinees 5-21 years after pre- or post-exposure regimens, using cell-culture vaccines for either i.m. or i.d. administration. Neutralizing antibody was detected in the sera of all subjects and following i.d. booster injections on days 0 and 3, all except one subject showed an accelerated antibody response. *Malerczyk C et al (2007)* found neutralizing antibody concentrations ≥ 0.5 IU/ mL and anamnestic responses in all of 10 persons who 15 years earlier had received primary PCECV immunization, followed by one booster dose after one year. *Brown D et al (2008)* demonstrated durable immune responses among 89 individuals who 1-12 years earlier had received a primary i.d. series of HDCV. Antibody concentrations (≥ 0.5 IU/ml) were found consistently, including in the 8 persons who had been immunized 10-12 years earlier.

References

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Malerczyk C, Briggs DJ, Dreesen DW, Banzhoff A. Duration of immunity: an anamnestic response 14 years after rabies vaccination with purified chick embryo cell rabies vaccine. *J Travel Med.* 2007 Jan-Feb;14(1):63-4.

Suwansrinon K, Wilde H, Benjavongkulchai M, Banjongkasaena U, Lertjarutorn S, Boonchang S, Suttisri R, Khowplod P, Daviratanasilpa S, Sitprija V. Survival of neutralizing antibody in previously rabies vaccinated subjects: a prospective study showing long lasting immunity. *Vaccine.* 2006 May 1;24(18):3878-80.

Thraenhart O, Kreuzfelder E, Hillebrandt M, Marcus I, Ramakrishnan K, Fu ZF, Dietzschold B. Long-term humoral and cellular immunity after vaccination with cell-culture rabies vaccines in man. *Clin Immunol Immunopathol.* 1994 Jun;71(3):287-92.