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Anticoagulant Rodenticides and Wildlife: Concluding Remarks

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Chapter 14
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Rodents are known to affect human society globally in various adverse ways (Chap. 1). Since historic times, they have been vectors for a wide range of human and livestock diseases. Almost all agricultural activity worldwide, both past and present, has been subject to attack and fouling by rodents, which may therefore threaten our ability to feed ourselves.

More recently, rodents have presented new problems, for example by causing damage to power supplies and electrical infrastructure, and by colonising (with inadvertent help from humans) remote islands and predating the eggs and chicks of what are often rare and endemic species of significant conservation value. The overall result of this multi-faceted conflict with mankind is a widespread demand for continuous control of commensal rodents, and in some cases other species.

Anticoagulant rodenticides (ARs) have been, and currently remain, the cornerstone of rodent control throughout the world (Chap. 2). Although alternative methods exist, they are less effective for control of large scale outbreaks or infestations, such as across agricultural areas. Other reasons further explain why ARs have become a mainstay of chemical control, and these are related to their mode of toxicity and pharmacokinetics. Briefly, AR mode of action (and toxicity) involves binding to vitamin K epoxide reductase sites, especially in the liver, and preventing the activation of

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clotting factors, eventually resulting in coagulopathy (Chap. 3). In terms of efficacy and safety, there are two important beneficial consequences of this mode of toxicity. First, the delayed onset of physiological effects reduces the likelihood that bait shyness will develop. Second, Vitamin K_1 is an effective antidote that mitigates the action of ARs. Accidental ingestion of ARs by livestock, companion animals, humans and wildlife can therefore be simply and effectively treated, a key benefit for poisons that are so widely used and potentially available to non-target organisms.

Anticoagulant rodenticides have the potential to harm a wide range of non-target species because they affect the blood clotting cascade, a highly conserved physiological mechanism amongst vertebrates. Due to this non-selectivity, their undoubted benefits for rodent control have to be balanced against the environmental risks that these compounds pose. There has been significant research effort world-wide in the last 25 years to better characterise and understand the risks of non-target exposure and poisoning. In this book, we have brought together and described the current state of understanding of these risks.

Although ARs have been used for decades, pharmacokinetic and toxicokinetic data have principally been generated from studies on laboratory mammals and concentrated on acute effects associated with lethal coagulopathy (Chaps. 3 and 4). There are, therefore, relatively limited laboratory data on other (particularly chronic and sub-lethal) effects in wildlife species and there are significant gaps in our knowledge that are relevant for assessing risk to wildlife. An important gap is an understanding of the cause of the large inter- and intra-species differences in sensitivity to ARs amongst the small number of species that have been tested. It is not clear where non-target taxa, that may be at most risk of exposure, are ranked within species-sensitivity distributions. Knowledge and understanding of Vitamin K status in non-target species as it relates to AR sensitivity, as well as other causal and confounding factors affecting sensitivity, are lacking. Ecological risk assessments for ARs would be significantly improved with additional knowledge in these areas. Other major gaps in knowledge include whether there are AR-mediated sub-lethal effects, unrelated to coagulopathy, that are significant (Chap. 3), the extent and importance of trans-placental and *in ovo* transfer of ARs, and the impacts of sequential exposures to ARs as are known to occur in wildlife.

Although there is much we do not know, it is clear that the pharmacokinetics and toxicity of ARs not only make them effective poisoning agents but also fundamentally mediate the comparative risk that different ARs pose to non-target species (Chaps. 3 and 4). Studies have shown that second-generation anticoagulant rodenticides (SGARs) are more acutely toxic than first-generation compounds (FGARs), although the difference in potency is diminished when exposure is chronic. SGARs are also more persistent in body tissues, with two- to five-fold longer hepatic half-lives. Differences in acute toxicity among compounds are most likely to affect the extent to which primary exposure in non-targets results in mortalities. The proliferation of SGAR use over FGARs may have increased the risk of primary poisoning amongst non-targets in general, and in particular amongst bird species. For example, the differences in acute toxicity of some SGARs (e.g., brodifacoum, difethialone) between birds and mammals are modest when compared with the seemingly large

differences in toxicity of FGARs between birds and mammals. However, it is the enhancements both in acute toxicity and tissue half-life in SGARs that are important in determining the extent of secondary exposure and poisoning of predators and scavengers, and that helps explain why many secondary exposure and poisoning studies have focussed on SGARs.

