[Template:Other uses](/wiki/Template:Other_uses" \o "Template:Other uses) [Template:Infobox medical condition](/wiki/Template:Infobox_medical_condition) **Rabies** is a [viral disease](/wiki/Viral_disease) that causes acute [inflammation of the brain](/wiki/Encephalitis) in humans and other [mammals](/wiki/Mammals).<ref name=WHO2013/> Early symptoms can include fever and tingling at the site of exposure.<ref name=WHO2013/> These symptoms are followed by one or more of the following symptoms: violent movements, uncontrolled excitement, fear of water, an inability to move parts of the body, confusion, and [loss of consciousness](/wiki/Loss_of_consciousness).<ref name=WHO2013/> Once symptoms appear, the result is nearly always death.<ref name=WHO2013/> The time period between contracting the disease and the start of symptoms is usually one to three months; however, this time period can vary from less than one week to more than one year.<ref name=WHO2013/> The time is dependent on the distance the virus must travel to reach the [central nervous system](/wiki/Central_nervous_system).<ref name=Robbins>[Template:Cite book](/wiki/Template:Cite_book)</ref>

Rabies is caused by [*lyssaviruses*](/wiki/Lyssavirus) including: [rabies virus](/wiki/Rabies_virus) and [Australian bat lyssavirus](/wiki/Australian_bat_lyssavirus).[[1]](#cite_note-1) Rabies is spread when an infected animal scratches or bites another animal or human.<ref name=WHO2013/> Saliva from an infected animal can also transmit rabies if the saliva comes into contact with the eyes, mouth, or nose.<ref name=WHO2013/> Globally, dogs are the most common animal involved.<ref name=WHO2013/> More than 99% of rabies cases in countries where [dogs](/wiki/Dog) commonly have the disease are caused by [dog bites](/wiki/Dog_bites).<ref name=Tint2010>[Template:Cite book](/wiki/Template:Cite_book)</ref> In the [Americas](/wiki/Americas), [bat](/wiki/Bat) bites are the most common source of rabies infections in humans, and less than 5% of cases are from dogs.<ref name=WHO2013/><ref name=Tint2010/> Rodents are very rarely infected with rabies.<ref name=Tint2010/> The [rabies virus](/wiki/Rabies_virus) travels to the brain by following the [peripheral nerves](/wiki/Peripheral_nervous_system). The disease can only be diagnosed after the start of symptoms.<ref name=WHO2013/>

Animal control and vaccination programs have decreased the risk of rabies from dogs in a number of regions of the world.<ref name=WHO2013/> Immunizing people before they are exposed is recommended for those who are at high risk. The high-risk group includes people who work with bats or who spend prolonged periods in areas of the world where rabies is common.<ref name=WHO2013/> In people who have been exposed to rabies, the [rabies vaccine](/wiki/Rabies_vaccine) and sometimes rabies [immunoglobulin](/wiki/Immunoglobulin) are effective in preventing the disease if the person receives the treatment before the start of rabies symptoms.<ref name=WHO2013/> Washing bites and scratches for 15 minutes with soap and water, [povidone iodine](/wiki/Povidone_iodine), or detergent may reduce the number of viral particles and may be somewhat effective at preventing transmission.<ref name=WHO2013>[Template:Cite web](/wiki/Template:Cite_web)</ref>[[2]](#cite_note-2) Only five people have survived a rabies infection after showing symptoms, and this was with extensive treatment known as the [Milwaukee protocol](/wiki/Milwaukee_protocol).[[3]](#cite_note-3)[[4]](#cite_note-4) Rabies causes about 24,000 to 60,000 deaths worldwide per year.<ref name=Giesen2015>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>[[5]](#cite_note-5) More than 95% of human deaths caused by rabies occur in [Africa](/wiki/Africa) and [Asia](/wiki/Asia).<ref name=WHO2013/> Rabies is present in more than 150 countries and on all continents but Antarctica.<ref name=WHO2013/> More than 3 billion people live in regions of the world where rabies occurs.<ref name=WHO2013/> A number of countries, including Australia, Canada, Japan, the United States, and Western Europe, do not have rabies among dogs.[[6]](#cite_note-6)[[7]](#cite_note-7) Many small island nations do not have rabies at all.[[8]](#cite_note-8)

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## Signs and symptoms[[edit](/index.php?title=(none)&action=edit&section=1)]

