I. Rationale of Treatment

Physicians must evaluate each possible rabies exposure. Consult local or state public health officials if questions arise about the need for treatment. Consider the following factors before specific antirabies treatment is initiated.

1. Species of Biting Animal

Bats

Bats have been documented in the 49 continental states, and bats are increasingly implicated as important wildlife reservoirs for variants of rabies virus transmitted to humans. Transmission of rabies virus can occur from minor, seemingly underappreciated exposures to bats (see Table 1).

2. Circumstances of Biting Incident

An unprovoked attack might be more likely than a provoked attack to indicate the animal is rabid. Bites inflicted on a person attempting to feed or handle an apparently healthy animal, particularly after provocation, are usually those associated with a rabid animal. Contact of saliva with intact skin) do not constitute exposures. Rare reports of aerosol exposure have been received from laboratory and bat-infested cave settings. (1)

Rabies Immune Globulin (Human) USP, Heat Treated, Imogam

The likelihood of rabies in a domestic animal varies regionally, and the need for post-exposure prophylaxis also varies on the basis of regional epidemiology (see Table 1). (1)

1. Local Treatment of Wounds

Thoroughly wash and flush all bite wounds and scratches immediately or as early as possible (for about 15 minutes, if possible) with soap and a cleansing agent and copious amounts of water. Where available, apply an iodine-containing, or similarly viricidal, topical preparation to the wound. (3)

2. Specific Treatment

Administer post-exposure antirabies vaccination with rabies vaccine in addition to administering Rabies Immune Globulin (RIG). However, for persons who have previously received complete vaccination regimens (pre-exposure or post-exposure) with a cell culture vaccine or another vaccine. Administer only vaccine to these persons (i.e., previously unvaccinated persons, the administration of both human rabies immune globulin (RIG) and vaccine is indicated in conjunction with the standard series of Rabies Vaccine vaccinations, is indicated for individuals suspected of exposure to rabies virus in such wildlife, unless the animal is available for diagnosis and public health authorities are facilitating expeditious laboratory testing, or if the brain tissue from the animal has already tested negative (see Table 1). (1)

Other Wild Animals

Small rodents (e.g., squirrels, chipmunks, rats, mice, hamsters, guinea pigs, and gerbils) and lagomorphs (including rabbits and hares) are rarely infected with rabies and have not been known to transmit rabies to humans. In all cases involving rodents, the state or local health department should be consulted before a decision is made to initiate post-exposure prophylaxis (see Table 1). (1)

III. Post-exposure Treatment of Rabies

The essential components of rabies post-exposure prophylaxis are wound treatment and, for previously unvaccinated persons, the administration of both human rabies immune globulin (RIG) and vaccine. Whether the vaccine or vaccine alone is indicated in such exposure situations, the state or local health department following a provoked or unprovoked exposure to determine the best course of action based on current public health recommendations. (1)

Bite

Any penetration of the skin by teeth. Nonbite

Scratches, abrasions, open wounds or mucous membranes contaminated with saliva or other potentially infectious material such as brain tissue from a rabid animal. Indirect contact and activities (e.g., petting or handling an animal, contact with blood, urine or feces, and contact of saliva with intact skin) do not constitute exposures. Rare reports of aerosol exposure have been received from laboratory and bat-infested cave settings. (1)

Pre-exposure prophylaxis should be initiated as soon as possible following suspected rabies virus exposure to such wildlife. Consult the local or state health department following a provoked or unprovoked exposure to determine the best course of action based on current public health recommendations. (1)

IV. Vaccination Status of Biting Animal

A properly immunized animal has a minimal chance of developing rabies and transmitting the virus. (1)

II. Post-exposure Treatment of Rabies

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Pre-exposure prophylaxis should be initiated as soon as possible following suspected rabies virus exposure to such wildlife. Consult the local or state health department following a provoked or unprovoked exposure to determine the best course of action based on current public health recommendations. (1)

V. Recommendations

The following recommendations are only a guide. Apply these in conjunction with the knowledge of the animal species involved, circumstances of the bite or other exposure, vaccination status of the animal, and presence of rabies in the region. Consult local and state public health officials if questions arise about the need for rabies prophylaxis.
INFORMATION FOR VACCINE RECIPIENTS OR PARENTS/GUARDIANS

Before administration, inform patients, parents or guardians of the benefits and risks of administration of Imogam Rabies – HT. Instruct patients, parents or guardians to report any serious adverse reactions to their healthcare provider.

