Vulture culture at threat from diclofenac

VULTURES (Accipitridae), the only known obligate scavengers, have been in severe decline across the Asian subcontinent for the past 20 years. Due to the loss of population (97.5 per cent to 99 per cent depending on the species), three vultures of the genus Gyps are on the critically endangered International Union for Conservation of Nature (IUCN) list, despite having been the most abundant large raptors in the world until the early 1990s. They are at risk of global extinction, being extremely difficult to breed in captivity (they mate for life and produce only one chick per year).

Research revealed the main cause of the vulture population collapse was the veterinary use of NSAID diclofenac on livestock. Vultures are exposed to the drug when scavenging on animals treated in the few days preceding death. Following exposure to diclofenac-contaminated tissues (or some other NSAIDs, Table 1), vultures develop kidney failure and reduced excretion of uric acid. This leads to extensive deposition of urate crystals in tissues (vesical gout) and death in a couple of days. The toxic dose in vultures is below the recommended dose to treat livestock (the LD50 in vultures is 0.225mg/kg, while cattle and other animals are treated with doses of 2.5mg/kg). As hundreds of vultures can feed from a single carcass, entire populations can be wiped out by only very small numbers of contaminated carcasses. Population modelling has shown rates of diclofenac contamination as low as 0.13 per cent to 0.75 per cent of carcasses is sufficient to account for the population collapse.

Obligate scavengers’ decline has major ecological (and socio-economic) consequences, as wild and domestic animal carcasses persist longer in the environment, thus increasing disease transmission in livestock, and also allowing increased carrion contact with facultative scavengers (raptors, scavenging storks, corvids, and mammalian scavengers such as canids and rats). Less specialised scavengers visit carcasses only after highly specialised ones have done so (Figure 1), thus vulture declines allow mammalian scavenger species to increase in numbers.

Repercussions

The decline of vultures may also affect disease transmission, as vultures are resistant to many bacterial toxins and organisms in decomposing tissue and can reduce the chance of diffusion of many infectious diseases by rapidly disposing of a carcass (for example anthrax, bubonic plague, tuberculosis). Vulture absence also increases close encounters, usually aggressive in nature, between terrestrial scavengers (dogs in India, hyenas and jackals in Africa), potential hosts of infectious agents able to infect other wild and domesticated species (rabies and distemper). All this poses a threat to human health – a 2008 study estimated that in India, concurrently with the vulture decline, there had been an increase in the feral dog population of at least 5.5 million dogs, resulting in more than 38.5 million additional bites and 47,300 extra deaths from rabies.

One study put the resulting cost to the Indian economy at £20bn. Other zoonotic diseases may also be spread by increased numbers of rats.

Diclofenac has been banned in India, Nepal and Pakistan since 2006, reducing the contamination of cattle carcasses to around 6.5 per cent in 2007 to 2008. Vulture numbers have stabilised or slightly increased throughout the region, although scavenging populations are very low. Bangladesh followed, banning diclofenac in 2010. Unfortunately, misuse of human forms of diclofenac in the veterinary sector still poses a threat to vultures, together with widespread use of other toxic or untested veterinary drugs in South Asia. Considerable efforts have been made to prevent veterinary diclofenac from being licensed (or to ban its use) in Africa, where large populations of vultures still exist. At the moment, diclofenac (already out of patent) is manufactured by a South American pharmaceutical company that in 2008 was exporting the drug to 15 African countries.

Of the nine different existing vulture species in southern Africa, seven are considered threatened. In particular, the Cape griffon vulture (Gyps coprotheres, Figure 2) is already at risk of extinction, with only 7,000 breeding pairs as of 2013 remaining in the wild (data correct at spring, 2014), and the Ruppell’s griffon vulture (Gyps rueppellii) is endangered. These vultures have very wide foraging behaviour, covering tens of thousands of kilometers a year, through different countries. This means registration of diclofenac or other toxic drugs in any southern African country poses a major risk to vulture populations of the entire region. Similarly, vulture populations in Kenya (where there are no restrictions on the distribution and sale of veterinary diclofenac) have declined by 60 per cent in recent years and six out of the eight resident species are now on the red IUCN list. In northern Africa vultures of the threatened species Neophron percnopterus (Egyptian vulture) and Sarogyps calvus (red-headed vulture) are also susceptible to diclofenac. Recently, the most common and most abundant vulture in Africa, the African white-backed vulture, has been uplisted to endangered by the IUCN due to its rate of decline in 2013.

