# Human rabies post-exposure prophylaxis: a review of the treatment of accidents involving domestic cats

Profilaxia pós-exposição da raiva humana: uma revisão dos tratamentos envolvendo gatos domésticos

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**ABSTRACT**: Rabies is an anthropozoonosis that presents approximately 100% lethality and expensive preventive assistance. Many human post-exposure anti-rabies treatments indicated for people at risk of exposure to rabies virus, usually due to some aggression by a mammalian animal, are instituted annually. This study aimed to evaluate the initial care of post-exposure prophylaxis of human rabies in Belo Horizonte between 2007 and 2016, involving accidents with domestic cats. It was found 71.1% agreement between the treatments instituted by health services and the protocol of the Ministry of Health. Treatments classified as insufficient totaled 18.3% and excessive, 10.6%. The animals were healthy in 68% and observable in 68.4% of the cases. Treatments involving the use of anti-rabies vaccine totaled 87.7%. The most frequent treatment adopted by the health services was observing the animals associated with the human anti-rabies vaccination in 56.7% of the cases. Imperfections in the filling of the notifications must be revised to enable improvements for future analyses. As for human prophylactic anti-rabies care, forming a multidisciplinary health team including veterinarians would be well on the way to improving the service offered.

KEYWORDS: rabies; post exposure prophylaxis; domestic cats; human anti-rabies prophylaxis.

**RESUMO**: A raiva é uma antropozoonose que apresenta aproximadamente 100% de letalidade e alto custo na assistência preventiva. É instituído anualmente, um elevado número de tratamento antirrábico humano pós-exposição, o qual é indicado para pessoas que se encontram sob risco de exposição ao vírus rábico, geralmente devido a alguma agressão por animal mamífero. Este trabalho teve como objetivo avaliar o atendimento inicial da profilaxia pós-exposição da raiva humana, em Belo Horizonte, entre os anos de 2007 a 2016, envolvendo acidentes com gatos domésticos. Encontrou-se 71,1% de concordância entre os tratamentos instituídos pelos serviços de saúde e o protocolo do Ministério da Saúde. Tratamentos classificados como insuficientes totalizaram 18,3% e excessivos 10,6%. Os animais eram sadios em 68% e observáveis em 68,4% dos casos. Tratamentos que envolviam o uso de vacina antirrábica totalizaram 87,7%. O tratamento adotado pelos serviços de saúde com maior frequência foi a observação do animal associada à vacinação antirrábica humana em 56,7% dos casos. É necessário que imperfeições no preenchimento das notificações sejam revistas de forma a possibilitar melhorias para análises futuras. Quanto ao atendimento antirrábico profilático humano, a formação de uma equipe multidisciplinar de saúde com inclusão de médicos veterinários seria uma forma de aprimorar o serviço oferecido.

PALAVRAS-CHAVE: Raiva; profilaxia pós-exposição; gatos domésticos; profilaxia antirrábica humana.

## **INTRODUCTION**

Despite being one of the oldest diseases known to man, rabies is still considered a severe public health problem in all regions of the world where the virus still circulates (STEELE; FERNANDEZ, 1991). Post-exposure prophylaxis of human rabies should be instituted for people at risk of exposure to the rabies virus, usually after biting, scratching, or even licking a mammal.

The patient under treatment must undergo a medical anamnesis according to the *Human Anti-rabies Care Form*,

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followed or not by an initial treatment based on the conditions of the animals involved, associated with the type of exposure to the rabies virus, the affected anatomical region, the depth of the injury and the number of injuries (Figure 1) (BRASIL, 2014, BRASIL, 2017).

In most countries where the rabies virus is present, dogs are still the leading transmitters of rabies to humans due to the difficulties in implementing measures to control the disease. However, in countries where canine rabies is well controlled and wild rabies is present, domestic cats may play a significant role as transmitters of the rabies virus to humans due to their keen hunting instinct that allows them to interact with wild species (BUNN, 1991).

Between 2010 and 2021 In Brazil, 40 human rabies cases were recorded. Nine transmissions occurred by dogs, 20 by bats, four by non-human primates, four by felines, and two by foxes, and in one case, the transmitting animal species could not be identified (MINISTÉRIO DA SAÚDE, 2021).

