Rabies Vaccine and Rabies Immune Globulin (RabIg) Administration (Post Exposure Prophylaxis)

I. How to Access Rabies Vaccines and Rabies Immune Globulin

Rabies vaccine and immune globulin require a request from the primary care physician to the Medical Officer of Health of the local public health unit to be released. Community health nurses will require a doctor's order to administer rabies vaccine and rabies immune globulin.

For additional vaccination information please refer to the most recent Canadian Immunization Guide, part 4 - Active Vaccines available at http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-eng.php.

II. Vaccine Dose & Route

There are two inactivated vaccines available: human diploid cell rabies vaccine (HDCV or IMOVAX®) and purified chick embryo cell rabies vaccine (PCECV or RabAvert®). See Section VI on Contraindications regarding use of PCECV in individuals with egg allergies.

The intramuscular (IM) dose is 1.0 ml. Each 1.0 ml dose of HDCV or PCECV vaccine contains at least 2.5 international units (IU) of rabies antigen. A series of multiple doses of the vaccine is required for post-exposure prophylaxis. See Section IV on Post-Exposure Prophylaxis (PEP) for number of doses and schedule.

Rabies vaccine should be administered IM into the deltoid muscle in older children and adults or into the vastus lateralis muscle (anterolateral thigh) in children less than one year of age. **Rabies vaccine should never be administered in the gluteal muscle due to variable absorption.**

The rabies vaccine and Rabies Immune Globulin (RabIg) should be given at different anatomical sites on day 0 using a separate needle and syringe. For subsequent vaccine doses, the limb where RabIg was administered can be used.

When possible, an immunization series should be completed with the same product. However, if this is not possible, PCECV and HDCV are considered interchangeable.

If a dose of vaccine is given at less than the recommended interval, that dose should be ignored and the dose given at the appropriate interval from the previous dose. If a dose is delayed, it should be given as soon as possible and the schedule resumed respecting the appropriate intervals from the latest dose. If there has been substantial deviation from the recommended schedule, post-vaccination serology should be obtained 7 to 14 days after completing the series.

Table 1. Rabies Vaccines

Vaccine Type	Name	Route/Site	Indications	Dosage
Human diploid cell rabies vaccine (HDCV)	IMOVAX®	IM (gold standard) Deltoid site, vastus lateralis site	· Pre-exposure · Post-exposure · Both primary series and booster doses	1 IM dose (1.0 ml) = ≥ 2.5 IU rabies antigen.
Purified Chick Embryo Culture (PCECV)	RabAvert®	IM (gold standard) Deltoid site, vastus lateralis site	· Pre-exposure · Post-exposure · Both primary series and booster doses	1 IM dose (1.0 ml) = ≥ 2.5 IU rabies antigen.

Canadian Immunization Guide, PHAC, 2012.

III. Rabies Immune Globulin (RabIg) Dose & Route

RabIg is not indicated and should not be given to anyone who has been previously appropriately immunized.

If anatomically possible, RabIg should be thoroughly infiltrated into the wound and surrounding area. See Appendix A on infiltrating a wound with RabIg. Any remaining volume of RabIg should be administered IM using a separate needle and syringe at a site distant from the site of vaccine administration. For large remaining volumes, injection sites must be verified with prescriber.

The IM dose of RabIg is calculated as 20 IU/kg of body weight for all age groups. Because of possible interference of RabIg with the immune response to the rabies vaccine, the dose of RabIg should not be exceeded.

Use the following formulae to calculate the correct dose:

20 IU/kg x (client weight in kg) ÷ 150 IU/ml = dose in ml

9.09 IU/lb x (client weight in lb) ÷ 150 IU/ml = dose in ml

RabIg is supplied in 2 ml vials containing 150 IU/ml. Table 2 indicates the number of vials that will need to be ordered based on the client's weight.

Table 2: Number of 2 ml vials of RabIg to be ordered per Total Body Weight of Client

TOTAL WEIGHT		# OF VIALS	TOTAL WEIGHT		# OF VIALS
≤ 33 lbs	≤ 15 kg	1	>165 – 198 lbs	>75 – 90 kg	6
>33 – 66 lbs	>15 – 30 kg	2	>198 – 231 lbs	>90-105 kg	7
>66 – 99 lbs	>30 - 45 kg	3	>231 – 264 lbs	>105 – 120 kg	8
>99 – 132 lbs	>45 – 60 kg	4	>264 – 297 lbs	>120 – 135 kg	9
>132 – 165 lbs	>60 – 75 kg	5	>297 – 330 lbs	>135 – 150 kg	10

Guidance Document for the Management of Suspected Rabies Exposures, MOHLTC, September, 2013.

Note: this table assists with ordering the correct number of vials; it is **not** a calculation of dosage.