The focus of this book is specifically about the impacts of ARs on wildlife, and the ability to clearly identify AR-mediated effects is fundamental to this topic. The mere presence of AR residues in tissues demonstrates exposure, but does not indicate that the animal succumbed from AR-mediated effects. A combined approach of clinical investigation, measurement of blood parameters and detection of tissue residues often can enable unequivocal diagnosis, but there are significant difficulties (Chap. 5). Knowledge of the pathophysiology of ARs aids in recognizing ante-mortem and post-mortem toxicosis. Ante-mortem symptoms, such as lethargy, subdued behaviour and unresponsiveness are generally not very specific. However in combination with observations on changes in blood parameters, such as increased clotting times, diagnosis is far more apparent. Many studies however rely on examination not of live animals but on necropsy and measurements of tissue residues in wildlife carcasses. Symptoms such as pallor of the mucous membranes (e.g., in oral cavity) can be an indicator of toxicosis, as is the presence of signs of haemorrhage. Histopathological lesions provide supportive evidence of severe blood loss, haemorrhage, or hypoxic damage, but are not solely indicative of AR toxicosis. Microscopic evidence of haemorrhage in heart, lung, kidney, liver and skeletal muscle, and tissue necrosis have also been reported but their prevalence is not always dose-related to AR-exposure. Furthermore, differentiating between haemorrhages resulting from poisoning as opposed to traumatic injury can be difficult.

Overall, the combining of data obtained through various routes of investigation and disciplines (e.g., clinical observation and treatment, pathological evaluation and forensics) will help provide the most complete picture of whether AR-mediated effects have occurred, but unequivocal diagnosis is difficult (Chap. 5). There are likely to be diagnostic errors, especially when only data from macroscopic post-mortems are available and when necropsies are conducted by researchers with limited experience. Assessment of probability of death, when possible, in relation to the residues in tissues collected from carcasses, may be a means of assessing overall AR-induced mortality in populations (Chaps. 6 and 7). This is hampered by the fact that it is unclear whether current reported levels of toxicity are over or underestimates. However, what is more likely to be under-detected, or go completely undetected, is if exposure to ARs elicits behavioural changes that predispose animals to other lethal risks, such as being more easily predated or involved in accidents (e.g., electrocution, vehicular strikes). Quantifying how many individuals may be “indirectly” affected in this way is a major challenge.

There have been many wildlife studies in which AR tissue residues (primarily in liver) have been the principal measurements recorded (Chap. 6). These investigations were conducted to determine the nature and extent of primary and secondary exposure and comprise the bulk of all the investigations on ARs in wildlife. They have concentrated on exposure rather than effects, probably because of the aforementioned

difficulties in diagnosing effects. Such residue measurements provide valuable information on exposure, as the long tissue half-lives of SGARs provide an "exposure signal" that is integrated over days and months. While liver residues are informative of exposure, they are of less value for risk assessment where there is a need to estimate dietary AR concentrations for predators. In such cases, total body concentrations of prey animals are recommended, but data on anticoagulant body burdens in non-target (and often even target) prey species are generally lacking.

