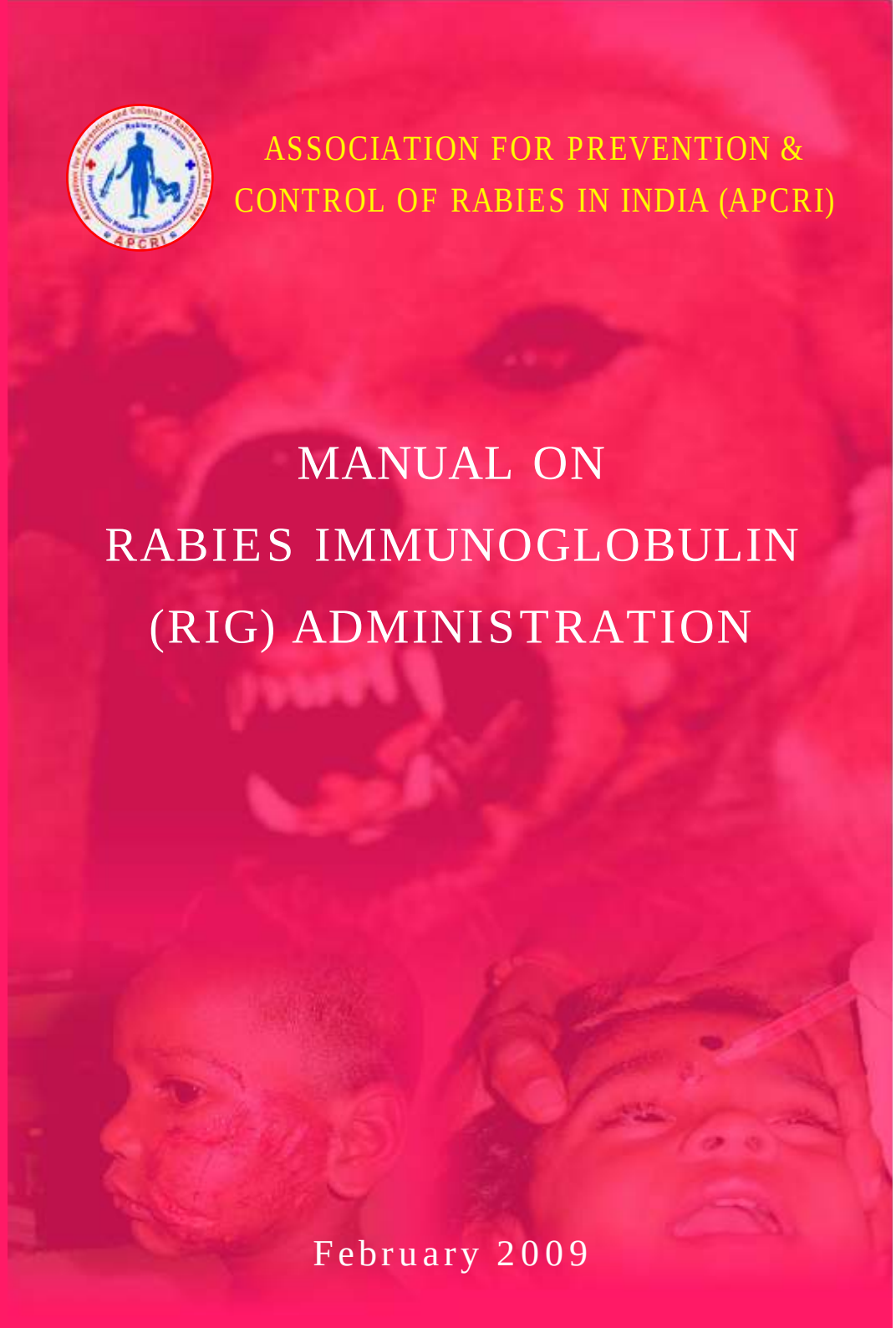

ASSOCIATION FOR PREVENTION &
CONTROL OF RABIES IN INDIA (APCRI)

MANUAL ON
RABIES IMMUNOGLOBULIN
(RIG) ADMINISTRATION

February 2009

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CONTENTS

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Foreword

Rabies is a practically 100 percent fatal disease even today, if not treated appropriately and in a timely fashion. All animal bite victims should be given proper wound care and timely and full doses of any modern anti-rabies vaccine. Because vaccines take about 2 weeks to produce sero-protective titers of antibodies, the persons are still vulnerable to rabies during this window period, when only the use of Rabies Immunoglobulins (RIGs) is life saving. Timely and proper administration of RIGs can neutralize the virus in the wounds - thus aborting the risk of developing rabies.

RIGs are indicated in all Category III exposures and in Category II exposures that occurring in immunosuppressed persons. Unfortunately due to a number of reasons RIGs are grossly under used in our country. A survey conducted by Association for Prevention and Control of Rabies in India (APCRI) in the year 2003 showed that the usage of RIGs was as low as about 2% ; about 5% of the rabies deaths could have been certainly prevented by the use of RIGs. Amongst the various reasons of the low usage of RIGs, the important once are fear amongst doctors of anaphylaxis following the RIG administration and a general lack of guidelines about its administration.

In this backdrop, this “Manual on RIG Administration” being brought out by APCRI is very timely and will very clearly address the commonly encountered queries of the users. It will go a long way in removing the fears about the RIG administration from the minds of treating doctors.