Table 1: RABIES POST-EXPOSURE PROPHYLAXIS GUIDE, UNITED STATES (1)

<table>
<thead>
<tr>
<th>Animal Type</th>
<th>Evaluation and Disposition of Animal</th>
<th>Post-exposure Prophylaxis Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dogs, cats, and ferrets</td>
<td>Healthy and available for 10 days observation</td>
<td>Persons should not begin prophylaxis unless animal develops clinical signs of rabies.</td>
</tr>
<tr>
<td>Rabid or suspected rabid</td>
<td>Immediately begin prophylaxis.</td>
<td>Unknown (e.g., escaped)</td>
</tr>
<tr>
<td>Wild skunks, raccoons, foxes, and most other carnivores; bats</td>
<td>Regarded as rabid unless animal proven negative by laboratory tests</td>
<td>Consider immediate prophylaxis.</td>
</tr>
<tr>
<td>Livestock, small rodents, lagomorphs (rabbits and hares), large rodents (woodchucks and beavers), and other mammals</td>
<td>Consider individually</td>
<td>Consult public health officials. Bites from squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, other small rodents, rabbits, and hares almost never require antirabies post-exposure prophylaxis.</td>
</tr>
</tbody>
</table>

*During the 10-day observation period, begin post-exposure prophylaxis at the first sign of rabies in a dog, cat, or ferret that has bitten someone. If the animal exhibits clinical signs of rabies, it should be euthanized immediately and tested.

†Initiate post-exposure prophylaxis as soon as possible following exposure to wildlife or another animal suspected of having rabies or any other animal not under observation that has tested negative. Other factors that might influence the urgency of decision-making include the species of the animal, the general appearance and behavior of the animal, whether the encounter was provoked by the presence of a human, and the severity and location of bites. Discontinue vaccine if appropriate laboratory diagnostic test (i.e., the direct fluorescent antibody test) is negative.

‡The animal should be euthanized and tested as soon as possible. Holding for observation is not recommended.

CONTRAINDICATIONS

Do NOT administer Imogam Rabies – HT in repeated doses once vaccine treatment has been initiated. Repeating the dose may interfere with maximum active immunity expected from the vaccine.

WARNINGS

• Administration of rabies post-exposure prophylaxis is a medical urgency, not a medical emergency, but decisions must not be delayed.

• Although no post-exposure vaccine failures have occurred in the US since cell culture vaccines have been routinely used, failures have occurred abroad when some deviation was made from the recommended post-exposure treatment protocol or when less than the currently recommended amount of antirabies sera was administered. (1)

• Rabies Immune Globulin (Human) USP, Heat Treated, Imogam Rabies – HT, is made from human plasma. Because this product is made from human plasma, it may carry a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses. An alcohol fractionation procedure used to purify the immunoglobulin component removes and/or inactivates both enveloped and non-enveloped viruses to a certain extent. An added heat treatment process (80°C, 10 hours) further inactivates both enveloped and non-enveloped viruses. Despite these measures, it is still theoretically possible that known or unknown infectious agents may be present. Report all infections thought by a physician possibly to have been transmitted by this product to the Pharmacovigilance Department, Sanofi Pasteur Inc., 1-800-822-2463.

• Prior to administration, review the patient history for possible sensitivity to human immune globulin. Epinephrine injection (1:1000) must be immediately available shoud an acute anaphylactic reaction occur.

• Persons with IgA deficiency have increased potential for developing antibodies to IgA and could have anaphylactic reactions to subsequent administration of blood products containing IgA. (4) (5)

PRECAUTIONS

• Imogam Rabies – HT is not for intravenous administration. Do NOT administer intravenously.