In December 2021, the municipality of Belo Horizonte recorded a case of rabies in a domestic cat. It is noteworthy

that there have been no human rabies cases in Belo Horizonte since 1984, and the last records of feline and canine rabies occurred in 1985 and 1989. In the same municipality, between the years 2004 and 2021, there was a significant increase in bats positive for the rabies virus, with all specimens of frugivorous and insectivorous habits with 24 bats positive for rabies in the year 2021 alone (PBH, 2021).

Feline species pose a considerable challenge for public health in the context of rabies control, focusing on viral antigenic variants typical of wild animals. The behavioral characteristics of the species make cats a relevant link between air cycle rabies, feline rabies, and rabies in humans (GENARO, 2010).

This work aimed to write and evaluate the indication of post-exposure anti-rabies treatment related to accidents with domestic cats in the city of Belo Horizonte/MG, between 2007 and 2016.

## **MATERIAL AND METHODS**

An observational, retrospective, and descriptive study was carried out based on the analysis of the Post-exposure Anti-Rabies

	Conditions of the offending animals				
Type of exposure	Dog or cat not suspected of rabies at the time of aggression	Dog or cat suspected of rabies at the time of aggression	Angry, missing, or dead dog or cat		
Indirect contact	No tre	vater			
Light accident Superficial wounds, usually single, on the trunk, upper and lower limbs, caused by biting or scratching. Skin licking with a superficial lesion.	Wash with soap and water. Observe the animal for ten days after exposure. If the animal remains healthy during the observation period, close the case. If the animal dies, disappears, or becomes rabid, administer four doses of the human rabies vaccine (days 0, 3, 7, and 14).	Wash with soap and water. Start the prophylactic regimen with two doses of the vaccine (days 0 and 3). Observe the animal for ten days after exposure. If the animal remains healthy during the observation period, close the case. If the animal dies, disappears, or becomes rabid, administer the human rabies vaccine up to four doses (days 7 and 14).	Wash with soap and water. Start the prophylactic regimen with serum and four doses of the vaccine (days 0, 3, 7, and 14).		
Serious accident Deep or tearing, multiple or extensive wounds anywhere on the body. Mucosal or skin licking with severe injury. Wounds on the head/neck/ face, hands, digital pulps, and soles of the feet.	Wash with soap and water. Start the prophylactic regimen with two doses of the vaccine (days 0 and 3). Observe the animal for 10 days after exposure. If the animal remains healthy during the observation period, close the case. If the animal dies, disappears, or becomes rabid, administer the human rabies vaccine up to four doses (days 7 and 14).	Wash with soap and water. Start the prophylactic regimen with serum and two doses of the vaccine (days 0 and 3). Observe the animal for 10 days after exposure. If the animal remains healthy during the observation period, close the case. If the animal dies, disappears, or becomes rabid, administer the human rabies vaccine up to four doses (days 7, 14).	Wash with soap and water. Start the prophylactic regimen with serum and four doses of the vaccine (days 0, 3, 7, and 14).		

Source: Adapted from Technical Standards for Human Rabies Prophylaxis, 2014 and IN no. 26-SEI/2017-CGPNI/DEVIT/SVS/MS, of July 17, 2017. Figure 1. Scheme for prescribing post-exposure prophylaxis of human rabies in Brazil.

Care Forms from the Notifiable Diseases Information System (SINAN). The historical series from 2007 to 2016 was determined using a single notification form model for human antirabies prophylaxis from SINAN used from 2007 onwards. The data used involved accidents with domestic cats from 2007 to 2016, totaling 3,585 service notifications in the city of Belo Horizonte/MG. 996 (27.8%). Some notifications were excluded due to incomplete information and pre-exposure and re-exposure treatments. Therefore, a database containing 2,589 notification forms was obtained. Excel® software version 2013 was the program for preparing the database, calculating the absolute and relative frequencies, and elaborating tables.