I congratulate APCRI office bearers for this excellent initiative. I am very optimistic about the usefulness of this manual in increasing the much desired wider use of RIGs in preventing Rabies deaths in India.

Dr. R.L. Ichhpujani
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(Hon. Advisory Board, APCRI)

Dr. G. Sampath

Preface

India reports the maximum number of deaths due to Human Rabies. The incidence of animal bites is also very high in our country.

Timely and proper Post Exposure Prophylaxis (PEP) can prevent this dreaded disease. Administration of Rabies Immunoglobulin (RIG) is an important component of PEP.

However the usage of RIGs is very low in our country due to various reasons like lack of awareness and fear in the minds of the practicing physicians.

I hope this manual will increase the awareness about passive immunity and also be useful to the practicing physicians in administering RIGs to the patients.

Dr. G. Sampath
President
APCRI

1. Introduction

Rabies is viral encephalitis caused by a RNA virus (Genus: *Lyssavirus*, Family: Rhabdoviridae) & is practically 100% fatal even today. It is a Zoonotic disease & endemic in India. The animals commonly responsible for transmission of rabies in India are dogs, cats and wild animals like mongoose, foxes & jackals.

According to WHO-APCRI National Multicentric Rabies Survey (2004), there are an estimated 17.4 million animal bite cases and 20,000 deaths due to human rabies annually in India. This corresponds to about 36% of the total global deaths due to human rabies.

Following exposure to a rabid animal, proper wound care, vaccination with modern anti-rabies vaccines and administration of rabies immunoglobulins can prevent rabies and thereby save many lives.

The attending physician must provide correct post-exposure rabies prophylaxis (PEP), failing which the patient may succumb to rabies and the physician may be sued for compensation under Consumer Protection Act.

However, it is observed that both physicians and patients give little importance to RIG administration.

2. Post Exposure Prophylaxis (PEP)

Post Exposure (or post bite) Prophylaxis against rabies includes the following steps:

1. Categorization of animal bite wound(s).
2. Local treatment of wound(s).
3. Administration of Rabies Immunoglobulins (RIG).
4. Anti Rabies Vaccination (ARV).

2.1 Categorization of animal bite wound(s)

The animal bite cases shall be categorized based on WHO guidelines for initiation of post exposure prophylaxis (Table-1)

Table 1: Type of contact, exposure and recommended post exposure prophylaxis

Category	Type of contact	Type of Exposure	Recommended post exposure prophylaxis
I	· Touching or feeding of animals. · Licks on intact skin.	None	· None, if reliable case history is available.
II	· Nibbling of uncovered skin. · Minor scratches or abrasions without bleeding.	Minor	· Local treatment of wounds. · Administer anti rabies vaccine
III	· Single or multiple transdermal bites or scratches · Licks on broken skin · Contamination of mucous membrane with saliva (i.e. licks)	Severe	· Local treatment of wounds. · Administer rabies immunoglobulin. · Anti rabies vaccine

Note:

i) Exposure to rodents, rabbits and hares seldom, if ever, require specific anti rabies post exposure prophylaxis.

ii) Bat transmitted rabies has not been reported in India and hence exposure to bats does not warrant post exposure prophylaxis.

2.2 Local treatment of wound(s)

Since the rabies virus usually enters the human body through a bite or scratch of a rabies infected animal, it is important to remove saliva containing the rabies virus at the site of bite by physical or chemical means.

This can be done by prompt and gentle thorough washing with soap or detergent and flushing the wound with running tap water for at least 15 minutes. After washing with water and soap, disinfectants like povidone iodine or surgical spirit (Viricidals) must be applied.

If soap or antiviral agent is not available, the wound should be thoroughly washed with water.

Washing of the wound must be done as long as the wound is raw, irrespective of the time lapsed since the exposure, because the rabies virus can persist at the site of bite/scratch for a long time. However, care must be taken not to disturb scabs, if formed.

In addition, tetanus prophylaxis, analgesics & antibacterial treatment/antibiotics may be given.

By mere washing of wounds & application of antiseptics, the risk of rabies will reduce by about 50 %.

Fig 1: Wound wash

Fig 2: Antiseptic application

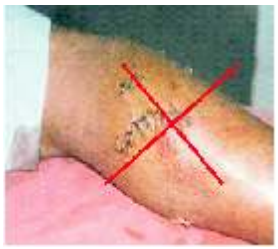

Fig 3: Don't suture the wounds

<u>Note:</u>

i) *Suturing of the wound(s) should be avoided.*

ii) *In case of lacerated wounds with severe bleeding, where suturing cannot be avoided, the wound should first be infiltrated with rabies immuno globulins (RIGs) and minimum number of stay sutures should be applied later.*

iii) *If suturing is needed for cosmetic purposes, it is preferably done 2 weeks after starting vaccination, as patient would develop protective antibodies by then.*

2.3 Anti rabies vaccination (ARV)

Modern anti rabies vaccines like Human Diploid Cell Vaccine (HDCV), Purified Chick Embryo Cell Vaccine (PCECV), Purified Verocell Rabies Vaccine (PVRV) & Purified Duck Embryo Vaccine (PDEV) must be administered as per WHO recommendations. These vaccines are highly effective and safe. The vaccination must be started immediately (in category II & III exposures) irrespective of the status of the biting animal.

