The global fight against rabies

Some countries such as the Philippines are taking valuable steps towards eliminating cases of human rabies but others, including India and Pakistan—which have well over a third of the global burden of the disease—could do far better. Talha Burki reports on the eve of World Rabies Day.

Sept 28 marks the second annual World Rabies Day. Spearheaded by the Alliance for Rabies Control, the event aims to draw attention to a long neglected disease.

Rabies kills at least 55 000 people every year worldwide (under-reporting and misdiagnosis may mean that the actual figure is higher). In Asia, the death toll numbers around 30 000. Deaths in Africa are trickier to map. In North Africa, the situation is under control; Libya has declared itself free of canine-rabies and, according to François Meslin—senior advisor on zoonotic diseases at WHO—Morocco and Tunisia could soon be in a similar position. South Africa and Tanzania are also well placed to eradicate the disease. But for vast swathes of the continent, information is scant. "We know rabies is there", points out Charles Rupprecht at the US Centers for Disease Control and Prevention, Atlanta, Georgia. "We know it's very intense, but we don't know how many cases, or where these cases are concentrated."

Meslin has helped develop a mathematical model to estimate the burden of rabies. It points to at least 24 000 deaths in Africa. "There were many hundreds of cases in Addis Ababa", Meslin told *The Lancet*. "If the model holds true for the rest of Ethiopia, then we're looking at 5000–10 000 cases, and this may even be an underestimate." Rabies is almost invariably fatal, a notoriously unpleasant death.

"We know all we need to know about rabies", affirms Henry Wilde, from the Queen Saovabha Memorial Institute in Bangkok, Thailand—WHO Collaborating Centre for Research on Rabies Pathogenesis and Treatment. WHO has endorsed several vaccines and issued directives for treating potentially dangerous animal bites. If followed correctly, these post-exposure prophylaxis (PEP) guidelines are virtually 100% effective—PEP is thought to prevent around 280 000 deaths per year. "The guidelines are very reasonable, even for developing nations", says Wilde. But more than any other disease, rabies requires a nationally coordinated response.

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Human rabies vaccines need multiple applications, so it is not usually practical for developing populations to vaccinate the entire population. Hence it is crucial that canine-rabies is controlled—dog bites account for over 99% of human rabies. For this to happen, 75% of dogs must be vaccinated. Malaysia is an excellent example, says Wilde, of a country that eliminated rabies by concerted culling, neutering, and vaccination of the dog population.

This kind of response is impossible in places without a working infrastructure, such as parts of sub-Saharan Africa. But this is not the case in the Indian sub-continent. "Pakistan has good roads, universities, and people", said Wilde. "They can build an atomic bomb, yet they can't get rid of rabies."

Pakistan has an estimated 2000–5000 cases every year. "The government isn't interested", asserts Naseem Salahaddin, infectious disease specialist at Liaquat University, Karachi. There has never been an epidemiological study of the disease, she told *The Lancet*. She added that medical staff are inadequately trained and infectious disease specialists are in short supply. PEP's first step specifies washing the wound with soap and water, a simple measure that can reduce rabies incidence by up to 65%. Wilde notes that in Thailand, which has almost eliminated rabies, district nurses spend 20 min washing dog-bite injuries. "The dog-bite management centres I've visited in India and Pakistan don't spend even one second washing the wound", stated Wilde.

Furthermore, Pakistan is one of five countries that have not switched to WHO recommended cell-culture vaccines (the others are Burma, Bangladesh, Peru, and Argentina). Pakistan continues to use domestically

Alliance for Rabies Control

A parade in Bicol, Philippines, on World Rabies Day, 2007

Reuters

75% of the dog population should be vaccinated against rabies

produced nerve-tissue vaccine. The most recent meeting of WHO Expert Consultation on Rabies issued a recommendation that these vaccines be discontinued. Nerve tissue vaccines, they added, "have been found to be reactogenic and some are of low immunogenicity". Shahab Khazi at Pakistan's National Institute of Health, agrees. "We know this vaccine is obsolete. We've tried in the past to switch, and we hope to make the change soon."