For analyzing the variables, the used fields of the Human Anti-Rabies Care form were: municipality of notification, type of exposure to the virus, anatomical location of the wound, wound, type of wound, animal condition, animal subject to observation, indicated treatment. To determine the lesion characteristics, it was necessary to choose the most relevant for transmitting the rabies virus, when there was more than one lesion (Araújo et al., 2020).

The comparison of the prescribed treatment with that recommended by the Ministry of Health was performed using formulas developed in Excel according to Cabral et al. (2018), adapted by Araújo (2017). The analysis of the agreement between the treatments performed by the health service and that proposed by the Ministry of Health used the weighted *Kappa coefficient* with the STATA 12<sup>®</sup> *software*, considering the value of p≤0.05 for distortions between the proposed comparisons. For the treatments indicated by the health service without compliance with the Ministry of Health's protocol, two categories were classified, excessive and insufficient.

The CEP UFMG (CAAE: 62506616.1.0000.5149) and CEP SMSA-PBH (CAAE: 62506616.1.3001.5140) approved the present study in the Plataforma Brasil System,

according to resolution 466/12 that discusses research involving human beings.

## **RESULTS AND DISCUSSION**

Table 1 showed a 71.1% (1,843) agreement between the treatments instituted by the health service and those recommended by the Ministry of Health (MS), represented by the sum of the treatments present in the main diagonal of the table. This result corroborates Cabral et al. (2018), who found a 67.2% agreement between the treatment performed by the health service and that recommended by the Ministry of Health. Fernandes (2013) also observed a 70% agreement. Moriwaki et al. (2013) found a 58.4% agreement.

Above the main diagonal are the treatments insufficiently adopted by the health service, and below the main diagonal are the treatments excessively adopted by the health service.

Among the treatments adopted by the health service in accordance with the Ministry of Health, the treatment combining the animals' observation and the use of the human rabies vaccine stood out, representing 48.3% (1,251/2589). It corroborates Cabral et al. (2018), who found 46.5% of the consultations involving animal observation associated with the use of the human rabies vaccine in accordance with the Ministry of Health's protocol.

In the statistical analysis of the agreement, a weighted Kappa index = 0.5124 and p<0.001 was observed, demonstrating that the agreement found in this study between the treatments instituted by the health service and recommended by the Ministry of Health goes beyond chance and suggests that the model used for indicating the human anti-rabies treatment was effective.

The procedure most frequently adopted by the health service was observing the animals associated with the human rabies vaccination in 56.7% (1468/2589) of the notification

		Procedure recommended by the Ministry of Health					
		Treatment waiver n (%)	Animal observation n (%)	Observation of the animal and vaccine n (%)	Vaccine n (%)	Vaccine and serum n (%)	Total adopted by the health service n (%)
	Treatment waiver	0 (0.0%)	3 (0.1%)	13 (0.5%)	4 (0.2%)	23 (0.9%)	43 (1.7%)
Procedure	Animal observation	2 (0.1%)	134 (5.2%)	134 (5.2%)	0 (0.0%)	7 (0.3%)	277 (10.7%)
	Animal observation and vaccine	14 (0.5%)	87 (3.4%)	1,251 (48.3%)	3 (0.1%)	113(4.4%)	1,468 (56.7%)
adopted for	Vaccine	5 (0.2%)	13 (0.5%)	105 (4%)	57(2.2%)	182(7%)	362 (14.0%)
health service	Vaccine and serum	1 (0.0%)	2 (0.1%)	29 (1%)	6 (0.2%)	401(15.5%)	439 (17.0%)
	Total recommended by the Ministry of Health	22 (0.9%)	239 (9.2%)	1,532 (59%)	70 (2.7%)	726 (28.1%)	2,589 (100%)

#### Table 1. Domestic cats in Belo Horizonte between 2007 and 2016.

forms, and they were not consistent with the protocols of the Ministry of Health, with 14.8% (217/14 68) of these prescribed appointments were not in compliance with the MS. The result found in the present work corroborates Corrêa et al. (2014), who observed 57.7% of adoption of the treatment that involves observation of the animals involved in accidents and use of the human rabies vaccine, with Cabral et al. (2018), who found 57.2% and the Ministry of Health (2016) which found 50.4% adoption of the same treatment by health services. Abreu and Crizóstomo (2014) found 85% of the same treatment indication.