• Never administer Rabies Immune Globulin (Human) in the same syringe or into the same anatomical site as the vaccine dose. Because Rabies Immune Globulin (Human) may partially suppress active production of antibody, no more than the recommended dose should be given. (1)

INFORMATION FOR VACCINE RECIPIENTS OR PARENTS/GUARDIANS

Before administration, inform patients, parents or guardians of the benefits and risks of administration of Imogam Rabies – HT. Instruct patients, parents or guardians to report any serious adverse reactions to their healthcare provider.

DRUG INTERACTIONS

Postpone immunization with live vaccines until at least three months after Imogam Rabies – HT administration because of the possibility that antibodies in the globulin preparation may interfere with the immune response to the vaccine.

PREGNANCY

Animal reproduction studies have not been conducted with Imogam Rabies – HT. It is also not known whether Imogam Rabies – HT can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Administer Imogam Rabies – HT to a pregnant woman only if clearly needed.

Because of the potential consequences of inadequately treated rabies exposure and limited data that indicate that fetal abnormalities have not been associated with rabies vaccination, pregnancy is not considered a contraindication to post-exposure prophylaxis. If there is substantial risk of exposure to rabies, pre-exposure prophylaxis may also be indicated during pregnancy. (1)

LACTATION

Immunoglobulins are excrated in maternal milk. Caution should be exercised when Imogam Rabies – HT is administered to a nursing woman.

ADVERSE REACTIONS

Systemic prophylactic treatments occasionally are complicated by adverse reaction. (1)

Data From Clinical Studies

The safety profile of Imogam Rabies – HT (heat treated) was compared to Rabies Immune Globulin (Human), Imogam Rabies (non-heat treated), in a clinical trial involving 16 volunteers in each of 4 treatment groups (64 total subjects). Local and systemic adverse reactions were classified by the description of the reaction and by its severity. (1) Both Imogam Rabies – HT and Imogam Rabies were without reported serious adverse reactions or allergic reactions. Two subjects reported severe headaches, one in the Imogam Rabies – HT placebo group and one in the Imogam Rabies + Imovax Rabies group, and one third of the volunteers reported moderate systemic (headache and malaise) reactions. These were equally distributed among the 4 treatment groups with no significant differences between the groups. Three-quarters of the local adverse reactions (redness, pain, erythema, induration, pruritus, regional adenopathy) were mild. The safety profile did not differ between groups, although Imogam Rabies – HT produced fewer and milder local reactions at the injection site. (6)

Data From Post-marketing Experience

The following additional adverse reactions have been identified during postapproval use of Imogam Rabies – HT. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to Imogam Rabies – HT exposure.

Cardiac Disorders

Hypotension, tachycardia

Gastrointestinal Disorders

Nausea, vomiting

General Disorders and Administration Site Conditions

Fever, chills

Immune System Disorders

Anaphylaxis, allergic reaction

Skin and Subcutaneous System Disorders

Rash, pruritus

Data From Literature

Although not reported specifically for Rabies Immune Globulin (Human), geniogonococcal edema and nephrotic syndrome have been reported after injection of immune globulin (IG), a product similar in biochemical composition but without antibodies active. (7)

Reporting of Adverse Reactions

Encourage reporting by patients, parents or guardians of all suspected adverse reactions occurring after Rabies Immune Globulin (Human) administration. Report suspected reactions following treatment with Rabies Immune Globulin (Human) to the FDA at 1-800-FDA-1088 or www.fda.gov medwatch. Also report these events to the Pharmacovigilance Department, Sanofi Pasteur Inc., Discovery Drive, Swiftwater, PA 18370 or call 1-800-822-2463.

DOSAGE AND ADMINISTRATION

For wound infiltration and intramuscular administration only. Imogam Rabies – HT is administered using a sterile needle and syringe. Inspect parenteral drug products visually for particulate matter and/or discoloration prior to administration, whenever solution and container permit. If either of these conditions exists, do not administer the product.

Use Imogam Rabies – HT in conjunction with rabies vaccines such as Rabies Vaccine, Imovax Rabies, for intramuscular immunization, a vaccine prepared from human diploid cell cultures. Never administer Rabies Immune Globulin (Human) in the same syringe or into the same anatomical site as rabies vaccine.