Europe

Four species of old world vultures breed regularly in Europe: two species that are endangered or threatened (Egyptian vulture and crested vulture, respectively) and two species that globally are of least concern: griffon vulture and bearded vulture.

The latter (Gypaetus barbatus, Figure 3), although not endangered worldwide, has been almost extinguished from its historic European range. At present, there are 125 breeding pairs in Spain, thanks to 30 years of repopulation effort. The Iberian peninsula, together with France and Italy, includes the bulk (approximately 95 per cent) of the European vulture population. Spain plays a critical role for vulture population recovery across Europe – through normal dispersion or human-induced reintroduction. Italy is similarly very important, as the Italian Alps are key to restore the migration flows and the connections of the healthier vulture populations in western Europe with the struggling Eastern Europe/Russian ones. Until recently, European vulture numbers were relatively low (when compared with those of Asia and Africa), while now (after south Asian population collapse and African decline) Europe is probably the continent in the old world with most vultures in absolute numbers. Diclofenac does not have a central marketing approval for veterinary use in Europe. However, in 2009 to 2010 the Italian authorities licensed its use in livestock and, in March 2012, two products containing diclofenac were authorised for use on bovines, pigs and horses in Spain. The drug has also been exported from Italy to other EU and non-EU countries (Czech Republic, Estonia, Latvia, Serbia and Turkey).

Nowhere on the data sheet or on the risk assessment report of the drug is mentioned the well-known impact on vultures. A VMD spokes- man said: “As a precautionary measure the VMD will not approve any requests from vets to import products containing diclofenac. Further- more, we have agreed not to issue any export certificates.
the carcases of free-ranging domestic livestock kept in the fields or in special places called mudalies. These can include dump sites, equivalent to African "vulture restaurants," had been shut down in 2011 allowing also the disposal of animals intensively produced. This was designed to help the vultures, as the mudalies are an essential food source for many of the birds, and the closures had threatened vulture numbers. But the introduction of defonacin could turn the mudalies into a threat, as carcasses are not tested for the drug's presence. Further, there are also an unknown number of non-authorised carcass dumps that are not controlled. If defonacin becomes widespread in Europe, carcasses would have to be collected and incinerated (at huge cost).

Some unpublished data suggests the drug may be toxic to other species. No vultures are present in the UK, but if defonacin is toxic to other birds of prey then the problem becomes relevant here as well. A campaign has begun to get the EU to change its guidelines so the drug can be banned. Vulture Conservation Foundation, BirdLife International, the RSPB and other conservation associations, together with the IUCN vulture specialist group are asking for a complete ban of the use of defonacin and acetylsalicylic acid (the latter not yet marketed, but also a potential threat). The identification of NSAIDs that are effective for treating livestock, but also non-toxic to vultures facilitates, the removal of defonacin from veterinary usage. Toxic effects have been observed on the kidneys of birds after treatment with a few different NSAIDs (Table 1), with marked interspecific differences. Studies have established the safety of individual NSAIDs to vultures and, the only safe alternative has been found to be meloxicam. Multiple studies have confirmed the safety of this drug to vultures; in particular, Naddeo et al in 2008 have shown its safety following repeated exposures, and evaluated its oral and intramuscular pharmacokinetics in Cape, white-backed, Egyptian and fappat-faced vultures. No signs of toxicity were seen in the tested birds, and a very rapid half-life of elimination of this drug was observed (0.42±0.1 h following IM administration and 0.32±0.17 h per os). This rapid metabolism makes it unlikely that meloxicam could accumulate: drug elimination should be complete five to seven hours post-exposure, and a vulture would have to consume numerous meals in one day for accumulation to occur. If you'd like to support the campaign, the petition can be found at www.care.org/imp-acet/3484d5-nike-european-union-diego-defense-the-vulture-ill-is-now-available-on-eu-market-ban-it-now?

References
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