This study's result is probably due to the characteristics of the animals involved in accidents reported by the patients during care. These animals were more frequently presented as healthy and observable (64%) (Table 2) due to the high number of patients with injuries on the hands, feet (62.2%), head, neck, face (6.6%), and mucosa (1%), totaling 69.8%. This characterizes severe accidents involving indication of rabies vaccination (Araújo et al., 2020).

Observable animals are the ones that have a guardian who ensures that the animals do not have access to the street without supervision for 10 days after the accident.

The treatment involving vaccination associated with antirabies serum showed that the health service adopted this procedure in 17% (439/2589) of the consultations (Table 1), differing from Cabral et al. (2018), who observed a 2.6% indication for the same treatment. The Ministry of Health's recommendation for the same treatment occurred in 28.1% (726/2589) of the cases analyzed, a fact that is justified when evaluating the conditions of the animals involved in the cases declared by the patients in 32% of the notification forms, such as suspicious, rabid, and dead/missing animals (Table 2). According to Table 1, in this same treatment, there was a 15.5% agreement (401/2589) between the treatment instituted by the health service and that recommended by the Ministry of Health, with a prescription error due to insufficient treatment in 12.6% (325/2589) of the notifications.

The procedure adopted by the health service with less frequency was the dispensation of treatment (1.7%), all of which were insufficient and did not comply with the procedures recommended by the Ministry of Health (Table 1). Cabral et al. (2018) found similar results, in which treatment was not dispensed (1.4%) as recommended by the Ministry of Health.

When evaluating the conditions of the animals (Table 2), we observed that in 68% of the visits (1760/2589), these animals were declared healthy (no signs suggestive of rabies), and in 68.4% (1773/2589) were subject to observation (there was the possibility of observing the animal for ten days following medical care). Abreu and Crizóstomo (2014) observed 86% of healthy and observable animals in a study where the dog was the predominant species. Cabral et al. (2018) observed 80% of healthy dogs and 83.4% subject to observation.

It was noted that in 23.4% (607/2589) of the records, the patients declared that their domestic cats had died or disappeared, differing from Cabral (2015), who worked with human anti-rabies care in which dogs were the animals involved. Cabral (2015) observed that in 8.9% of the records of human anti-rabies care, patients declared that the dogs had died or disappeared after the accident. It is suggested that cats have greater access to the streets than dogs, leading to inter and intraspecific interactions that may contribute to transmitting disease-causing agents, including rabies. Ellis (2009) argues that domestic cats are natural predators and hunters and thus explore the environment to locate prey and food. Bats infected by the rabies virus may have wing paralysis or disjointed movements, which can attract cats and capture with the possible transmission of the rabies virus (GENARO, 2010).

The condition variable of the animals involved in accidents is essential for defining adequate treatment; however, of the 3,585 initial notification forms, 90 (2.5%) met blank, and notification forms were excluded from the analysis. Despite its relevance, this variable is not mandatory; therefore, the notification can be sent unfilled (SINAN NET, 2014). Cabral (2015) found that 4.1% of his initial database did not have information about the condition of the animals.

As to the possibility of observing the animals (Table 2) in 24% of the notifications, this information was blank. According to the SINAN NET 5.0 dictionary, this variable is not mandatory; however, the possibility of observing the animals becomes an important tool when deciding on the conduct to be adopted by the health professionals (SINAN NET, 2014).

 Table 2. Characterization of post-exposure human anti-rabies care in reported accidents with domestic cats in Belo Horizonte-MG

 between 2007 and 2016, according to the condition of the animals involved and the possibility of observing them.

Animals' condition	Possibility of observing the animals					
	Year n (%)	No n (%)	In White* n (%)	Total n (%)		
Sound	1,658 (64.0%)	80 (3.1%)	22 (0.9%)	1,760 (68.0%)		
Suspect	114 (4.4%)	103(4.0%)	2 (0.1%)	219 (8.5%)		
Rabid	1 (0.0%)	2 (0.1%)	0 (0.0%)	З (0.1%)		
Dead / missing	0 (0.0%)	11 (0.4%)	596 (23.0%)	607 (23.4%)		
Total	1,773 (68.4%)	196 (7.6%)	620 (24.0%)	2,589 (100%)		

\*Blank: not completed by the health service.