[right|thumb|A person with rabies, 1959](/wiki/File:Rabies_patient.jpg) The [period](/wiki/Incubation_period) between infection and the first [symptoms](/wiki/Influenza-like_illness) (incubation period) is typically 1–3 months in humans.<ref name=Giesen2015/> [Incubation periods](/wiki/Incubation_period) as short as four days and longer than six years have been documented, depending on the location and severity of the contaminated wound and the amount of virus introduced.<ref name=Giesen2015/> Initial signs and symptoms of rabies are often nonspecific such as fever and headache.<ref name=Giesen2015/> As rabies progresses and causes [inflammation of the brain and/or meninges](/wiki/Meningoencephalitis), signs and symptoms can include slight or partial [paralysis](/wiki/Paralysis), [anxiety](/wiki/Anxiety), [insomnia](/wiki/Insomnia), [confusion](/wiki/Confusion), [agitation](/wiki/Wikt:restlessness), abnormal behavior, [paranoia](/wiki/Paranoia), terror, and [hallucinations](/wiki/Hallucination), progressing to [delirium](/wiki/Delirium) and [coma](/wiki/Coma).<ref name=Robbins/><ref name=Giesen2015/> The person may also have hydrophobia.<ref name=WHO2013/>

Death usually occurs 2 to 10 days after first symptoms. Survival is rare once symptoms have presented,<ref name=Giesen2015/> even with the administration of proper and intensive care.[[9]](#cite_note-9) Jeanna Giese, who in 2004 was the first patient treated with the [Milwaukee protocol](/wiki/Milwaukee_protocol),[[10]](#cite_note-10) became the first person ever recorded to have survived rabies without receiving successful [post-exposure prophylaxis](/wiki/Post-exposure_prophylaxis). An [intention-to-treat analysis](/wiki/Intention-to-treat_analysis) has since found this protocol has a survival rate of about 8%.[[11]](#cite_note-11)

### Hydrophobia[[edit](/index.php?title=(none)&action=edit&section=2)]

[thumb|A rabid dog](/wiki/Image:Rabid_dog.jpg) Hydrophobia ("fear of water") is the historic name for rabies.[[12]](#cite_note-12) It refers to a set of symptoms in the later stages of an infection in which the person has difficulty swallowing, shows panic when presented with liquids to drink, and cannot quench his or her thirst. Any mammal infected with the virus may demonstrate hydrophobia.<ref name=NHS/>

Saliva production is greatly increased, and attempts to drink, or even the intention or suggestion of drinking, may cause excruciatingly painful spasms of the muscles in the throat and [larynx](/wiki/Larynx). This can be attributed to the fact that the virus multiplies and assimilates in the [salivary glands](/wiki/Salivary_gland) of the infected animal for the purpose of further transmission through biting. The infected animal's ability to transmit the virus would reduce significantly if it could swallow saliva and water.[[13]](#cite_note-13) Hydrophobia is commonly associated with furious rabies, which affects 80% of the infected people. The remaining 20% may experience a paralytic form of rabies that is marked by muscle weakness, loss of sensation, and paralysis; this form of rabies does not usually cause fear of water.<ref name=NHS>[Template:Cite web](/wiki/Template:Cite_web)</ref>

