Neutralizing Antibodies to Rabies Following Injection of Rabies Immune Globulin into Gluteal Fat or Deltoid Muscle
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Background: This experiment was carried out to determine whether there is any difference in circulating rabies antibody when rabies immune globulin is administered into fat or muscle tissue.

Methods: Blood samples were taken at 24 and 48 hours after administering 40 IU/kg body weight of purified equine rabies immune globulin (ERIG) into deltoid muscle, or fatty gluteal tissue of grossly obese subjects.

Results: Both groups revealed barely detectable antibody levels.

Conclusions: No conclusion was possible concerning the absorption kinetics of immune globulin from fat or muscle. However, it was evident that circulating antibody levels, using the recommended 40 IU/kg dose of ERIG, were extremely low and probably less than the required protective level at the possible bite site. This study supports current recommendations for local infiltration of virus inoculation sites with human or equine rabies immune globulin.

Materials and Methods

Subjects presenting to our outpatient clinic with WHO category I or II rabies exposures, hence patients that would normally not be given RIG,1 were recruited for this study in a nonrandomized manner. Eleven animal bite patients with normal Body Mass Index (BMI) 18.5–24.9, nine overweight ones with BMI of 25–29.9, eight obese ones with BMI over 30, and one underweight subject with a BMI of 15.1,3 were given purified equine rabies immune globulin (ERIG, Institute Pasteur, Paris batches 5212 and 5658, potency 220 IU/mL) at 40 IU/kg. They also received the first intradermal injection of their tissue culture rabies vaccine series, according to the WHO approved, Thai Red Cross postexposure schedule (Purified Vero Cell Rabies Vaccine, PVRV, Institute Merieux, batch A0254, potency 3.17 IU per 0.5 mL).

Group I was given the ERIG into the gluteal region using a 23 gauge needle injecting perpendicularly 3.5 cm deep, presumably into fatty tissue. Group II received the ERIG in the same way into deltoid muscle. The determination whether injections were into fat or muscle tissue was made by the first author, an experienced nurse, by palpating the area. Blood was drawn 24 and 72 hours later, and the circulating rabies neutralizing antibody titer was determined using the method of J.S. Smith.6 Informed consent was obtained from all patients. The Ethics Committee of the Thai Red Cross Society approved this study.

Results and Discussion

This study was carried out in 1990, and it was not previously reported since we did not note any significant differences between the serum antibody levels in obese or lean subjects, and whether injections were made into the gluteal or deltoid area. Levels were barely above the cut-off point (0.03 IU/mL) in all groups. All

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antibody titers were well below 0.5 IU/mL, the lowest acceptable level by WHO standards. Only 2 out of 29 subjects had titers above 0.3 IU/mL at 24 hours and they dropped to 0.12 IU/mL 24 hours later. A recent more detailed study of the kinetics of RIG by J. Lang et al. also revealed that circulating antibody levels were low, and in the same range as those found in our earlier unpublished study. Classical studies by Dean and Baer showed that it is the RIG that is injected into virus inoculation sites that saved the life of animals challenged with a LD 50 dose of rabies virus. Recent reports of rabies postexposure vaccine failures suggest that incomplete, or no RIG infiltration of wounds, may have played a role in at least some of these deaths. The WHO expert committee on rabies recommended in 1996 that all wounds be injected with RIG. As much as possible, or all of the calculated dose of RIG should be used for this. If wounds are extensive and multiple, RIG is to be diluted to allow complete injection of all potential inoculation sites. WHO also recommended that RIG not be injected into fatty tissues.

The Thai Red Cross has since 1986 been engaged in a vigorous educational campaign, directed at the public and health care providers, stressing the importance of prompt WHO standard postexposure rabies treatment. However, old concepts take a long time to disappear and a recent hospital survey in Thailand, and one in Pakistan, discovered that a majority of respondents were still not aware of, or ignored current WHO recommendations for safe, and proven effective postexposure rabies treatment. Many respondents did not use RIG, or limited the dose injected into wounds to one-half of the calculated total amount, giving the rest intramuscularly into the gluteal region. Our old study, and that of Lang et al., support Dean and Baer's seminal work that documented the value of wound injection with RIG. These studies indicate that RIG injected into gluteal muscle or fat, may not provide enough early circulating antibody to neutralize virus at the bite sites. Rabies vaccine alone can not be expected to induce protective antibody levels sooner than 10 days after the start of a postexposure schedule. Whether there is any difference in circulating antibody titers when RIG is injected into muscle or fat can not be answered by this study. Antibody levels were barely detectable in both groups and therefore our data did not allow a valid comparison between the two groups.

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References