Comparing the procedures adopted by the health service and those recommended by the Ministry of Health, it was observed that the behaviors excessively adopted by the health service represented 10.3%, while 18.6% were classified as insufficient (Table 3). Moriwaki et al. (2013) observed that 13.4% of the conducts were excessive and 28.1% were insufficient; Fernandes (2013) found that 16% of the procedures were insufficient and 7% were excessive; Cabral et al. (2018) observed that 21.2% of the conducts were excessive and 11.5% were insufficient.

Among the health service's behaviors classified as excessive, we can highlight the adoption of human rabies vaccination alone in 4.8% (123/2589) of the consultations (Table 3), of which, in 95.93% (118 /123), the possibility of observing the animals was not considered (Table 1). In these cases, treatment would begin with two doses of the human rabies vaccine (days 0 and 3), and if the animal remained healthy until the end of the 10-day observation period, the case would be closed without administering the other doses (BRASIL, 2014). In this way, unnecessary patient exposure to immunobiologicals would be avoided, and costs would reduce.

In 1.5% (38/2589) notifications, the adoption of vaccine-associated rabies serum was excessive. Observation of the animals associated with the vaccine occurred excessively in 3.9% (101/2589) of attendance records. Patients subjected to excessive treatments using immunobiologicals are subject to undesirable side effects. Since 2002, with the Fuenzalida and Palácios vaccine's replacement with the cell-culture vaccine, the adverse effects of rabies prophylaxis have been reduced, as it is considered a safer vaccine (BRASIL, 2014; THRAENHART et al., 2004; WEEKLY, 2017).

As for the procedures classified as insufficient, treatments in which the vaccine or vaccine-associated anti-rabies serum were unnecessary, which are the treatments recommended by the Ministry of Health, can be highlighted as the most severe cases.

The health service adopted treatment waiver in 1.7% (43/2589) of attendance records (Table 3) and 0.9% (23/2589) (Table 1); the recommendation of the Ministry of Health would be vaccination associated with serum. Despite the low frequency found, 0.9%, this is a critical prescription error

since it is a severe disease and the patients could have become infected if the virus had been present in the saliva of the animals involved in accidents.

In 7% (182/2589) of the consultations, patients' vaccination was the treatment insufficiently adopted by the health service. In these cases, vaccination-associated rabies serum would be recommended. In 4.5% (116/2589) of the consultations, the procedure for observing the animals involved in accidents associated with human rabies vaccination was insufficiently adopted, and in 113 (Table 1), the Ministry of Health's recommendation would be the serum-associated vaccination. The animals' observation by the health service in 141 (5.5%) insufficient forms would have the total prescription of immunobiologicals according to the protocol of the Ministry of Health; however, they were not administered to the patients.

In addition to the patients' physical injuries and the conditions of the animals involved in accidents, it is crucial to analyze the epidemiological situation of rabies in the places where the accidents occurred. Awareness of epidemiological data on the circulation of the rabies virus in synanthropic wild animal species in urban areas is essential because they can introduce other variants of the virus in regions where the urban rabies cycle by dog variants is under control if the dog and cat populations have low-rabies vaccination coverage.

It is notorious that vaccination coverage above 80% in dogs and cats prevents virus circulation in the respective populations (BRASIL, 2022). However, developing a reliable population estimate for these domestic species is necessary to achieve the vaccination target.