## Cause[[edit](/index.php?title=(none)&action=edit&section=3)]

[thumb|](/wiki/File:Rabies_Virus_EM_PHIL_1876.JPG)[TEM](/wiki/Transmission_electron_microscopy) [micrograph](/wiki/Micrograph) with numerous rabies [virions](/wiki/Virion) (small, dark grey, rodlike particles) and [Negri bodies](/wiki/Negri_bodies) (the larger [pathognomonic](/wiki/Pathognomonic) cellular inclusions of rabies infection) Rabies is caused by a number of [*lyssaviruses*](/wiki/Lyssavirus) including: [rabies virus](/wiki/Rabies_virus) and [Australian bat lyssavirus](/wiki/Australian_bat_lyssavirus).[[1]](#cite_note-1) The rabies virus is the [type species](/wiki/Type_species) of the Lyssavirus [genus](/wiki/Genus), in the family[*Rhabdoviridae*](/wiki/Rhabdoviridae), order [*Mononegavirales*](/wiki/Mononegavirales). Lyssaviruses have helical symmetry, with a length of about 180 [nm](/wiki/Nanometre) and a cross-section of about 75 nm.<ref name=Sherris>[Template:Cite book](/wiki/Template:Cite_book)</ref> These viruses are [enveloped](/wiki/Viral_envelope) and have a single-stranded [RNA](/wiki/RNA) genome with [negative sense](/wiki/Negative-sense#Negative-sense). The genetic information is packed as a [ribonucleoprotein](/wiki/Ribonucleoprotein) complex in which RNA is tightly bound by the viral nucleoprotein. The [RNA genome](/wiki/RNA_genome) of the virus encodes five genes whose order is highly conserved: nucleoprotein (N), phosphoprotein (P), matrix protein (M), glycoprotein (G), and the viral RNA polymerase (L).[[14]](#cite_note-14) Once within a muscle or nerve cell, the virus undergoes replication. The trimeric spikes on the exterior of the membrane of the virus interact with a specific cell receptor, the most likely one being the [acetylcholine](/wiki/Acetylcholine) receptor, [acetyl](/wiki/Acetyl). The cellular membrane pinches in a procession known as [pinocytosis](/wiki/Pinocytosis) and allows entry of the virus into the cell by way of an [endosome](/wiki/Endosome). The virus then uses the acidic environment, which is necessary, of that endosome and binds to its membrane simultaneously, releasing its five proteins and single strand RNA into the cytoplasm.[[15]](#cite_note-15) The L protein then transcribes five mRNA strands and a positive strand of RNA all from the original negative strand RNA using free nucleotides in the cytoplasm. These five mRNA strands are then translated into their corresponding proteins (P, L, N, G and M proteins) at free ribosomes in the cytoplasm. Some proteins require post-translative modifications. For example, the G protein travels through the rough [endoplasmic reticulum](/wiki/Endoplasmic_reticulum), where it undergoes further folding, and is then transported to the [Golgi apparatus](/wiki/Golgi_apparatus), where a sugar group is added to it ([glycosylation](/wiki/Glycosylation)).[[15]](#cite_note-15) Where there are enough proteins, the viral polymerase will begin to synthesize new negative strands of RNA from the template of the positive strand RNA. These negative strands will then form complexes with the N, P, L and M proteins and then travel to the inner membrane of the cell, where a G protein has embedded itself in the membrane. The G protein then coils around the N-P-L-M complex of proteins taking some of the host cell membrane with it, which will form the new outer envelope of the virus particle. The virus then buds from the cell.[[15]](#cite_note-15) From the point of entry, the virus is [neurotropic](/wiki/Neurotropic_virus), traveling quickly along the neural pathways into the [central nervous system](/wiki/Central_nervous_system). The virus usually first infects muscle cells close to the site of infection, where they are able to replicate without being 'noticed' by the host's immune system. Once enough virus has been replicated, they begin to bind to acetyl choline receptors (p75NR) at the neuromuscular junction.[[16]](#cite_note-16) The virus then travels through the nerve cell axon via retrograde transport, as its P protein interacts with dynein, a protein present in the cytoplasm of nerve cells. Once the virus reaches the cell body it travels rapidly to the Central Nervous System (CNS), replicating in motor neurons and eventually reaching the brain.<ref name=Robbins/> After the brain is infected, the virus travels centrifugally to the peripheral and autonomic nervous systems, eventually migrating to the salivary glands, where it is ready to be transmitted to the next host.

### Transmission[[edit](/index.php?title=(none)&action=edit&section=4)]

[Template:Main article](/wiki/Template:Main_article)

All warm-blooded species, including humans, may become infected with the rabies virus and develop symptoms. [Birds](/wiki/Bird) were first artificially infected with rabies in 1884; however, infected birds are largely if not wholly asymptomatic, and recover.<ref name=serological>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Other bird species have been known to develop rabies [antibodies](/wiki/Antibody), a sign of infection, after feeding on rabies-infected mammals.[[17]](#cite_note-17)<ref name=Owls>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

The virus has also adapted to grow in cells of [poikilothermic](/wiki/Poikilotherm) ("cold-blooded") vertebrates.[[18]](#cite_note-18)[[19]](#cite_note-19) Most animals can be infected by the virus and can transmit the disease to humans. Infected [bats](/wiki/Bat),[[20]](#cite_note-20)[[21]](#cite_note-21) [monkeys](/wiki/Monkey), [raccoons](/wiki/Raccoon), [foxes](/wiki/Fox), [skunks](/wiki/Skunk), [cattle](/wiki/Cattle), [wolves](/wiki/Wolf), [coyotes](/wiki/Coyotes), [dogs](/wiki/Dog), [mongooses](/wiki/Mongoose) (normally yellow mongoose)[[22]](#cite_note-22) and [cats](/wiki/Cat) present the greatest risk to humans.

