

SUCCESSFUL TREATMENT OF ACUTE SYSTEMIC ANAPHYLAXIS IN A WESTERN LOWLAND GORILLA (*GORILLA GORILLA GORILLA*)

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Abstract: This brief communication describes the successful treatment of acute systemic anaphylaxis in a wild-born but captive infant western lowland gorilla (*Gorilla gorilla gorilla*) in the Republic of Congo. The infant demonstrated signs of acute respiratory distress, lingual swelling, and reaction to intradermal tuberculin, given 55 hr earlier. Details of the treatment with steroids, anesthetic induction, and i.v. epinephrine are all reported, and potential antigens that may have initiated the anaphylactic shock are discussed.

Key words: Anaphylactic shock, epinephrine, *Gorilla gorilla gorilla*, type 1 hypersensitivity, western lowland gorilla.

BRIEF COMMUNICATION

Anaphylaxis is an acute immunoglobulin E-mediated systemic reaction in previously sensitized people or animals. The introduction of an antigen to a patient's blood system to which the patient is already sensitized results in an antigen-antibody reaction.¹⁰ This causes a massive generalized release of inflammatory mediators from mast cells and basophils in response to the antigen.¹¹ The inflammatory mediators, histamines and leukotrienes, mediate smooth-muscle contraction and venous dilatation, thereby increasing venous capacity and decreasing venous return.¹¹ Arterial dilatation subsequently decreases arterial pressure, and capillary permeability increases because of the presence of histamine.¹¹ These responses cause a loss of plasma into tissues and leads to urticaria and angioedema.¹¹ Fluid accumulation may cause pulmonary edema and possibly obstructive angioedema in the upper respiratory tract. Hypovolemia and shock can follow.¹¹ In humans, triggers for anaphylaxis are known to include foods (peanuts; tree nuts; and various fruits, such as apples and peaches),

parenteral enzymes, blood products, β -lactam antibiotics, other drugs, allergen immunotherapy, and insect stings.¹¹ The reaction is typically known as type I or immediate hypersensitivity; however, delayed-type reactions and biphasic reactions (with an immediate and a delayed reaction 2 to 4 hr later) have been reported.¹²

In domestic animals, most anaphylactic reactions affect the pulmonary system, although exceptions include gastrointestinal reactions in canines and dermatologic reactions in horses.^{1,8} In humans, anaphylaxis usually affects the bronchopulmonary tree.⁶ Gorillas, as great apes, have much in common taxonomically and physiologically with humans, and consequently, would be expected to share similar disease processes.¹⁴

In February 2006, a wild-born orphaned female western lowland gorilla (*Gorilla gorilla gorilla*) was confiscated in the Republic of Congo and placed under the care of the Projet Protection des Gorilles, a gorilla rehabilitation and reintroduction project.⁵ The animal was estimated to be 2 yr old and had been in captivity for approximately 6 mo before confiscation. It was severely underweight, weighing 8.0 kg, and had a shotgun pellet subcutaneously over her pectoral muscle but was otherwise apparently healthy. Chest auscultation revealed nothing abnormal. Stool samples were negative for endoparasites by fecal egg flotation when using a modified Sheather's solution.

The gorilla was anesthetized 4 days after confiscation as part of the quarantine protocol. After preinduction administration of diazepam (Valium®, 1%, Roche Pharmaceuticals Ltd., 92200 Neuilly-sur-Seine, Île-de-France, France; 0.75 mg/kg p.o.), anesthesia was induced with ketamine (Narketan 10®, Vetoquinol UK Ltd.,

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Buckingham, Buckinghamshire, MK18 1PA, United Kingdom; 8.75 mg/kg i.m.). Two supplemental doses of ketamine (1 mg/kg i.v. and 1.25 mg/kg i.v.) were given 5 and 20 min, respectively, after initial induction. The procedure and anesthesia were unremarkable. Viscotears® (Novartis, Farnham, Surrey, GU16 7RS, United Kingdom) drops were applied to both conjunctivas to prevent corneal drying. The gorilla was seronegative to hepatitis B antigen (capture enzyme immunoassay), human immunodeficiency virus (HIV)1, and HIV2 (by both enzyme-linked immunosorbent assay and indirect immunofluorescence assay).^{2,13} Hematology (erythrocyte, platelet, hemoglobin, mean corpuscular hemoglobin concentration, leucocyte, monocyte, basophil, eosinophil, neutrophil, mean corpuscular hemoglobin, and mean corpuscular volume) and biochemistry (total and direct bilirubin, calcium, cholesterol, creatinine, glucose, lactate dehydrogenase, protein, and urea) results were unremarkable. Tests were performed in a commercial laboratory in Brazzaville by using human biochemistry panels. Results were compared with data from more than 80 gorillas and appeared unremarkable. During anesthesia, the shotgun pellet was removed, and the incision was closed by using simple interrupted 3.0 polyglactin 910 (Vicryl®, Ethicon, Somerville, New Jersey 08807, USA) sutures. Ivermectin (Dectomax®, Pfizer Ltd., Sandwich, Kent, United Kingdom; 0.3 mg/kg i.m.) was administered in the quadriceps muscle for routine deworming. Amoxicillin (Amoxypen LA®, Intervet UK Ltd., Walton, Buckinghamshire, MK7 7AJ, United Kingdom; 18.75 mg/kg i.m.) was administered in the quadriceps muscle to prevent local infection and subsequent wound dehiscence. Intradermal tuberculosis (TB) testing was performed by using 0.1 ml mammalian old tuberculin (M.O.T.®, Colorado Serum Co., Denver, Colorado 80216, USA) in the right upper eyelid. Paracetamol (Effergan® Pediatric 3% oral suspension, UPSA Laboratories, 92500 Rueil Malmaison, Île-de-France, France; 10 mg/kg p.o.) was given before surgery and twice daily for 2 days after the surgery to prevent irritation around the sutures. Anesthetic recovery was smooth, but effects of the diazepam preanesthetic medication, in particular, drowsiness, were noticed up to 4 hr after administration. The right upper eyelid showed marked swelling within 1 hr of the tuberculin injection and still showed a marked generalized reaction at 24 hr. Swelling continued to decrease thereafter, and, by 55 hr after injection, the eyelid appeared normal.