Table 3. Rabies Immune Globulin

RabIg Type	Name	Route/Site	Indications	Dosage
RabIg (Rabies Immune Globulin)	IMOGAM® Rabies Pasteurized	If anatomically possible, thoroughly infiltrate into the wound and surrounding area. Remainder of dose to be administered IM at a site distant to the vaccine (verify site for large volume with prescriber)	Post exposure	20 IU/kg body weight for all age groups.
RabIg (Rabies Immune Globulin)	HYPERRAB® S/D	If anatomically possible, thoroughly infiltrate into the wound and surrounding area. Remainder of dose to be administered IM at a site distant to the vaccine (verify site for large volume with prescriber)	Post exposure	20 IU/kg body weight for all age groups.

Canadian Immunization Guide, PHAC, 2012

Note: According to the Parenteral Drug Therapy Manual (The Ottawa Hospital, 2012), "The maximum volume, which may be given in any single IM injection, is 3 ml for adults and 2 ml for children. An exception is for the deltoid injection where a maximum of 2 ml should not be exceeded (approximately 1 ml or less is preferred)".

IV. Post-Exposure Prophylaxis (PEP)

Schedule

The post-exposure prophylaxis schedule for rabies vaccine depends on the rabies immunization status of the individual.

Unimmunized Immunocompetent Individuals

Post-exposure prophylaxis of previously unimmunized individuals consists of both rabies immune globulin (RabIg) and rabies vaccine. The RabIg provides immediate passive protection until the exposed person mounts an immune response to the rabies vaccine.

RabIg

Rabies Immune globulin should be given on the first day of initiation of therapy (day 0).

If RabIg was not given on day 0, there is no value in administering it more than eight days after initiation of the approved vaccine course, since vaccine-induced antibodies begin to appear within one week.

Rabies Vaccine

The first dose of rabies vaccine, for previously unimmunized immunocompetent persons should be administered as soon as possible after exposure (Day 0). Additional doses should be administered on days 3, 7, and 14 after the first vaccination, for a total of four separate doses.

Unimmunized Immunocompromised Individuals

Unimmunized immunocompromised persons (including those taking corticosteroids or other immunosuppressive agents, and those who have immunosuppressive illnesses) and those taking chloroquine and other antimalarials should receive five doses of rabies vaccine on days 0, 3, 7, 14 and 28 with one dose of RabIg on day 0.

Previously Immunized Individuals

RabIg should not be given to someone who has been previously immunized.

In previously appropriately immunized individuals who require post-exposure prophylaxis, two doses of either HDCV or PCECV vaccine are recommended. The first dose should be administered immediately after exposure (Day 0) followed by the second dose on Day 3.

Table 4: Summary of PEP Schedules

	Day 0	Day 3	Day 7	Day 14	Day 28	RabIg (On day 0)
A) Previously Unimmunized Immunocompetent	YES 1.0 ml	YES 1.0 ml	YES 1.0 ml	YES 1.0 ml	NO	Dose determined by weight – refer to formula on page 2
B) Previously Unimmunized Immunocompromised	YES 1.0 ml	YES 1.0 ml	YES 1.0 ml	YES 1.0 ml	YES 1.0 ml	Dose determined by weight – refer to formula on page 2
C) Previously Immunized	YES 1.0 ml	YES 1.0 ml	NO	NO	NO	NO

Canadian Immunization Guide, PHAC, 2012.

Note: When determining days on which to administer vaccine doses, days are counted from the dose given on day 0.

V. Adverse Events

HDCV

Local injection site reactions such as pain, erythema, swelling, pruritus and induration at the injection site were reported in 60% to close to 90% of recipients. Mild systemic reactions such as headache, nausea, abdominal pain, muscle aches and dizziness were reported in about 6% to 55% of recipients.

Anaphylactic reactions to this vaccine have occurred in up to 1 in 10,000 vaccine recipients. Systemic allergic reactions with generalize urticaria and accompanied in some cases by arthralgia, angioedema, fever, nausea and vomiting have been reported. These reactions are uncommon in individuals receiving primary immunization.

PCECV

Local injection site reactions were reported in 11% to 57% of recipients, consisting of pain, tenderness, swelling, erythema and induration at the injection site lasting for 2 to 3 days. Systemic reactions are generally less common (i.e. 1% to 10% of recipients) and may consist of malaise, myalgia, arthralgia, headache and fever. Lymphadenopathy, nausea and rash have been reported occasionally.

Anaphylaxis following immunization has been reported, although causal association with vaccination has not been established.

RabIg

Local injection site pain, erythema and induration are commonly reported following administration of RabIg, as are systemic reactions such as headache and low-grade fever. The majority of reported events were mild.