Rabies may also spread through exposure to infected [bears](/wiki/Bears), [domestic farm animals](/wiki/Livestock), [groundhogs](/wiki/Groundhog), [weasels](/wiki/Weasel), and other [wild carnivorans](/wiki/Carnivora). [Lagomorphs](/wiki/Lagomorphs), such as [hares](/wiki/Hare) and [rabbits](/wiki/Rabbit), and small [rodents](/wiki/Rodent) such as [chipmunks](/wiki/Chipmunk), [gerbils](/wiki/Gerbil), [guinea pigs](/wiki/Guinea_pig), [hamsters](/wiki/Hamster), [mice](/wiki/Mice), [rats](/wiki/Rat), and [squirrels](/wiki/Squirrel), are almost never found to be infected with rabies and are not known to transmit rabies to humans.[[23]](#cite_note-23) Bites from mice, rats, or squirrels rarely require rabies prevention because these rodents are typically killed by any encounter with a larger, rabid animal, and would, therefore, not be carriers.[[24]](#cite_note-24) The [Virginia opossum](/wiki/Virginia_opossum) is resistant but not immune to rabies.[[25]](#cite_note-25) The virus is usually present in the nerves and [saliva](/wiki/Saliva) of a symptomatic rabid animal.[[26]](#cite_note-26)[[27]](#cite_note-27) The route of [infection](/wiki/Infection) is usually, but not always, by a bite. In many cases, the infected animal is exceptionally aggressive, may attack without provocation, and exhibits otherwise uncharacteristic behavior.[[28]](#cite_note-28) This is an example of a viral pathogen [modifying the behavior of its host](/wiki/Behavior-altering_parasites_and_parasitoids) to facilitate its transmission to other hosts.

Transmission between humans is extremely rare. A few cases have been recorded through [transplant surgery](/wiki/Organ_transplant).[[29]](#cite_note-29) After a typical human infection by bite, the virus enters the [peripheral nervous system](/wiki/Peripheral_nervous_system). It then travels along the [afferent nerves](/wiki/Afferent_nerve_fiber) toward the [central nervous system](/wiki/Central_nervous_system).[[30]](#cite_note-30) During this phase, the virus cannot be easily detected within the host, and vaccination may still confer cell-mediated immunity to prevent symptomatic rabies. When the virus reaches the [brain](/wiki/Brain), it rapidly causes [encephalitis](/wiki/Encephalitis), the prodromal phase, which is the beginning of the symptoms. Once the patient becomes symptomatic, treatment is almost never effective and mortality is over 99%. Rabies may also inflame the [spinal cord](/wiki/Spinal_cord), producing [transverse myelitis](/wiki/Transverse_myelitis).[[31]](#cite_note-31)[[32]](#cite_note-32)

## Diagnosis[[edit](/index.php?title=(none)&action=edit&section=5)]

Rabies can be difficult to diagnose, because, in the early stages, it is easily confused with other diseases or with aggressiveness.<ref name=Merck>[Template:Cite book](/wiki/Template:Cite_book)</ref> The [reference method](/wiki/Gold_standard_(test)) for diagnosing rabies is the fluorescent antibody test (FAT), an [immunohistochemistry](/wiki/Immunohistochemistry) procedure, which is recommended by the [World Health Organization](/wiki/World_Health_Organization) (WHO).[[33]](#cite_note-33) The FAT relies on the ability of a detector molecule (usually fluorescein isothiocyanate) coupled with a rabies-specific antibody, forming a conjugate, to bind to and allow the visualisation of rabies antigen using fluorescent microscopy techniques. Microscopic analysis of samples is the only direct method that allows for the identification of rabies virus-specific antigen in a short time and at a reduced cost, irrespective of geographical origin and status of the host. It has to be regarded as the first step in diagnostic procedures for all laboratories. Autolysed samples can, however, reduce the sensitivity and specificity of the FAT.[[34]](#cite_note-34) The [RT PCR](/wiki/Reverse_transcription_polymerase_chain_reaction) assays proved to be a sensitive and specific tool for routine diagnostic purposes,[[35]](#cite_note-35) particularly in decomposed samples[[36]](#cite_note-36) or archival specimens.[[37]](#cite_note-37) The diagnosis can be reliably made from brain samples taken after death. The diagnosis can also be made from saliva, urine, and cerebrospinal fluid samples, but this is not as [sensitive](/wiki/Sensitivity_and_specificity) and reliable as brain samples.[[34]](#cite_note-34) Cerebral inclusion bodies called [Negri bodies](/wiki/Negri_bodies) are 100% diagnostic for rabies infection but are found in only about 80% of cases.<ref name=Sherris/> If possible, the animal from which the bite was received should also be examined for rabies.[[38]](#cite_note-38) The [differential diagnosis](/wiki/Differential_diagnosis) in a case of suspected human rabies may initially include any cause of [encephalitis](/wiki/Encephalitis), in particular infection with viruses such as [herpesviruses](/wiki/Herpesviridae), [enteroviruses](/wiki/Enteroviruses), and [arboviruses](/wiki/Arboviruses) such as [West Nile virus](/wiki/West_Nile_virus). The most important viruses to rule out are [herpes simplex virus](/wiki/Herpes_simplex_virus) type one, [varicella zoster virus](/wiki/Varicella_zoster_virus), and (less commonly) enteroviruses, including [coxsackieviruses](/wiki/Coxsackie_virus), [echoviruses](/wiki/Echovirus), [polioviruses](/wiki/Poliovirus), and human [enteroviruses](/wiki/Enterovirus) 68 to 71.[[39]](#cite_note-39) New causes of viral encephalitis are also possible, as was evidenced by the 1999 outbreak in Malaysia of 300 cases of encephalitis with a mortality rate of 40% caused by [Nipah virus](/wiki/Nipah_virus), a newly recognized [paramyxovirus](/wiki/Paramyxovirus).[[40]](#cite_note-40) Likewise, well-known viruses may be introduced into new locales, as is illustrated by the recent outbreak of encephalitis due to West Nile virus in the eastern United States.[[41]](#cite_note-41) Epidemiologic factors, such as season, geographic location, and the patient's age, travel history, and possible exposure to bites, rodents, and ticks, may help direct the diagnosis.