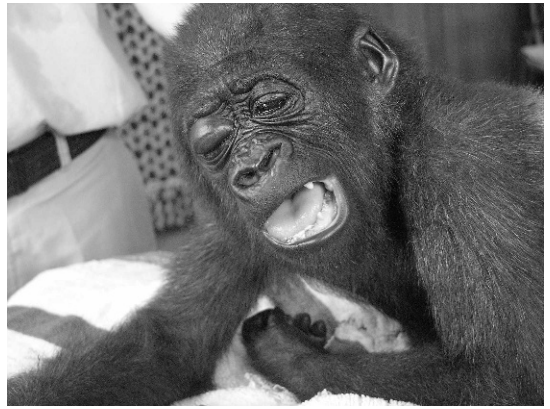


Figure 1. The infant western lowland gorilla (*Gorilla gorilla gorilla*) in respiratory distress with lingual and intradermal tuberculosis testing site (right eyelid) swelling during the anaphylactic reaction.

Two days after anesthesia, the gorilla started coughing while eating plain bread, which suggested inhalation of bread crumbs. This progressed within 20–30 min to severe coughing, labored breathing, nasal dilatation, and gasping. Airway obstruction, pneumothorax, and anaphylaxis were differential diagnoses. Fifteen minutes after onset, dexamethasone (Dexasone®, Intervet UK Ltd., Walton, Buckinghamshire, MK7 7AJ, United Kingdom; 0.25 mg/kg i.m.) was given, and a bag valve mask (Ambubag®, Ambu A/S, 2750 Ballerup, Copenhagen, Denmark) with a human infant face mask was used to manually aid respiration. Ampicillin (Amoxypen LA®, Intervet UK Ltd., Walton, Buckinghamshire, MK7 7AJ, United Kingdom; 18.75 mg/kg i.m.) was administered prophylactically in case of subsequent surgical intervention or aspiration pneumonia. The Heimlich maneuver was also performed several times in attempts to clear a possible foreign body airway obstruction, but no such obstruction was detected. It was unclear if lung sounds were reduced on one side. After 30 min, lingual swelling was observed, as well as significant swelling of the right eyelid (TB test site) (Fig. 1). The infant was manually restrained and sedated with ketamine (6.25 mg/kg i.v.) to allow further treatment. Epinephrine (Epinephrine Injectable [RX]® 1:1000, Phoenix Pharmaceuticals Inc., St. Joseph, Missouri 64507, USA; 0.0125 mg/kg i.v.) was administered, which increased the heart rate and was followed by mild arrhythmias with irregularly timed and strength heartbeats detected by auscultation for a very short period. Lingual and eyelid swelling had worsened, and copious clear nasal discharge

was present. Attempts to pass a 6.0-mm internal diameter endotracheal tube were unsuccessful because of severe lingual and oropharyngeal swelling. Fluids were cleared from the nasal cavity and pharynx, and the tongue was depressed digitally to establish an airway. The airway was maintained in this manner for approximately 1 hr post-onset, until breathing became less labored. Approximately 15 min after epinephrine administration, the breathing appeared normal. At 2 hr after onset, frothy mucus was coughed up, with no evidence of foreign material. At that time, the right upper eyelid swelling had resolved. Teeth grinding (an indication of stress or discomfort) and inappetence alone continued for the next 48 hr.

The infant was again anesthetized for TB testing 1 mo later. Anesthesia with ketamine (6.5 mg/kg i.m.) was unremarkable, and repeated intradermal TB testing with M.O.T. was negative, which showed no reaction, despite the exact same bottles of ketamine and M.O.T. being used. Two mo after the reaction, the gorilla exhibited a mild apparent reaction to a measles, mumps, and rubella vaccine (MMR®, Aventis-Pasteur, 69181 Leimen, Baden-Württemberg, Germany; i.m.) given in the quadriceps muscle under manual restraint. Signs included vomiting and diarrhea after 30 min and showing rapid and irregular breathing after 3 hr. This continued throughout the day despite administration of Loratadine oral anti-histamine syrup (Claritin Allergy 1 mg/ml Syrup, Schering-Plough Ltd., Shire Park, Welwyn Garden City, Herts AL7 1TW; 0.75 mg/kg). Signs dissipated within 24 hr, and the gorilla made a complete recovery.

