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Author(s)	新屋, 惣
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Name

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Risk assessment of toxic effects of pesticide exposure in wild terrestrial mammals
（陸生野生哺乳類における農薬暴露による毒性影響のリスクアセスメント）

This research aims to contribute to wildlife conservation by assessing the risks of pesticide exposure to wild mammals. This is crucial as many wildlife species are affected by pesticides. Chapter 1 investigates neonicotinoids in wild raccoons' urine in Hokkaido, comparing their metabolic capabilities to rats. Several neonicotinoids and their metabolites were detected. Raccoons showed lower metabolic capacity for neonicotinoids than rats, indicating higher susceptibility. Despite exposure levels being below safety thresholds, potential additive and synergistic effects of multiple neonicotinoids warrant further research. Chapter 2 examines pesticide exposure in wild raccoons in cropland and masked palm civets in metropolitan in Japan. Analyzing stomach contents revealed raccoons primarily consumed corn with high exposure to neonicotinoids, while civets consumed various crops and industrial antifungal agents. Although maximum exposure levels were below the acceptable daily intake for humans, synergistic effects and acute toxicity risks require more investigation. This underscores the need for long-term research on pesticide impacts on wildlife. Chapter 3 explores the genetic and metabolic responses of musk shrews to acetamiprid. The study identified various CYP genes and their relationships with other mammals. Musk shrews exhibited high expression of certain CYP isoforms and faster clearance rates of acetamiprid compared to mice. This highlights the importance of considering species-specific metabolic traits in assessing environmental contaminants and positions musk shrews as a valuable model for studying pesticide toxicity in wildlife. Chapter 4 investigates the effects of pesticide exposure on pathogen reservoir animals using mice and *Leptospira* as models. Diazinon exposure in mice reduced urinary excretion of *Leptospira* and lowered kidney tissue levels of the pathogen, suggesting an enhanced immune response. This implies that diazinon exposure could reduce leptospirosis transmission risk to humans. Further research is needed on the effects of various pesticides on infectious diseases in wildlife.

This study highlights that many wild mammal species are threatened by human activities, including pesticide exposure. Japan's pesticide regulations are less stringent compared to the EU, where stricter controls have led to increased wildlife populations. Japan's high pesticide use per land area necessitates more data on pesticide exposure across different wildlife species to reassess current limits. Also, research must consider interspecies differences in pesticide sensitivity, especially in carnivores at the top of the ecological pyramid, which are more vulnerable to chemicals. Effective risk management should be based on data from the most sensitive species. Limited research on the detoxification potential of pesticides in top predators calls for aggregated data. Furthermore, there is a gap in studying the effects of chemical exposure on reservoir animals of infectious diseases, which could influence disease transmission risks to humans. Collaborative research between toxicology and microbiology is essential. Overall, the study reveals ongoing pesticide exposure in wild mammals in Japan. Although exposure levels were not high, the possibility of co-exposure to multiple pesticides poses toxic risks due to interspecies sensitivity differences. Pesticide exposure could also impact pathogen infection status in reservoir wildlife, altering infectious risks to humans. Future research should focus on diverse areas, various mammalian species, and the effects of pesticide exposure on infectious disease reservoirs.