Cheaper rabies diagnosis will become possible for low-income settings: accurate rabies diagnosis can be done at a tenth of the cost of traditional testing using basic [light microscopy](/wiki/Light_microscopy#Optical_microscopy) techniques.[[42]](#cite_note-42)

## Prevention[[edit](/index.php?title=(none)&action=edit&section=6)]

[Template:Main article](/wiki/Template:Main_article) Almost all human cases of rabies were fatal until a vaccine was developed in 1885 by [Louis Pasteur](/wiki/Louis_Pasteur) and [Émile Roux](/wiki/Émile_Roux). Their original vaccine was harvested from infected rabbits, from which the virus in the nerve tissue was weakened by allowing it to dry for five to ten days.[[43]](#cite_note-43) Similar nerve tissue-derived vaccines are still used in some countries, as they are much cheaper than modern cell culture vaccines.[[44]](#cite_note-44) The human diploid cell rabies vaccine was started in 1967. Less expensive purified chicken embryo cell vaccine and purified [vero cell](/wiki/Vero_cell) rabies vaccine are now available.[[38]](#cite_note-38) A [recombinant vaccine](/wiki/Recombinant_vaccine) called V-RG has been used in Belgium, France, Germany, and the United States to prevent outbreaks of rabies in undomesticated animals.[[45]](#cite_note-45) Immunization before exposure has been used in both human and nonhuman populations, where, as in many jurisdictions, domesticated animals are required to be vaccinated.[[46]](#cite_note-46) The number of recorded human deaths from rabies in the United States has dropped from 100 or more annually in the early 20th century to one or two per year due to widespread vaccination of domestic dogs and cats and the development of human vaccines and immunoglobulin treatments. Most deaths now result from bat bites, which may go unnoticed by the victim and hence untreated.[[47]](#cite_note-47) The Missouri Department of Health and Senior Services Communicable Disease Surveillance 2007 Annual Report states the following can help reduce the risk of contracting rabies:[[48]](#cite_note-48)

* Vaccinating dogs, cats, and ferrets against rabies
* Keeping pets under supervision
* Not handling wild animals or strays
* Contacting an animal control officer upon observing a wild animal or a stray, especially if the animal is acting strangely
* If bitten by an animal, washing the wound with soap and water for 10 to 15 minutes and contacting a healthcare provider to determine if post-exposure prophylaxis is required

September 28 is [World Rabies Day](/wiki/World_Rabies_Day), which promotes the information, prevention, and elimination of the disease.[[49]](#cite_note-49)