2.3.1 Vaccination schedules

- Intra muscular Regimen (Essen) : All modern anti rabies vaccines must be administered intra muscularly on Days 0, 3, 7, 14 and 28 into deltoid muscle (in adults) or antero-lateral aspect of thigh (in children).

  These vaccines should not be administered in the gluteal region as the gluteal fat may retard vaccine absorption resulting in delayed and lower seroconversion.

Fig 4: IM injection into thigh muscle

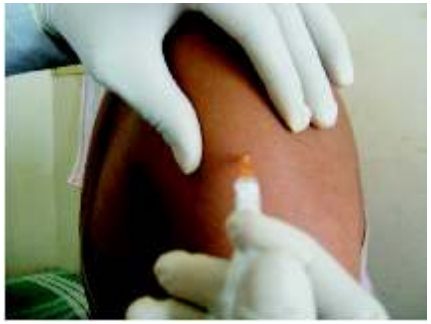

Fig 5: IM Injection into Deltoid muscle

- Intra dermal Regimen (Updated Thai Red Cross Regimen : 2-2-2-0-2): Purified chick embryo cell rabies vaccine (PCECV) & different brands of Purified vero cell rabies vaccine (PVRV) are approved for use through intradermal route in the country by Drug Controller General of India (DCGI). In this regimen 0.1 ml of vaccine is administered intradermally on each deltoid region on days 0, 3, 7 & 28.

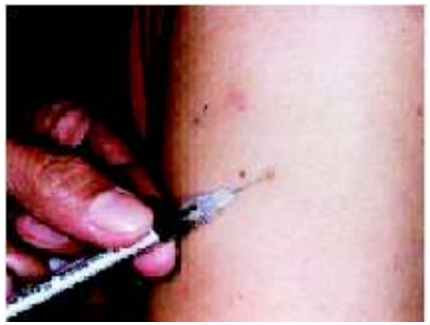

Fig 6: Insertion of needle for ID inoculation

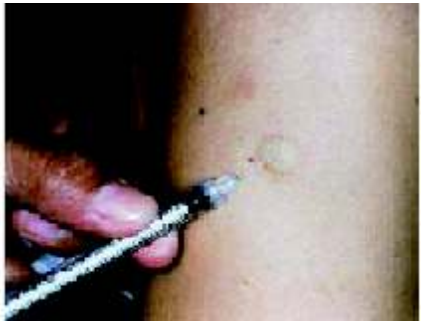

Fig 7: Bleb raised on ID inoculation

<u>Note:</u> i) *There is no single dose vaccine.*

ii) *Day'0' is the first day of vaccination and not the day of bite.*

2.4 Rabies Immunoglobulins (RIGs)

Rabies Immunoglobulin (RIG) is a life saving drug in all category III exposures. WHO-APCRI Indian Rabies Survey (2004) revealed that the use of RIGs was as low as 2 % in our country & one of the reasons for non use of RIGs by medical profession is the fear of anaphylaxis. However anaphylaxis is quite rare with currently available RIG preparations, as they are highly purified.

Till 2001, the Equine RIG was manufactured in only one Government facility at Central Research Institute, Kasauli, Himachal Pradesh and the Human RIGs were imported and very expensive. Subsequently the production of purified ERIGs was started at different private facilities in the country, thus ensuring their continuous availability and at an affordable price too. Therefore, the onus is now on the medical profession to use them in all deserving cases and to prevent human rabies deaths.

2.4.1 History of RIGs/ARS

Use of rabies immunoglobulin for prevention of rabies dates back to 1890, when Babes for the first time demonstrated its utility in experimental animals. From then onwards, till 1945 many experiments and field studies were done to assess the usefulness of passively administered rabies antibody in prevention of rabies. But these provided conflicting results ranging from 100% protection to no protection.

The usefulness of rabies immunoglobulin was conclusively demonstrated in 1945 by Habel and his colleagues after a series of carefully controlled animal experiments. These studies proved that post exposure treatment with anti rabies serum (ARS) given at the site of the bite soon after virus injection, along with vaccine, was much more effective than vaccine alone. In 1955, Koprowsky and others could reproduce similar results.

The dramatic life saving effect of administration of RIGs in man was demonstrated in a group of persons bitten by a rabid wolf in Iran in 1954. Of the 4 persons given vaccine alone, 3 died of rabies, whereas only 1 of the 12 administered equine rabies antiserum and vaccine succumbed to rabies.

Following these events, the WHO coordinated a series of experiments with Professor Atanasiu from Pasteur Institute, Paris to determine the optimal dose of RIG, so that active immunity induced by vaccination is not significantly suppressed. The combined use of vaccine and serum became a standard post exposure treatment after the recommendation by WHO in 1966.

For production of RIG, several animals were used, but RIG produced in horses became more popular because large quantities could be obtained. Till 1960, equine rabies immunoglobulin (ERIG) used was not purified and led to the incidence of serious side effects like anaphylaxis and serum sickness. In late 1960s, highly purified and enzyme digested ERIG became available. This has resulted in fewer side effects.

Use of human serum for production of RIG was initiated by Hosty as early as 1959. In 1971 Cabasso standardized the production of human rabies immunoglobulin (HRIG) and determined the optimal dosage.

