INTRADERMAL APPLICATION OF MODERN
(CELL-CULTURE AND EMBRYONATING EGG)
RABIES VACCINES FOR HUMAN
RABIES POST-EXPOSURE TREATMENT
(SUMMARY)

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1 INTRODUCTION.

In developing countries, where more than 99% of all human rabies deaths occur, nervous tissue anti-
rabies vaccines are still the most widely used because of their relatively low cost and despite their
variable potency and the risk of neurological complications. The supplies of modern and safe vaccines
for many developing countries are grossly inadequate whereas the demand for affordable and safe
human post-exposure treatment (PET) is increasing in the developing world. Although the costs of
modern vaccines are decreasing, the current price of a full intramuscular vaccine treatment is far be-
yond what an average family in Africa or Asia can afford.

Multi-site intradermal administration of small doses of cell culture rabies vaccines which have been
shown to protect humans bitten by proven rabid animals and to reduce the costs of PET by 60%, is an
effective way of decreasing the cost of these much more potent, safe modern vaccines, and of in-
creasing the neutralising antibody response. In many developing countries, however, rabies vaccines
are being given intradermally under inappropriate conditions and according to regimens whose effi-
cacy is unproven.

A WHO Expert Committee held in 1991 recommended intradermal application of modern rabies vac-
cines. This recommendation was re-assessed in January 1992 and re-evaluated by 2 WHO consulta-
treatment and the correct technique of intradermal immunisation against rabies» was published in
1996. This document (WHO/EMC/ZOO.96.6) updates and supersedes the recommendations of the
8th report of the Expert Committee on Rabies published in 1992 (TRS 824) on PET.

2 RECOMMENDED INTRADERMAL REGIMENS.

An "ideal" vaccine regimen for PET should require a minimum quantity of vaccine, few visits to the
clinic and rapid induction of immunity. These features need to be combined to produce an economical,
efficient, safe regimen.

The TRC 222011 and the 804011 regimens have fulfilled these requirements. They have been used in
restricted areas, mainly by experienced personnel. From 1985 to 1994 however approximately 70 000
TRC intradermal regimens where given in Thailand with more than 29 000 in category 3 exposure.

The 2-site intradermal method (222011) for use with purified vero cell rabies vaccine (PVRV), with
purified chick embryo cell vaccine (PCECV) and purified duck embryo vaccine (PDEV) con-
­sists of injecting one intradermal dose at each of 2 sites on day 0, 3, 7 and a single site on day
28 and 90; the intradermal dose per site is one fifth of the volume after reconstitution of a sin-
gle immunising intramuscular dose, i.e. the intradermal dose is 0.1 ml/site for PVRV; and the
intradermal dose is 0.2 ml/site for PCEC and PDEV. PDEV should become available in 0.5 ml
after reconstitution in 1998.

The 8-site (804011) regimen for use with human diploid cell (HDC) and PCEC vaccines where intra-
­muscular dose is 1ml consists of injecting on the first day, 1 ml of vaccine divided between
8 intradermal sites (deltoids, anterior thighs, supra scapular and lower quadrant of the abdo-


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men); and on day 7, 4 x 0.1 ml intradermal injections (deltoids and thighs), and single 0.1 ml intradermal boosters on days 28 and 90.

3 WHO GUIDELINES.

WHO has recently published precise instructions on the currently recognised methods of intradermal vaccination, to make optimum use of restricted resources, and on precautions to be taken to prevent vaccine contamination from multidose vials, as well as viral cross-infection. The guidelines also provide new information on the use of immunoglobulin and other aspects of rabies PET.

These guidelines provide up-dated knowledge of the correct methods of using modern tissue culture and embryonating egg vaccines intradermally which is very poor in tropical areas with endemic dog rabies, where exposure to rabid animals is frequent, vaccine is scarce, there is little money and no RIG available. Under these conditions the WHO document aims at preventing the use of a variety of untested, potentially dangerous intradermal regimens which are being used in some places. As mentioned before the only regimens which have been demonstrated to be immunogenic today are the 222011 and the 804011. The volume of the standard intramuscular dose varies between different products, and some producers are in the process of changing from a 1 ml to an 0.5 ml ampoule. Attention should therefore be paid to the volume of the product after reconstitution.

These guidelines should be suitable for distribution to large and small clinics and rural health centres and to government organisations deciding on vaccine policies.

4 FUTURE RESEARCH.

There is a need for (a) new intradermal vaccine regimen(s) using products formulated in 0.5 ml vials. Immunogenicity studies in non-exposed volunteers must identify a satisfactory regimen before efficacy is tested in patients needing PET.

- The immunogenicity of a regimen beginning with 4-site intradermal injections (0.1 ml/site), e.g. 40202 (days 0-7-28) using the entire 0.5 ml vial on day 0 should be studied.

- The effect of smaller doses (0.05 ml/site) in 8 sites, still using one 0.5 ml vial on day 0, could be investigated. The 8-site intradermal PET regimen has only been tested with HDCV and PCEC in 1 ml vials.

- The value of giving a final injection on day 90 should be tested.

5 CONCLUSIONS.

Implementing intradermal methods for PET would increase the use of PET globally. It was emphasised that these regimens are of comparable immunogenicity to the intramuscular regimen and very much more effective and safer than vaccines of nervous tissue origin. There is no contraindication to the use of an intradermal regimen.

The decision to implement economical intradermal PET rests with government agencies which select policies for rabies prophylaxis in their own countries. Dissemination of information from such an authority by instruction of physicians, nurses and other health care workers is very important. Local or regional advisers, who could be contacted easily to give practical advice, would enhance the acceptance of the new methods.
REFERENCES