It is perhaps surprising that there have been comparatively few studies on primary exposure in wildlife (Chap. 6) compared with the number on secondary exposure. This is despite the fact that primary exposure is likely to result in higher dose rates to individuals than secondary exposure and would probably be more likely to cause acute mortalities. The studies that have been conducted indicate that the taxa most at risk of primary exposure include invertebrates, reptiles, birds and mammals. Comparatively little is known about primary exposure and effects in invertebrates, reptiles or even birds; hence further investigations are needed. Studies on non-target small mammals indicate that there are both key ecological (Chap. 6) and landscape (Chap. 8) interactions between bait placement and receptor species that influence primary exposure. Typically, it is the more granivorous/herbivorous species that are most widely exposed, as the vast majority of AR use involves the application of cereal baits. Other types of baits are used in and around buildings, which may result in other species being exposed, including more omnivorous and even carnivorous species. This may play an important role in more urban areas. Animals foraging close to bait stations, typically within 100 metres, are more likely to be exposed to ARs, although this distance can be greater for the more mobile rodent and other species for example birds, and can depend on habitat configuration. In contrast, localised spatial interactions are less important when considering aerial bait applications, because of the large-scale and relatively indiscriminate nature of bait distribution. However, co-occurrence between non-target animals and AR treatments does not mean that exposure to ARs actually occurs because species traits, such as dietary and habitat preferences, home range size and mobility, all influence the likelihood of exposure. Adoption of a trait-based approach, together with consideration of the spatial interactions between the compound and non-target species, are likely to both enhance *a priori* identification of primary exposure risk and help identify appropriate mitigation measures. It is notable that studies to date suggest a surprisingly high degree of exposure (as evidenced by tissue residues) in shrews and hedgehogs, which are predominantly insectivorous, a trait that would not indicate high likelihood of exposure (Chaps. 6). Exposure in shrews and hedgehogs may be both primary and secondary through consumption of contaminated insects, and possibly carrion. It is possible that specialist feeders are more plastic in their diet selection, and that exposure through multiple pathways is more common for many individuals, than is presumed.

Overall, it is evident from a range of studies that primary exposure can lead to acute mortalities in non-targets and, in some instances, has caused declines in species abundance (Chaps. 6 and 7). Populations are likely to recover partly through reduced density-dependent mortality, and such recovery may be relatively rapid in

species with high intrinsic rates of reproduction. In non-isolated populations, immigration may also contribute to recovery. However, prolonged or permanent baiting can exert a continuous mortality pressure, and may encourage immigration into what effectively become ecological sink areas. Further studies are needed to quantify the interaction between baiting practices (e.g., formulation, placement, density and especially duration) and population effects. Furthermore, given the unexpected high occurrence of residues in shrews and hedgehogs, there is a need to determine if small insectivores are particularly susceptible to AR exposure, accumulation or effects.

It might be expected that secondary exposure in predators would reflect opportunistic feeding behaviour and the highly variable nature of primary exposure in prey. However, the often greater life-span and larger foraging areas of predators compared with prey, coupled with the bioaccumulation of ARs in tissues such as the liver, mean that secondary exposure is integrated both temporally and spatially. This explains the finding that 58% (2414 out of 4187) of predators analyzed in worldwide field monitoring studies have AR tissue residues, evidence that secondary exposure to ARs in populations of predators is a global phenomenon (Chap. 7). Because of the diversity of their prey, not all of which feed on rodenticides, exposure might be expected to be lower in generalist predators than in rodent-specialists. A review of the literature indeed suggests that the proportion of animals exposed is greatest in mammals that specialize on rodents and less in non-specialist mammals; interestingly, this difference between generalists and specialists was not apparent in birds. Studies further suggest that the most "at-risk" predators are nocturnal opportunistic predators for which rodents are a key component of their diet, seasonally or year-round. The ecological factors that drive the uptake of ARs in predators and likelihood of exposure (Chap. 9) are context specific. They depend on the landscape that the predators inhabit and the management of habitats within that landscape. For example, there is significant potential for ARs to move into food-chains when they are mass-applied to agricultural fields, but predators that consume rats and hunt in urban environments, where rodent control is commonplace, may be disproportionately exposed. In general, the likelihood of exposure in predators will vary with the scale and duration of bait availability to prey, the proportion of prey exposed, the temporal trends in prey density, the foraging tactics of predators, and the propensity of poisoned rodents to be captured and consumed.