2.4.2 Indications for RIGs

According to WHO, all <u>transdermal bites or scratches</u> viz. wounds that bleed, irrespective of site, number and severity are <u>Category III exposures</u>. It is a common misbelief that only severe, multiple wounds & bites on head and neck are category III exposures.

The following situations need rabies immunoglobulins.

- ✓ All Category III exposures.
- ✓ Bites by all wild animals viz. by mongoose, jackal, fox etc.
- ✓ Even Category II exposures in immunocompromised/immunosuppressed individuals including HIV infected people & AIDS patients.

<u>*Note:*</u>

i) RIGs should also be administered in Category III exposures even by vaccinated pet animals.

ii) RIGs can be used in pregnant women and lactating mothers.

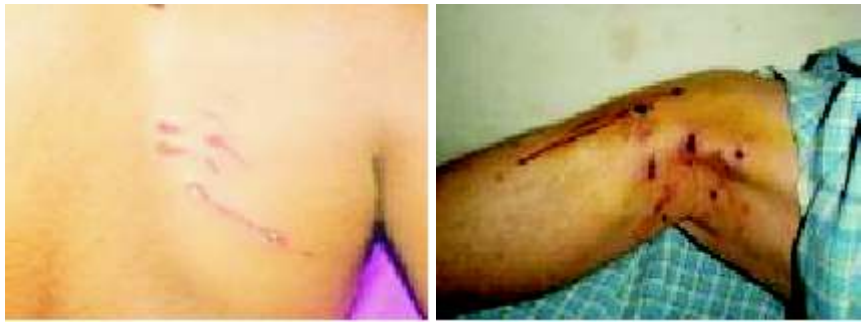

Fig 8 & 9 : category III exposures

2.4.3 Importance of RIGs

Administration of Rabies Vaccine stimulates production of neutralizing antibodies by the patient's immune system. Protective levels of antibodies are seen 7 to 14 days after the initial dose of vaccine. Adequate serotitres can be expected in all the vaccinees by day 14. Moreover when the bites are on the head, neck, face & hands, the incubation period will be shorter.

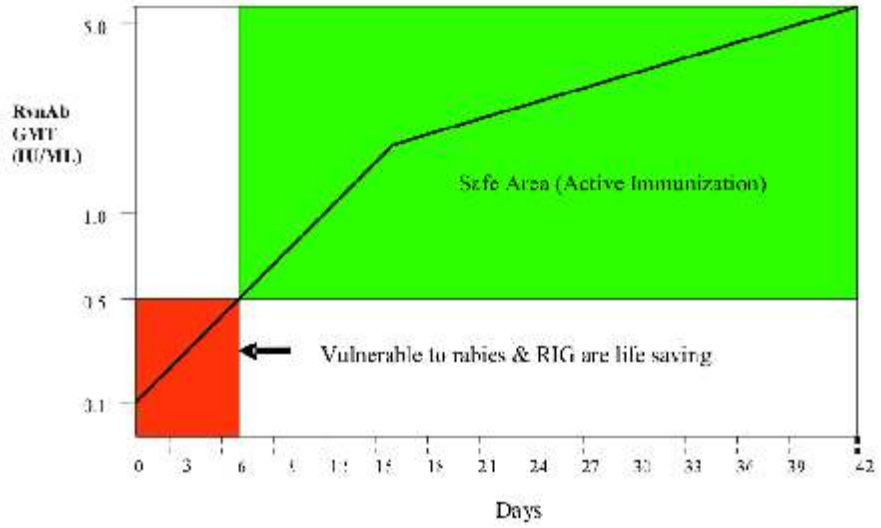

Figure10: Immune response following vaccine administration

Thus the patients are vulnerable to develop rabies during this window period of 7 to14 days despite the timely and full course of any anti rabies vaccine and with proper wound care.

Hence, administration of RIGs, after thorough cleansing of wounds, is life saving as their timely and proper administration neutralizes the virus in the wound and aborts the risk of developing rabies. The Rabies Immunoglobulin (RIG) or Anti Rabies Serum (ARS) are readymade anti rabies antibodies which provide passive immunity and offer immediate protection.

<u>Note:</u> RIGs are always to be used along with rabies vaccine as early as possible & are never to be used alone to treat animal bite victims. A full course of vaccination should follow thorough cleansing of wounds and passive immunization.

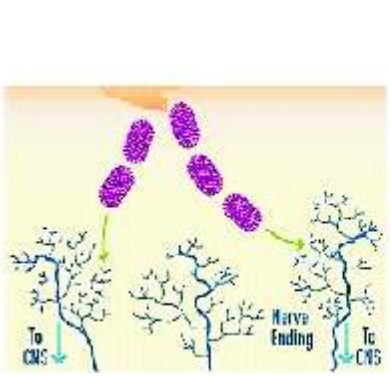

Fig 11: Virus entry into nerve endings

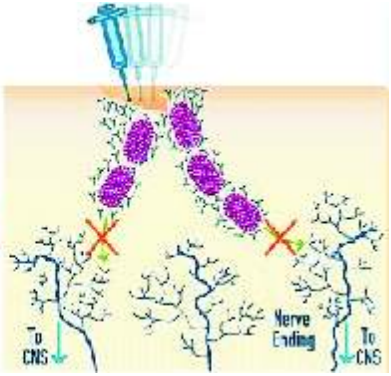

Fig 12: Virus neutralization by RIG

2.4.4. Types of RIGs

(a) Human Rabies Immunoglobulins (HRIG):

These are imported and expensive. These are available as 2ml vials with a potency of 150 IU/ml. These are homologous in origin & have a longer half-life when compared to ERIG & are hence given at half the dose of ERIG. HRIG infiltration doesn't require prior skin testing.