The recommended dose of Imogam Rabies – HT is 20 IU/kg (0.133 mL/kg) or 9 IU/lb (0.06 mL/lb) of body weight administered at the time of the first vaccine dose. (3) (8) (9) Multiple vials may be required for a single effective dose.

For example, a 70 kg individual will need 0.133 mL/kg × 70 kg = 9.31 mL. This would require 4 full vials of Imogam 2 mL vials plus a partial vial to deliver the recommended dose.

Because Rabies Immune Globulin (Human) may partially suppress active production of antibody, do not give more than the recommended dose. (1) (11) Discard any remaining product.
If anatomically feasible, use the full dose of Rabies Immune Globulin (Human) to thoroughly infiltrate the area around and into the wounds. Inject any remaining dose intramuscularly, using a separate needle, at a site distant from vaccine administration. (1) (10)

HOW SUPPLIED
Imogam Rabies – HT is supplied in a 2 mL single-dose vial with a minimal potency of 150 International Units per milliliter (IU/mL). Multiple vials may be needed for a single effective dose.
Single-dose vial, 2 mL NDC 49281-190-58. Packaged as NDC 49281-190-20.

STORAGE
Store Imogam Rabies – HT in the refrigerator at 2° to 8°C (35° to 46°F). DO NOT FREEZE.

CLINICAL STUDIES
Controlled human trials of Rabies Immune Globulin (Human) have not been performed; however, extensive field experience from many areas of the world indicates that post-exposure prophylaxis combining local wound treatment, local infiltration of rabies immune globulin (RIG), and vaccination is uniformly effective when appropriately administered. (1)

Rabies antibody provides passive protection when given immediately to individuals exposed to rabies virus. (12) Studies of Rabies Immune Globulin (Human), (11) Imogam Rabies, given with the first of five doses of Sanofi Pasteur SA HDCV (7) confirmed that passive immunization with 20 IU/kg of Rabies Immune Globulin (Human) provides maximum circulating antibody with minimum interference of active immunization by HDCV.
A double-blind randomized trial (6) was conducted to compare the safety and antibody levels achieved following intramuscular injection of Imogam Rabies – HT (heat treated) and Rabies Immune Globulin (Human). Imogam Rabies (non-heat treated). Each Rabies Immune Globulin (Human) was administered on day 0, either alone or in combination with the human diploid cell Rabies Vaccine (Imovax Rabies) using the standard post-exposure prophylactic schedule of day 0, 3, 7, 14, and 28.
Sixty-four healthy veterinary student volunteers were randomized into four parallel groups of 16 each to receive the following Rabies Immune Globulin (Human) and vaccine regimens:
- Imogam Rabies – HT + Imovax
- Imogam Rabies + placebo
- Imogam Rabies – HT + placebo
- Imogam Rabies + Imovax

The treatment of both Rabies Immune Globulin (Human) and vaccine corresponded to the post-exposure recommended dose of 20 IU/kg of Rabies Immune Globulin (Human) and was administered in three equally divided IM injections of under 5 mL in either gluteus. Serum rabies antibody levels were assessed before treatment and on days 3, 7, 14, 28, 35, and 42 by the Rabies Fluorescent Focus Inhibition Test (RFFIT).
Serum antibody levels were similar in the Imogam Rabies – HT and Imogam Rabies groups. By day three, 60% of each group had detectable antibody titers of ≥0.05 IU/mL. By day 14, the geometric mean titers (with 95% confidence interval) were 19 IU/mL (11-38) in the Imogam Rabies + placebo group and 31 IU/mL (20 to 48) in the Imogam Rabies + vaccine group. These differences were not statistically significant.

REFERENCES
4 Fudenberg HH. Sensitization to immunoglobulins and hazards of gamma globulin therapy, pp 211-220 in Merler E, Editor Immunoglobulins: biologic aspects and clinical uses, National Academy of Sciences, Wash., DC. 1970.

Product Information as of December 2020

Manufactured by:
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