## Treatment[[edit](/index.php?title=(none)&action=edit&section=7)]

[Treatment after exposure](/wiki/Postexposure_prophylaxis) can prevent the disease if administered promptly, generally within 10 days of infection.<ref name=Sherris/> Thoroughly washing the wound as soon as possible with soap and water for approximately five minutes is effective in reducing the number of viral particles.[[50]](#cite_note-50) [Povidone-iodine](/wiki/Povidone-iodine) or alcohol is then recommended to reduce the virus further.[[51]](#cite_note-51) In the US, the [Centers for Disease Control and Prevention](/wiki/Centers_for_Disease_Control_and_Prevention) recommends people receive one dose of human rabies [immunoglobulin](/wiki/Immunoglobulin) (HRIG) and four doses of rabies vaccine over a 14-day period.[[52]](#cite_note-52) The immunoglobulin dose should not exceed 20 units per kilogram body weight. HRIG is expensive and constitutes most of the cost of postexposure treatment, ranging as high as several thousand dollars.[[53]](#cite_note-53) As much as possible of this dose should be injected around the bites, with the remainder being given by deep intramuscular injection at a site distant from the vaccination site.[[15]](#cite_note-15) The first dose of rabies vaccine is given as soon as possible after exposure, with additional doses on days three, seven and 14 after the first. Patients who have previously received pre-exposure vaccination do not receive the immunoglobulin, only the postexposure vaccinations on days 0 and 3.[[54]](#cite_note-54) The pain and side effects of modern cell-based vaccines are similar to flu shots. The old nerve-tissue-based vaccinations that require multiple painful injections into the abdomen with a large needle are inexpensive, but are being phased out and replaced by affordable World Health Organization intradermal-vaccination regimens.[[38]](#cite_note-38) Intramuscular vaccination should be given into the [deltoid](/wiki/Deltoid_muscle), not the [gluteal area](/wiki/Gluteal_muscles), which has been associated with vaccination failure due to injection into fat rather than muscle. In infants, the lateral thigh is recommended.[[55]](#cite_note-55) Awakening to find a bat in the room, or finding a bat in the room of a previously unattended child or mentally disabled or intoxicated person, is regarded as an indication for [post-exposure prophylaxis](/wiki/Post-exposure_prophylaxis) (PEP). The recommendation for the precautionary use of PEP in occult bat encounters where no contact is recognized has been questioned in the medical literature, based on a cost-benefit analysis.[[56]](#cite_note-56) However, a 2002 study has supported the protocol of precautionary administering of PEP where a child or mentally compromised individual has been alone with a bat, especially in sleep areas, where a bite or exposure may occur without the victim being aware.[[57]](#cite_note-57) Begun with little or no delay, PEP is 100% effective against rabies.[[10]](#cite_note-10) In the case in which there has been a significant delay in administering PEP, the treatment should be administered regardless, as it may still be effective.[[15]](#cite_note-15)

### Induced coma[[edit](/index.php?title=(none)&action=edit&section=8)]

[Template:See also](/wiki/Template:See_also) In 2004, American teenager Jeanna Giese survived an infection of rabies unvaccinated. She was placed into an [induced coma](/wiki/Induced_coma) upon onset of symptoms and given [ketamine](/wiki/Ketamine), [midazolam](/wiki/Midazolam), [ribavirin](/wiki/Ribavirin), and [amantadine](/wiki/Amantadine). Her doctors administered treatment based on the hypothesis that detrimental effects of rabies were caused by temporary dysfunctions in the brain and could be avoided by inducing a temporary partial halt in brain function that would protect the brain from damage while giving the immune system time to defeat the virus. After 31 days of isolation and 76 days of hospitalization, Giese was released from the hospital.[[58]](#cite_note-58) She survived with all higher level brain functions, but an inability to walk and balance.[[59]](#cite_note-59) On a podcast of NPR's [*Radiolab*](/wiki/Radiolab), Giese recounted, "I had to learn how to stand and then to walk, turn around, move my toes. I was really, after rabies, a new born baby who couldn't do anything. I had to relearn that all...mentally I knew how to do stuff but my body wouldn't cooperate with what I wanted it to do. It definitely took a toll on me psychologically. You know I'm still recovering. I'm not completely back. Stuff like balance and, um, I can't run normally."[[60]](#cite_note-60) Giese's treatment regimen became known as the "Milwaukee protocol", which has since undergone revision with the second version omitting the use of [ribavirin](/wiki/Ribavirin). Two of 25 patients survived when treated under the first protocol. A further 10 patients have been treated under the revised protocol, with a further two survivors.[[11]](#cite_note-11) The anesthetic drug [ketamine](/wiki/Ketamine) has shown the potential for rabies virus inhibition in rats,[[61]](#cite_note-61) and is used as part of the Milwaukee protocol.