Since HRIG has slower clearance than F (ab') 2 fragments from the body, it is advisable to use HRIG in multiple/severe exposures.

b) Equine Rabies Immunoglobulins (ERIG):

These are indigenously produced both in Government and Private sectors. These are available in adequate quantities on a continual basis at an affordable price. These are available as 5 ml vials (Potency of 300 IU / ml). These are heterologous in origin & produced from hyper immunized horses. Most of the Equine Rabies Immunoglobulins available now have F(ab')2 fragments. F(ab')2 is a specific part of the immunoglobulin which neutralizes the rabies virus and which has been freed from the reactogenic Fc fragment. Thus, the occurrence of adverse events has been significantly reduced.

2.4.5 Dosage of RIGs

Unlike modern rabies vaccines, which are independent of body weight of the patient for their dosage, the dosage for administration of RIGs is decided on the basis of body weight.

For HRIGs, the dosage is 20 IU per kg body weight subject to a maximum of 1500 IU.

For ERIGs, the dosage is 40 IU per kg body weight subject to a maximum of 3000 IU.

Note: *i) The dosage of RIG should not exceed the recommended dose calculated as per the body weight of the patient.*

ii) RIGs should be given as a single dose and should not be repeated.

2.4.6 When to administer RIGs

RIG is more effective if infiltrated immediately or within 24 hours of animal bite along with the first dose of vaccine. If vaccine alone was started, then RIG can be given upto 7 days after starting first dose of vaccine (3 doses of vaccine given on days 0, 3 & 7) as this will not interfere with the antibody production induced by the vaccine . However, RIG can be administered even a week or later after exposure to an animal, if the person has not received any vaccine.

However it should be remembered that RIGs should be administered at the earliest, after local wound treatment, to get the maximum benefit.

2.4.7 Precautions to be taken while administering RIGs

- The patient should <u>not</u> be on an empty stomach.
- The RIG vial(s) taken out from refrigerator should be kept outside for a few minutes before administration to the patient (to warm it to room / body temperature).
- While infiltrating RIG into bite wounds, care must be taken to avoid injecting into blood vessels and nerves. Sufficient care must also be taken while infiltrating RIG into bite wounds near the eyes and genital region. Anatomical feasibility must always be kept in mind while injecting RIG.
- While injecting into finger tips, care must be taken to avoid compartment syndrome.
- All emergency drugs and facilities for managing any adverse reactions must be available.
- <u>If ERIG is being administered</u>: Carefully elicit the history of any previous administration of horse sera viz. anti-tetanus, anti-diphtheria, anti-gas gangrene , anti snake venom serum & even anti-rabies sera (ERIG).
- Keep the patient under observation for at least one hour after ERIG administration and then send home.

2.4.8 Skin Sensitivity Testing & Interpretation

The guidelines of the manufacturer mandate a compulsory skin test to check for hypersensitivity before the full dose administration of Equine Rabies Immunoglobulin (ERIG). The skin test acts as a window, which helps us to identify the possible immunological response that will be mounted by the immune system of an individual to an allergen. The skin testing may detect the rare case of IgE mediated (type I) hypersensitivity to equine serum protein. However, majority of reactions to ERIG result from complement activation and are not IgE mediated and will not be predicted by skin testing.

Those administering ERIG should always be ready to treat anaphylactic reactions with Inj. Adrenaline. The dose is 0.5 mL of 0.1 % solution (1 in 1000, 1mg/mL) for adults and 0.01 ml/kg body weight for children injected subcutaneously.

Inj. Hydrocortisone hemisuccinate (1-2 mg/kg), Inj. Pheneramine Maleate (0.8 mg/kg), Inj. Ranitidine (1-2 mg/kg), Inj. Deriphyllin (0.5 mg/kg), Inj. Dopamine, intravenous fluids and oxygen cylinder should be kept ready & used if needed. ERIG should preferably be given in a hospital facility under close medical supervision.

Normally, one should follow the guidelines given in the package insert, which accompanies every vial of ERIG in the box. However, the general guidelines are as follows:

- Let the patient be in a sitting position.
- Record baseline pulse, blood pressure and respiratory rate of the patient.
- Draw 0.1 ml (4 units) of sterile normal saline into an insulin syringe and inject it intradermally into flexor aspect of right forearm. This will raise a bleb/swelling of about 4-5 mm (control injection).
- Take 0.1 ml of ERIG in another insulin syringe and draw 0.9 ml of sterile normal saline into the same syringe and gently rotate and mix it in syringe.

  Inject 0.1 ml of this 1:10 dilution of ERIG intradermally into the flexor aspect of left forearm raising a bleb/swelling of about 4-5 mm size (ERIG test dose).
- Keep a constant watch on the pulse, blood pressure and respiratory rate of the patient for the next 15 minutes & observe for any local or systemic reactions.