Across the border, in India, there are 20 000 cases of human rabies every year. It is the highest incidence in the world (as with Pakistan, rabies is not a reportable disease in India, so exact statistics are hard to find). Two in five people bitten by dogs will not seek treatment. Management for the disease is devolved to the Animal Welfare Board, under the auspices of the Ministry of Environment—in most other countries, rabies is the responsibility of the Ministry of Health.

Experts doubt whether veterinary staff in India have the experience and knowledge to do mass vaccinations of dogs, and question whether the official figure of 30 million animals is an underestimate. PEP guidelines are rarely followed, even in private clinics. "The outlook is terrible, we're failing", says Wilde. Government involvement is minimal. Non-governmental organisations work with local communities to combat rabies, notes Meslin, but he admits that this is not a sustainable solution.

Low literacy rates and ignorance compound the problem. 61% of the Indian populace can read, in Pakistan the figure is 50%. But rabies in India and elsewhere is concentrated among the poor people in rural areas—a demographic where illiteracy is higher than the national average. These people are often ignored by the authorities; experts estimate that 2·5 million applications of PEP have been misdirected towards better-off Indians in low-risk areas—a worrying trend given that India faces an annual deficit of 12 million doses of vaccine.

On the surface, the situation in China seems equally dispiriting—over 3300 cases of human rabies last year—a sharp increase from the 159 cases in 1996. The epidemic is concentrated in south eastern provinces. An explosion in the dog population is to blame, alongside a loosening of the previously strict animal control policies. Nevertheless, Meslin is optimistic. "China can reverse the tide", he says. "They have the technology, the knowledge, and the resources; they are producing a lot of vaccine, and they've identified the hotspots."

China has been accused of responding to rabies in a heavy-handed and indiscriminate manner. In 2006, *The Lancet Infectious Diseases* reported a "brutal cull of 50 000 dogs in several southern Chinese provinces". Dogs were taken from their owners and clubbed to death. WHO was moved to point out that such actions were unlikely "to have a significant impact on the spread of rabies".

Even in countries without China's resources much can be done, believes Debbie Briggs of Kansas State University, USA. She cites the Philippines: "they put rabies on the national curriculum, they taught children about how to interact with dogs, and in those parts of the country we saw a drop in rabies of 50%". Roughly half the victims of dog bites are children; they tend to be bitten on high-risk areas such as the head.

There are encouraging developments. Rupprecht is working with China on a single-dose vaccine for humans and animals, if successful this would greatly reduce the economic burden of the disease. The Bill & Melinda Gates Foundation recently agreed to include rabies in its portfolio. Funds have been earmarked but not yet disbursed.

Last year, WHO compiled a shortlist of ten countries ready for a comprehensive antirabies programme—countries (such as the Philippines) in which the total eradication of rabies is a real possibility. In Latin America, thanks largely to the efforts of the Pan-American Health Organisation, rabies is under control. Mexico is free of human rabies. Across the region, there are around 50 cases every year, half of which are transmitted by bats. Victims are from small localised communities: Peruvian miners, for example, are occasionally bitten by subterranean bats. Proofing houses against bats, and educating and vaccinating the populace are the next steps, says Meslin.

Meslin describes the situation in sub-Saharan Africa as "stagnant", and rabies has re-emerged in Vietnam. Briggs talks of fake vaccines being circulated in India, and of a worsening situation in Uzbekistan and Tajikistan—Tajikistan spends merely $8000 a year on preventive measures. Vietnam, China, and Pakistan all charge for cell-culture vaccines, a daunting prospect for most of those affected by rabies. The incidence in India and Pakistan remains stubbornly and needlessly high—well over a third of the global burden. "At the very least, the Pakistani Government should make a decision to identify the disease as a priority", suggests Salahaddin. Advice that is equally applicable to India.

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