On June 12, 2011, Precious Reynolds, an eight-year-old girl from [Humboldt County, California](/wiki/Humboldt_County,_California), became the third reported person in the [United States](/wiki/United_States) to have recovered from rabies without receiving PEP.[[62]](#cite_note-62)

## Prognosis[[edit](/index.php?title=(none)&action=edit&section=9)]

In unvaccinated humans, rabies is almost always fatal after [neurological](/wiki/Neurological) symptoms have developed.[[63]](#cite_note-63) [Vaccination](/wiki/Vaccination) after exposure, PEP, is highly successful in preventing the disease if administered promptly, in general within 6 days of infection. Begun with little or no delay, PEP is 100% effective against rabies.[[10]](#cite_note-10) In the case of significant delay in administering PEP, the treatment still has a chance of success.[[15]](#cite_note-15) 5 of the first 43 patients (12%) treated with the [Milwaukee protocol](/wiki/Milwaukee_protocol) survived, and those receiving treatment survived longer than those not receiving the treatment.[[64]](#cite_note-64)

## Epidemiology[[edit](/index.php?title=(none)&action=edit&section=10)]

[Template:Main article](/wiki/Template:Main_article) [[File:Rabies Free Countries Sourced 2010.svg|thumb|300px|Rabies-free countries (in green) [Template:As of](/wiki/Template:As_of). [Template:Farbindex](/wiki/Template:Farbindex)  
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In 2010, an estimated 26,000 people died from rabies, down from 54,000 in 1990.<ref name=Loz2012>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> The majority of the deaths occurred in Asia and Africa.[[63]](#cite_note-63) [India](/wiki/India) has the highest rate of human rabies in the world, primarily because of stray dogs,[[65]](#cite_note-65) whose number has greatly increased since a 2001 law forbade the killing of dogs.[[66]](#cite_note-66) Effective control and treatment of rabies in India is also hindered by a form of [mass hysteria](/wiki/Mass_hysteria) known as [puppy pregnancy syndrome](/wiki/Puppy_pregnancy_syndrome) (PPS). Dog bite victims with PPS (both male and female) become convinced that puppies are growing inside them, and often seek help from faith healers rather than from conventional medical services. In cases where the bite was from a rabid dog, this decision can prove fatal. Dr. Nitai Kishore Marik, former district medical officer of West Midnapur, states "I have seen scores of cases of rabies that reached our hospitals very late because of the intervention of faith healers. We could not save those lives."[[67]](#cite_note-67) An estimated 20,000 people die every year from rabies in India — more than a third of the global toll.[[66]](#cite_note-66) [Template:As of](/wiki/Template:As_of), China had the second-highest number of cases (approximately 6,000), followed by the Democratic Republic of the Congo (5,600).[[68]](#cite_note-68) The rabies virus survives in widespread, varied, rural animal reservoirs. Despite Australia's official rabies-free status,[[69]](#cite_note-69) [Australian bat lyssavirus](/wiki/Australian_bat_lyssavirus) (ABLV), discovered in 1996, is a strain of rabies prevalent in native bat populations. There have been three human cases of ABLV in Australia, all of them fatal.

In Asia and in parts of the Americas and Africa, dogs remain the principal host. Mandatory vaccination of animals is less effective in rural areas. Especially in developing countries, pets may not be privately kept and their destruction may be unacceptable. Oral vaccines can be safely distributed in baits, a practice that has successfully reduced rabies in rural areas of [Canada](/wiki/Canada), [France](/wiki/France), and the [United States](/wiki/United_States). In [Montréal](/wiki/Montréal), Quebec, Canada, baits are successfully used on raccoons in the Mont-Royal Park area. Vaccination campaigns may be expensive, and cost-benefit analysis suggests baits may be a cost-effective method of control.[[70]](#cite_note-70) In [Ontario](/wiki/Ontario), a dramatic drop in rabies was recorded when an aerial bait-vaccination campaign was launched.<ref name=Grambo>[Template:Cite book](/wiki/Template:Cite_book)</ref>