Fig 13: Administration of skin test dose

Interpretation

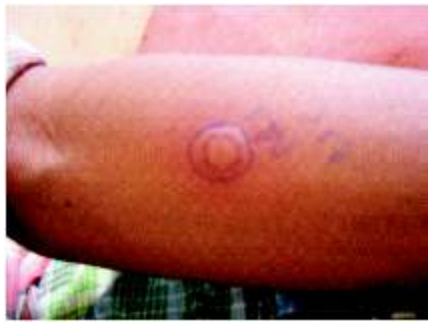

Fig 14: Induration & erythema

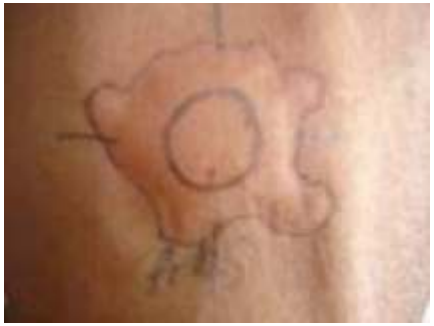

Fig15: Induration, erythema with pseudopodia

The skin sensitivity test (SST) is considered positive (Fig-14 & 15),

(1) If there is erythema and/or induration of >10 mm in the left forearm (ERIG test dose) and the control right forearm showing no such local dermal reaction.

(2) Any increase or abrupt fall in blood pressure, syncope, hurried/ difficult breathing, palpitation etc.

The skin sensitivity test (SST) is considered negative, when there is no reaction in both the forearms. A negative skin test must never reassure the physician that no anaphylactic reaction will occur subsequently.

The recent WHO recommendation states that there are no scientific grounds for performing a skin test prior to

administration of ERIG, because testing does not predict reactions and ERIG should be given whatever the result of the test (Ref.12).

However it is mandatory to follow the manufacturer's guidelines and perform the skin test as per the directions given in the product insert accompanying the ERIG. This would ensure compliance to the drug laws of the country and avoid any possible litigation under the Consumer Protection Act (COPRA).

The treating physician should be prepared to manage anaphylaxis which could occur at any stage of administration of ERIG irrespective of the outcome of the skin test. This could occur while administering the test dose itself or later while administering the full dose of ERIG.

2.4.9 Mode of Administration of full dose of RIGs

It is important to infiltrate all wounds with RIGs to neutralize the virus locally. Systemic [intramuscular] administration of RIGs is of very little value. The common mistake done by doctors (mostly for convenience) is to inject the full dose of RIGs intramuscularly, most often into gluteal region, which serves very little purpose. *The previous recommendation was to give anti rabies serum half into wounds and half intramuscularly, which is no longer recommended and may lead to treatment failure.*

As much of the calculated dose of RIG, as is anatomically feasible, should be infiltrated into & around all the wounds. Before pushing the RIG, confirm that the needle is not in any blood vessel by withdrawing the piston of the syringe to check for blood in the syringe.

As the RIG is being injected the needle should be slowly withdrawn while the piston of the syringe is pushed so that entire wound is infiltrated. The RIG shall be injected into the edges & base of the wound(s) till traces of RIG oozes out. It is preferable to use separate needles for infiltrating different wounds. Multiple needle injections into the wound should be avoided as far as possible.

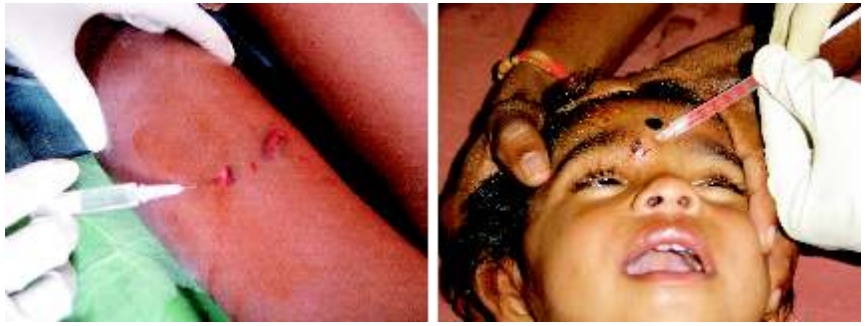

Fig 16: Infiltration of wounds with RIG

Insulin syringe and needle must be used to inject RIGs into wounds on face, neck & tip of fingers with minimal trauma.

If a finger or toe needs to be infiltrated, care must be taken not to cause a compartment syndrome, which can occur when an excessive volume of RIG is infiltrated under pressure (leading to impairment of the blood circulation and resulting in necrosis).

In the event that some volume of RIGs is left over after all wounds have been infiltrated, it should be administered by deep IM at an injection site distant from the vaccine injection site.

Sometimes significant quantity of RIG may ooze out of the wounds. In such cases this quantity of RIG should be replaced by fresh infiltration using an equivalent volume of RIGs.

Note: (i) In case of persons consuming milk of a rabid animal, there is a theoretical risk of rabies transmission. In these circumstances, if the milk is boiled before consumption, there is no risk and even vaccines are not required. If they have consumed raw milk, then the full dose of RIG has to be given systemically as it is not anatomically feasible to inject into oral cavity. This should be followed by a full course of vaccination. Similarly, following exposure due to sexual intercourse with a human rabies patient, full dose of RIG has to be given intramuscularly.

ii) If the rabid animal's saliva falls into the eyes, RIGs can be instilled as eye drops, after dilution (1:1) with sterile normal saline.