A diagnosis of anaphylaxis was made based on the clinical signs and response to therapy. The dietary and medical history was reviewed to try to determine a cause of the anaphylaxis (Table 1). The gorilla had reportedly consumed milk, from an unknown source but probably Nido® milk powder (Nestlé, 01 BP 1840, Abidjan, Cote d'Ivoire), and eaten bananas and bread while in captivity before confiscation. After confiscation, the gorilla had been offered fruit on a daily basis, including banana, passion fruit, orange, mango-steen (*Garcinia mangostana*), *Landolphia* fruits, and grapes. The day before the reaction, infant formula milk (Gallia Stage 2®, Nestlé), infant instant cereal (Cerelac®, Nestlé), and scrambled egg were given for the first time since arrival. Locally produced plain roasted peanuts were also given, however, the gorilla had eaten peanuts daily for 4 days before the reaction. The day of

Table 1. Potential antigen exposure and times before the anaphylactic reaction.

Potential antigen	Time before anaphylaxis (hr)				
	55	48	24	9	2.5
Ketamine	Yes				
Ivermectin	Yes				
Paracetamol ^a	Yes	Yes	Yes	Yes	
Amoxicillin ^b	Yes				
M.O.T. ^c	Yes				
Bread					
Peanuts		Yes	Yes	Yes	Yes
Formula milk ^a			Yes	Yes	Yes
Infant cereal ^a			Yes	Yes	
Egg			Yes		
Insect					Unknown

^a The gorilla infant was subsequently re-exposed to the same brands with no ill effects.

^b Long-acting (3 day) Amoxicillin given (Amoxypen LA, Intervet UK Ltd., Walton, Buckinghamshire, MK7 7AJ, United Kingdom).

^c Mammalian Old Tuberculin (M.O.T., Colorado Serum Co., Denver, Colorado 80216, USA). The gorilla infant was subsequently re-exposed to the same vial of M.O.T., with no repeated reaction.

the reaction, infant formula milk (Gallia Stage 2, and infant instant cereal (Cerelac) were fed 9 hr before the reaction; and infant formula milk (Gallia Stage 2), peanuts, fruit (banana and mangosteen) and bread were fed approximately 2.5 hr before the reaction. Peanuts and milk were considered as possible causes of the anaphylactic reaction; however, both had been given on more than one occasion before the reaction and most recently, more than 2 hr earlier. Neither fruits nor milk were considered to be a cause of the anaphylaxis, although fruit allergies are reported in humans. The same formula milk, bread (from the same source), and all the fruits were subsequently incorporated into the daily diet, without reaction, whereas peanuts were avoided. Although none were observed, insect bites or stings were also considered as possible causes.

Finally, iatrogenic causes were considered, such as antigen in the M.O.T., the amoxicillin, or the nonsteroidal anti-inflammatory drug, paracetamol. Both the M.O.T. and amoxicillin were used 55 hr before the onset of the reaction, and the paracetamol was given on five occasions, the last approximately 9 hr before the onset of the reaction. The M.O.T. and amoxicillin, therefore, were discounted.

Despite a literature review and an e-mail query to captive ape facilities in Africa, Europe, and the

United States, the authors did not find prior reported cases of severe anaphylaxis in non-human great apes. Inhalant allergies have been reported in chimpanzees, manifested as chronic respiratory disease but not as anaphylaxis.⁴ Anaphylaxis has been known to be induced by penicillin among rhesus macaques (*Macaca mulatta*) and crab-eating macaques (*Macaca fascicularis*) in laboratory situations (A. Saxon, pers. comm.). The incidence of anaphylaxis in non-human apes is unknown. However, in humans, prevalence data estimate that 1.24–16.8% of the U.S. population are at risk for anaphylaxis, the majority (about half) of all cases being idiopathic.⁷ The second most common types of anaphylaxis are induced by either food (peanuts in children, shellfish in adults) or by drugs (particularly antibiotics and nonsteroidal anti-inflammatory drugs).³ A cohort study of 969 children in the United Kingdom reported 2.2–5.5% of infants have food hypersensitivity reactions in the first year of life, and these reactions can have a genetic influence, with 1–4- and 6–9-yr-old south Asian children having 3.8 and 9.1 odds ratios, respectively, of having food-related wheezing compared with Caucasian children.⁹ Fatal reactions, however, are rare among humans (and one, therefore, may presume non-human apes), with only 0.002% of humans at risk of a fatal reaction.⁷ However, this case provides evidence that severe reactions may occur and require prompt medical treatment. The gorilla is currently still part of the reintroduction program more than 3 yr later and has not had a repeated episode.

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