Rabies is common among wild animals in the US. [Bats](/wiki/Bat), [raccoons](/wiki/Raccoon), [skunks](/wiki/Skunk) and [foxes](/wiki/Fox) account for almost all reported cases (98% in 2009). Rabid bats are found in all 48 contiguous states. Other reservoirs are more limited geographically; for example, the raccoon rabies virus variant is only found in a relatively narrow band along the East Coast. Due to a high public awareness of the virus, efforts at vaccination of domestic animals and curtailment of feral populations, and availability of [postexposure prophylaxis](/wiki/Postexposure_prophylaxis), incidents of rabies in humans are very rare. A total of 49 cases of the disease was reported in the country between 1995 and 2011; of these, 11 are thought to have been acquired abroad. Almost all domestically acquired cases are attributed to bat bites.[[71]](#cite_note-71) In [Switzerland](/wiki/Switzerland), the disease has been virtually eradicated after scientists placed chicken heads laced with live attenuated vaccine in the [Swiss Alps](/wiki/Swiss_Alps).[[72]](#cite_note-72) The foxes of Switzerland, proven to be the main source of rabies in the country, ate the chicken heads and immunized themselves.[[72]](#cite_note-72) [Italy](/wiki/Italy), after being declared rabies-free from 1997 to 2008, has witnessed a reemergence of the disease in wild animals in the [Triveneto](/wiki/Triveneto) regions ([Trentino-Alto Adige/Südtirol](/wiki/Trentino-Alto_Adige/Südtirol), [Veneto](/wiki/Veneto) and [Friuli-Venezia Giulia](/wiki/Friuli-Venezia_Giulia)), due to the spreading of an epidemic in the [Balkans](/wiki/Balkans) that hit [Austria](/wiki/Austria) too. An extensive wild animals vaccination campaign eradicated the virus from Italy again, and it regained the rabies-free country status in 2013, the last reported case of rabies being reported in a red fox in early 2011.[[73]](#cite_note-73)

## Research[[edit](/index.php?title=(none)&action=edit&section=14)]

Rabies has the advantage over other [pseudotyping](/wiki/Pseudotyping) methods for gene delivery in that the cell-targeting ([tissue tropism](/wiki/Tissue_tropism)) is more specific for difficult-to-reach sites, such as the [central nervous system](/wiki/Central_nervous_system) without invasive delivery methods, as well as being capable of [retrograde tracing](/wiki/Retrograde_tracing) (i.e., going against the flow of information at [synapses](/wiki/Synapses)) in neuronal circuits.[[82]](#cite_note-82) Recent evidence indicates artificially increasing the permeability of the [blood–brain barrier](/wiki/Blood–brain_barrier), which normally does not allow most immune cells across, promotes viral clearance.[[83]](#cite_note-83)[[84]](#cite_note-84)

## See also[[edit](/index.php?title=(none)&action=edit&section=15)]

[Template:Portal](/wiki/Template:Portal)

* [Global Alliance for Rabies Control](/wiki/Global_Alliance_for_Rabies_Control)
* [Neglected tropical diseases](/wiki/Neglected_tropical_diseases)
* [Rabies in popular culture](/wiki/Rabies_in_popular_culture)
* [World Rabies Day](/wiki/World_Rabies_Day)

## References[[edit](/index.php?title=(none)&action=edit&section=16)]

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## Further reading[[edit](/index.php?title=(none)&action=edit&section=17)]

* [Template:Cite book](/wiki/Template:Cite_book)
* [Template:Cite book](/wiki/Template:Cite_book)
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* [Template:Cite book](/wiki/Template:Cite_book)
* [Template:Cite journal](/wiki/Template:Cite_journal)

## External links[[edit](/index.php?title=(none)&action=edit&section=18)]

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* [Template:DMOZ](/wiki/Template:DMOZ)
* [Virus Pathogen Database and Analysis Resource (ViPR): Rhabdoviridae](http://www.viprbrc.org/brc/home.do?decorator=rhabdo)
* [World Rabies Day](http://www.worldrabiesday.org/)
* [OIE's Rabies Portal](http://www.oie.int/en/animal-health-in-the-world/rabies-portal/)
* [Aerophobia and Hydrophobia in Rabies Videos](http://www.doctorshangout.com/forum/topics/videos-of-aerophobia-and)
* [Template:Cite web](/wiki/Template:Cite_web)

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[Category:Cat diseases](/wiki/Category:Cat_diseases) [Category:Dog diseases](/wiki/Category:Dog_diseases) [Category:Wildlife diseases](/wiki/Category:Wildlife_diseases) [Category:Neurological disorders](/wiki/Category:Neurological_disorders) [Category:Rabies](/wiki/Category:Rabies) [Category:Rodent-carried diseases](/wiki/Category:Rodent-carried_diseases) [Category:Viral encephalitis](/wiki/Category:Viral_encephalitis) [Category:Viral infections of the central nervous system](/wiki/Category:Viral_infections_of_the_central_nervous_system) [Category:Zoonoses](/wiki/Category:Zoonoses) [Category:RTT](/wiki/Category:RTT)