Diagnosis of lethal secondary poisoning is difficult, as discussed earlier and in detail in Chap. 5, and so the extent to which secondary exposure causes mortalities in non-target predators is uncertain. Liver AR residues tend to be higher in mammals than birds but it is not clear if this is a reflection of differences in exposure, bioaccumulation potential, or toxicity. Detection of elevated residues could indicate either higher exposure or tolerance— more sensitive individuals and species may die before accumulating high residues, and their carcasses rarely found. Despite such difficulties in diagnosing fatalities, there have been studies documenting incidents in which relatively large numbers of individual predators have been identified as having been poisoned by ARs (e.g., Chap. 7). Some island eradications have also led to AR-mediated population declines of predators; current practices can now

involve capture, temporary removal and subsequent re-establishment of "at-risk" species. There remains no clear evidence of population declines that can be directly attributed to AR poisoning. However, cause-effect relations of chemical exposure leading to population declines are difficult to detect, attribute and seemingly rare. It is also argued (Chap. 12) that predator populations released from other pressures, such as persecution, have rapidly expanded despite their widespread exposure to ARs, suggesting that any effects caused by ARs may be small in comparison. The extent to which secondary poisonings may cause demographic effects is likely to vary among species, and even among populations. However, the global evidence of exposure, and the uncertainties about the magnitude and drivers of lethal and sub-lethal poisoning, dictate the need for continued AR monitoring in predators. This should include monitoring in humans, at least amongst groups that eat large amounts of game. Furthermore, the role and consequences of AR use on the top-down regulation of rodent populations by predators should also be taken into account when considering AR use.

Another key factor that has affected the interaction between ARs and wildlife is intrinsic resistance in target species. The genetic and physiological basis for resistance in target species has been the focus of much study (Chap. 10). The widespread replacement of FGARs by SGARs is partly the consequence of the development of resistance to FGARs in target species. This deployment of more potent and persistent SGARs has unquestionably increased the risk to wildlife from rodent control. There is also a possibility that, because of prolonged exposure, resistant rodent pest species may accumulate greater AR total body burdens than non-target (presumably more sensitive) species. However, there are relatively few studies on body burdens in free-living target species; this remains a knowledge gap. Furthermore, it is likely that resistance may have indirect effects by prolonging the duration of control campaigns, and thus extending the window of exposure for non-target species. Clearly, there is a need to monitor the onset of resistance in target species and, where detected, halt the use of compounds rendered less effective by resistance. The development of molecular techniques to detect resistance now makes conducting large scale genetic surveillance a reality. Characterisation of the resistance status of rodent populations can help guide selection of the most efficacious compounds and control methods.

The overall risk that ARs pose to wildlife is evident from the fact that their use is now regulated in many countries around the world (Chap. 11). Their continued authorisation reflects recognition of the benefits delivered by rodent control, and concerns that regulatory action might prevent access to effective rodent control for some sectors of society (e.g., lower economic strata) and thus limit associated benefits for health and well-being. While there are alternatives to ARs (Chap. 13) such as acute rodenticides (acting more rapidly than ARs; e.g., bromethalin, cholecalciferol, strychnine, zinc phosphide), they can also pose a significant hazard through direct consumption by many species, including people (especially children), livestock, and pets. Forcing a shift from ARs to other chemistries may simply substitute one set of risks for another. Furthermore, while it is generally accepted that contamination of wildlife and adverse effects on individuals are undesirable, and to

regulatory standards in principle unacceptable, the lack of clear evidence of long-term population-level effects on non-target wildlife raises challenging questions as to what level of mitigation is actually appropriate and acceptable (Chap. 13). It is perhaps not surprising therefore that the regulatory response to AR use is not universally agreed upon.