VI. Contraindications and Precautions

There are no contraindications to the use of rabies vaccine or RabIg after significant exposure to a proven rabid animal; however, care should be taken if post-exposure prophylaxis is to be administered to persons who are hypersensitive to the products or to any ingredient in the formulation or component of the container. Expert opinion should be sought in the management of these individuals.

Persons with egg allergies are not necessarily at increased risk of a hypersensitivity reaction to PCECV. If an alternative vaccine is not available, post-exposure prophylaxis using PCECV should be administered to a person with hypersensitivity to eggs with strict medical monitoring. Facilities for emergency treatment of anaphylactic reactions should be available.

Pregnancy and Lactation
Pregnancy and lactation are not contraindications to post-exposure rabies prophylaxis, but it is sensible to delay pre-exposure immunization of pregnant women unless there is a substantial risk of exposure.

For more details on contraindications and precautions, refer to the Canadian Immunization Guide, Part 4 http://www.phac-aspc.gc.ca/publicat/cig-gci/index-eng.php

VII. Simultaneous Administration with other Vaccines

There is no evidence that the administration of immune globulin interferes with the response to inactivated vaccines, or live vaccines for polio or yellow fever. However, an interval of 4 months should be maintained between the administration of MMR and varicella vaccines. If MMR or varicella vaccines were received less than 14 days prior to the administration of the immune globulin, they should be repeated 4 months after the immune globulin is administered, or serologic tests should be completed.

VIII. Serologic Testing

Because of the excellent immune response to rabies vaccine, healthy people immunized with an appropriate regimen do not require routine antibody testing after pre- or post- exposure rabies vaccination, unless one of the following applies:

- Pre – exposure vaccination was given by the intradermal route. Check serology at least 2 weeks after completion of the series
- There has been substantial deviation from the recommended post - exposure schedule. Check serology 7 to 14 days after completing the series
- The person has been immunized with a vaccine other than HDCV or PCECV. Check serology 7 to 14 days after completing the series.

APPENDIX A

INFILTRATING A WOUND WITH RabIg

If possible, the full dose of RabIg should be thoroughly infiltrated into the wound and surrounding area. If not anatomically feasible, any remaining volume of RabIg should be injected, using a separate needle and syringe, intramuscularly at a site distant from the site of vaccine administration.

When more than one wound exists, each wound should be locally infiltrated with a portion of the RabIg using a separate needle and syringe. In such instances, the RabIg can be diluted twofold to threefold in a solution of 0.9% sodium chloride in order to provide the full amount of RabIg required for thorough infiltration of all wounds. If the site of the wound is unknown, the entire dose should be administered intramuscularly at a separate site(s) from where the rabies vaccine is administered. Rabies vaccine and RabIg should never be mixed in the same syringe. If RabIg is not administered as recommended at the initiation of the rabies vaccine series, RabIg can be administered up to day 7 after vaccine is initiated.

A facial wound is not a contraindication for infiltration since the face presents a greater risk of contracting rabies.

INFILTRATING TECHNIQUE

EQUIPMENT

- 3-, 5- or 10 ml sterile syringe
- 23 – 25 gauge sterile needle, of a length suitable for the depth of the wound
- Rabies immune globulin
- 0.9% NaCl for dilution (if necessary)
- Non-sterile gloves
- Sterile dressing
- 70% isopropyl alcohol swabs

PROCEDURE

If possible, avoid suturing the wound. In the case of an already sutured wound, the area must be disinfected before infiltration of the RabIg. Note that this is a painful procedure.

1. Wash hands
2. Put on non-sterile gloves
3. Prepare the immunizing agent
    - Assess the number and seriousness of the wound site(s) because the RabIg must be distributed in proportion to the size and depth of the wounds.
    - Use a new syringe and needle when wounds are located at different sites (for example: face and forearm). If wounds are too close together, you can use the same needle and same syringe.

4. Introduce the needle into the edges of the wound, with the bevel facing upwards at an angle of 30 to 90°.
5. Aspirate slowly, pulling back on the plunger to ensure that the needle has not entered a blood vessel.
    - If a small amount of blood enters the syringe, correct the needle position and continue. If there is a lot of blood then discard equipment and start over.
    - Injecting slowly helps reduce pain, caused primarily by rapid distension of tissue
6. Slowly inject a portion of the RabIg into the tissue surrounding the wound until there is a slight local edema or a whitish area.
7. Withdraw the needle a few millimetres, change the angle and move the needle forward again to form a fan-shaped pattern.
8. Withdraw the needle then reinsert it close to the same area.
9. Repeat steps 4 to 7, going around the periphery of the wound.
10. Cover the wound with a sterile dressing.
11. Dispose of soiled equipment and gloves appropriately and wash hands.