RIG infiltration of multiple severe exposures:


Fig 17 & 18 : Multiple & severe animal/ dog bite cases

Animal bite wounds inflicted can be severe & multiple especially in children. In such cases the calculated dose of RIG may not be sufficient to infiltrate all wounds. In these circumstances it is advisable to dilute the RIG in sterile normal saline to a volume sufficient to inject all wounds. However, the total recommended dose of RIG (For ERIG – 3000 IU; For HRIG -1500 IU) must not be exceeded as it may suppress the antibody production induced by the vaccine.

For infiltration of larger wounds on extremities and other sites, 1 ½ inch long 24G needle may be used to reach the entire wound.

Note: *i) RIG should never be administered in the same syringe or at the same anatomical site as vaccine administration.*

ii) RIG should be infiltrated into already sutured wounds without disturbing the sutures.

iii) RIG can be safely injected into already infected animal bite wounds following proper wound cleansing and administration of appropriate antibiotics.

2.4.10 Treatment Options for cases with Skin test positivity

✓ Ideally, they should receive HRIG.

✓ If HRIG is not available or not affordable, then the patient should be managed at an anti rabies center or hospital where facilities are available to treat complications of ERIG administration especially anaphylaxis.

✓ Note: It is important that the private doctors identify a nearby private nursing home or hospital as a "RIGs Center" and promote it by referring all category III exposure cases. In case of Government facilities, the Community health center, Taluk/Tehsil hospitals, District hospitals and other bigger hospitals may be identified as RIGs centers.

2.4.11 Adverse reactions to RIGs

The common adverse events are pain & swelling at the site of RIG administration. Sometimes brief rise in body temperature is seen. If RIGs are accidentally injected intravenously, circulatory reactions like shock may be seen.

The currently available ERIGs are highly purified (pepsin digested and enzyme refined) products unlike the previously available crude horse antiserum (of 1960s with adverse drug reactions of up to 40 % among the recipients). Unfortunately, the medical profession has the same old fear of occurrence of anaphylaxis which used to be more common with crude ARS.

The incidence of anaphylactic reaction is 1: 45,000 cases (Ref.7) & hypersensitivity reaction to the skin test is 1-11 % (Ref.8). *Till date none has died of anaphylaxis following ERIGs. Consequently, ERIGs are lifesaving in all Category III cases and their benefits clearly outweigh the remote risk of anaphylaxis.*

Erythema & Serum sickness like reactions may occur in about 1 to 2 % subjects after six days of RIG administration. The clinical manifestations of serum sickness are fever, pruritis, rash, urticaria, erythema, lymphadenopathy and arthralgia. This can be treated with non steroidal anti-inflammatory drugs and antihistamines.

2.4.12 RIGs in re- exposure cases

a) In persons who have received previously (any time in the past) either pre-exposure vaccination (3 doses on day 0, 7 & 21/28) or post exposure prophylaxis (5 doses), there is no need for RIG administration because their immune system has already been primed and once they receive a booster dose of vaccine, their immune system will initiate an immediate anamnaestic response which is adequate to neutralize the virus. Hence, re-exposure cases need only two doses of modern anti rabies vaccine on days 0 & 3.

b) Persons who have received sheep brain vaccine (NTV) previously or persons who cannot remember the type & dose of rabies vaccine that they received previously, have to receive complete PEP including RIG.

2.4.13 Approach to a patient requiring RIGs, when none is available

1. Thorough wound cleansing.

2. Essen schedule of vaccination (intramuscular) with double dose on day '0' i.e., one dose each in left and right deltoid, followed by one dose on days 3,7,14 and 28 or 8-site (Oxford) intradermal regimen. However, these are not to be construed as substitute for RIGs in routine clinical practice.

2.4.14 Post exposure treatment failures in animal bite cases

In spite of receiving post exposure prophylaxis, there are reported treatment failures resulting in human rabies. There are various reasons for the same like;

1) Delay in starting treatment due to late reporting of patients.

2) No proper wound wash.

3) Application of irritants to bite wounds.

4) Suturing of animal bite wounds without local infiltration of RIG.

5) Non administration of RIGs.

6) RIGs administered, but there is incomplete infiltration of wounds or all the wounds are not infiltrated.

7) Administration of full dose of RIGs intramuscularly and without infiltration of the wounds.

8) Non administration of full doses of vaccine as per schedule.

9) Administration of rabies vaccines into gluteal region which may result in delayed & insufficient production of antibodies.

10) Inoculation of rabies virus directly into the nerve in extensive & deep bites, especially in bites on head, neck & face (high risk bites).

11) Immunocompromised patients.

3. Conclusion:

Rabies Immunoglobulins (RIGs) are essential and life saving in all Category III exposures. *The currently available Equine Rabies Immunoglobulins (ERIGs) are purified, safe, economical and effective.* HRIGs are to be used when they are available and can be afforded by the patients.