Although application of more stringent risk mitigation measures could pose a risk to efficacious rodent control, there are various mitigation measures that are reasonable and could be implemented (Chap. 12). Those include such measures as bait protection, replacing permanent baiting and its associated constant "leakage" of ARs into the environment with pulsed baiting that is initiated at the onset of infestation, restricting use by non-professionals, and avoiding use in areas of high non-target density. Such measures are primarily focused on reducing primary exposure to non-targets; however, they are unlikely to be particularly efficacious for species that cannot be prevented from accessing baits. This may be circumvented by increasing focus on prevention of the development of local populations and non-chemical control of target species, which may decrease the need for chemical control. Although reductions in non-target primary exposure would be expected to lead to a concomitant reduction in secondary exposure, this may be partly confounded by the increased availability of AR-poisoned target rodents to predators and scavengers. Reduction in secondary exposure may be improved through incorporation of varied chemical control methods along with pest control practices common in integrated pest management (IPM). These could include non-chemical control, habitat management, and, in agricultural habitats, the use of lure crops and supplemental feeding. Use of IPM may not only reduce non-target exposure to AR but also benefit resistance management. Barriers to adoption of IPM approaches include the perception that they do not work, work too slowly or are cumbersome, and are typically more laborious, expensive and time consuming than simply relying just on application of ARs. Therefore, it is important that the expectations of different stakeholders are considered and managed. Users may also need to be incentivised further through better communication about the risks to wildlife from ARs and the likelihood of resistance in targets that may result from an over-reliance on ARs. However, immediate tangible benefits may also be needed, and one possible option would be to link implementation of IPM and/or other mitigation measures to existing agricultural practices through the use of financial subsidy and levy schemes.

Finally, it seems appropriate for this book, in which we have focussed on the scientific evidence of how ARs affect wildlife, to end by considering key information gaps. These are the gaps that need to be filled to gain a better understanding of the risk that ARs pose to wildlife and the benefits delivered by mitigation measures and IPM. In terms of acute effects, better tools are needed to estimate the extent of AR-induced mortality in different wildlife populations. Currently, the bulk of available data on exposure relates to avian and mammalian predators from predominantly rural environments, yet we still have a poor ability to estimate how ARs affect those populations. Furthermore, although we know that there can be extensive sub-lethal exposure of non-target wildlife, we know little about the thresholds (dose or residues) that cause coagulopathy, and even less about exposure levels that affect

survival and reproductive fitness. If we in addition consider exposure scenarios and species about which we have less information, there is a real lack of knowledge about the extent and importance of exposure in lower vertebrates and invertebrates. Better information is also needed on exposure of wildlife in urban habitats where there is probably the greatest density and frequency of AR use, both professional and amateur. Until these knowledge gaps are better addressed, the discussion over the need for, or required extent of, mitigation or other interventions will continue. While lack of this information has the potential to paralyse decision-making about future interventions, and might be considered a priority, it is interesting to note that regulatory action and mitigation is proceeding in many countries (Chaps. 11 and 12). That is based on the undesirability of and public opposition to existing wide scale indiscriminate exposure and the potential loss of wildlife, including species that are charismatic and of high conservation value. Given that there is already a move towards mitigation and increased regulation, the key research priority may ultimately be to address the lack of scientific assessment of the effectiveness of both specific AR mitigation measures and of IPM approaches to rodent control. Study trials, monitoring and reporting of the effects of different measures on efficacy of pest species control, on non-target AR exposure, and on management of resistance, are sorely needed. If such knowledge gaps can be filled, it should result in a better understanding of the holistic costs and benefits of chemical and non-chemical control. Ultimately, it will enable us to answer the fundamental questions on how much rodent control is warranted, of what type, and what are the direct and indirect consequences of such activities on non-target wildlife.