Since domestic cats have a keen hunting instinct, even when well fed, they are potential bat predators in urban areas. Contact between these two species can reintroduce the rabies virus to domestic animals populations in regions with low vaccination coverage, and due to the proximity between humans and domestic animals, rabies can communicate to humans. Cats still have an outstanding characteristic compared to rabies by forming large colonies of feral cats where intense intra and interspecific relationships occur, thus increasing the chances of contact with wild animals infected by the rabies virus and transmitting it to other members of the colony (BERNSTEIN, 2007). In

Classification of procedures adopted by the health service
2007 and 2016, according to whether or not they are compatible with what is recommended by the Ministry of Health.
lable 3. Classification of post-exposure numan anti-rables care in reported accidents with domestic cats in Belo Horizonte-MG between

Classification of procedures adopted by the health service					
Type of treatment	Compatible n (%)	Insufficient n (%)	Excessive n (%)	Total n (%)	
Treatment waiver	0 (0.0%)	43 (1.7%)	0 (0.0%)	43 (1.7%)	
Animal observation	134 (5.20%)	141 (5.4%)	2 (0.1%)	277 (10.7%)	
Observation and vaccine	1,251 (48.3%)	116 (4.5%)	101 (3.9%)	1,468 (56.7%)	
Vaccine	57 (2.2%)	182 (7%)	123 (4.8%)	362 (14.0%)	
Vaccine and serum	401 (15.5%)	0 (0.0%)	38 (1.5%)	439 (17.0%)	
Total	1,843 (71.1%)	482 (18.6%)	264 (10.3%)	2,589 (100%)	

the United States, where urban-cycle rabies caused by canine variants has been eradicated, sylvatic rabies is a significant challenge for disease surveillance, and cats are the most reported animals for rabies among domestic species (DYER et al., 2014).

The analysis of the circumstances in which the aggression occurred and knowing the life habits of the animals are essential information to prescribe the anti-rabies care since it allows understanding whether it was a provoked or spontaneous aggression and if the animals involved are semi-domiciled or not, in which case, the possibility of contact with sick animals is evaluated. This information is not present in the human anti-rabies care form.

As for the possibility of observing the animals according to the treatments that involve observing these animals in accidents (observation and observation-associated human rabies vaccination) (Table 4), 67.4% (1745/2589) of notifications and 94.9% (1656/1745) of agreements with the Ministry of Health corroborate Cabral (2015), who observed 95.3% agreement for this analysis in a study involving accidents with dogs. Animals' observation is essential to define the treatment adopted since some treatments to be adopted depend on this observation.

**Table 4.** Characterization of post-exposure human anti-rabies care in reported accidents with domestic cats in Belo Horizonte-MG between 2007 and 2016, according to the possibility of observing the animals and the treatment adopted.

Type of treatment adopted					
Possibility of observing the animals involved	Just observation n (%)	Observation + vaccine n (%)	Total n (%)		
Year	268 (15.4%)	1,388 (79.5%)	1,656 (94.9%)		
No	4 (0.2%)	43 (2.5%)	47 (2.7%)		
Empty	5 (0.3%)	37 (2.1%)	42 (2.4%)		
Total	277 (15.9%)	1,468 (84.1%)	1,745 (100%)		

In 2.7% (47/1745) of the consultations, patients reported that it was impossible to observe the animals; however, the procedures adopted involved observation of the animals involved, suggesting an error in filling out the notification or error in prescribing the procedure adopted by the service. This fact corroborated Cabral et al. (201 8), who found a 2.1% inability to observe the animals involved associated with treatments in which it is necessary to observe the animals.

## CONCLUSION

Although rabies is an ancient disease known to man, it still proves to be a serious public health problem. Analyzes of SINAN's secondary anti-rabies prophylaxis databases are essential for making adjustments and improvements in health decision-making. Despite the high agreement found between the treatments instituted by the health service and the protocol that governs the prophylactic treatment after exposure to human rabies of the Ministry of Health, there are still insufficient and excessive prescriptions indicating that the service provided must be continuously updated, and somehow, knowledge must be recycled. Inconsistencies in filling in notifications made the analysis unfeasible in these cases, losing valuable information on human rabies prophylaxis, which is an important limiting factor for the study. The multidisciplinarity of the health teams involved in this service, including the presence of veterinarians, would be a way to improve the service offered as it is a severe disease of public health interest since domestic animals are an integral part of the rabies cycle. Few studies in the literature focus on domestic cats as transmitters of rabies to humans, and more studies related to the triad cycle that involves wild animals are necessary, especially bats, cats, and humans.

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