4. References & Suggested further readings

1. Alan C Jackson & William H Wunner, Rabies, 2nd edition, 2007 Elsevier publication, Great Britain.
2. George M Baer. The Natural history of Rabies, 2nd edition (1991), CRC press.
3. World Health Organization. WHO expert consultation on rabies, Technical Report Series, 931, 2005, Geneva, Switzerland (www.who.int/rabies).
4. National guidelines for rabies prophylaxis and intra dermal administration of cell culture rabies vaccines, National Institute of Communicable Diseases (Government of India), New Delhi, 2007.
5. Association for Prevention and Control of Rabies in India. Assessing Burden of Rabies in India, WHO sponsored national multi-centric rabies survey, May 2004, KIMS, Bangalore, India. [www.apcri.org].
6. H Wilde et al. Failure of rabies post exposure treatment in Thailand. Vaccine 1989; 7:49-52.
7. H Wilde et. al. Purified equine rabies immune globulin: a safe and affordable alternative to human rabies immune globulin, 1989. Bulletin of WHO vol.67 (5), 731-736.
8. H Wilde et.al. Equine Rabies Immunoglobulin: A product with an undeserved poor reputation, 1990. Am. J. Trop. Med. Hyg. Vol. 42(2). 175-178.
9. M.K. Sudarshan et. al. Evaluation of a new Premedication protocol for administration of Equine rabies immunoglobulin in patients with hypersensitivity. 2007. Indian Journal of Public Health. Vol.51. No 2 April-June, 91-96.
10. Palmira CUPO et. al Proposal of Abolition of the skin sensitivity test before ERIG application. SciELO, Brazil Jan/Feb 2001
11. Dean D.J., Baer G.M. and Thompson W.R. Studies on the local treatment of rabies infected wounds. Bull. WHO. 1963,28,472-486.
12. World Health Organization. Rabies vaccines, WHO position paper, Weekly Epidemiological Record, No.49/50, 82,425-436, 2007 (www.who.int/wer)

Annexure - I

Availability of different Rabies Immunoglobulins in India

Human Rabies Immunoglobulins (HRIG) Brands	Manufactured/Marketed by
Berirab-P	Manufactured by Aventis Behring, Germany & Marketed by Cadila Health Care, Ahmedabad
Imogam Rabies	Manufactured by Aventis Pasteur, France & Marketed by Ranbaxy, Gurgaon, Haryana.
Kamrab	Manufactured by Kamada, Israel & Marketed by Synergy Diagnostics, Ltd, Thane, Maharashtra

Equine Rabies Immunoglobulins (ERIG) Brands	Manufactured/Marketed by
Anti Rabies Serum (ARS)	Central Research Institute (CRI), Kasauli, Himachal Pradesh.
Equirab	Bharath Serums and Vaccines Ltd, Mumbai
Anti Rabies Serum	VINS, Hyderabad.
Abhayrig	Manufactured by VINS, Hyderabad & Marketed by Human Biologicals Institute, Hyderabad.
Vinrig	Manufactured by VINS, Hyderabad & Marketed by Ace Pharmaceuticals, Hyderabad
CARIG	Cadila Pharmaceuticals, Ahmedabad

Annexure - II

List of Participants who attended the National workshop on "Rabies Immunoglobulin Administration" held on 2nd March 2008 at KIMS, Bangalore.

Sl No	Name	Place
1	Dr R L Ichhpujani	New Delhi
2	Dr M K Sudarshan	Bangalore
3	Dr S N Madhusudana	Bangalore
4	Dr S Abdul Rehaman	Bangalore
5	Dr G Sampath	Hyderabad
6	Dr D H Ashwath Narayana	Bangalore
7	Dr R Jayakumar	Chennai
8	Dr C V Subramanium	Bangalore
9	Dr Amlan Goswami	Kolkata
10	Dr B J Mahendra	Mandya
11	Dr H S Ravish	Bangalore
12	Dr B G Parasuramalu	Bangalore
13	Dr G Praveen	Bangalore
14	Dr G M Venkatesh	Hassan
15	Dr N L Gangadhar	Bangalore
16	Dr N Shakila	Bangalore
17	Dr Shivaramakrishna	Mandya
18	Dr Shivayogi Mandakki	Sagara
19	Dr A N Rajendra	Mysore
20	Dr H M Balachandra	Mysore
21	Dr C A Narasimha	Mysore
22	Dr T S R Sai	Tirupathi
23	Dr D M Satapathy	Berhampur
24	Dr T R Behra	Berhampur
25	Dr Shobha Malini	Berhampur
26	Dr M N Siddique	Lucknow
27	Dr Sumit Poddar	Kolkata
28	Dr Ranjit Mankeshwar	Mumbai

Sl No	Name	Place
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30	Dr Nileena Koshy	Trissur
31	Dr Rajinish Kumar	New Delhi
32	Dr J S Anand	New Delhi
33	Dr Dhanya Kumar	Bangalore
34	Dr L T Gayathri	Bangalore
35	Dr Manjula	Bangalore
36	Dr K L Ravikumar	Bangalore
37	Mr Adeet Ghosh	Mumbai
38	Mr Taref Kanthawala	Mumbai
39	Mr Chintesh Dwidevi	Mumbai
40	Mr Mahesh	Chennai
41	Mr Balakumar	Chennai
42	Mr Jagdish Kumar	Bangalore
43	Mr Sarat Singh	Bangalore
44	Mr C Ramakrishna	Bangalore
45	Mr G Suchindranath	Bangalore
46	Mr Ramachandra G kulkarni	Bangalore
47	Mr Vinay Kumar Gupta	Bangalore

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Bharath Serums and Vaccines Ltd., (BSVL), Mumbai.

Human Biologicals Institute (HBI), Hyderabad.

Synergy Diagnostics Pvt. Ltd., Thane.

Annexure - III

List of experts who finalized the Manual on 'Rabies Immunoglobulin administration'

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