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Emerging Pathogens in the Context of Marine Mammal Health SARS-COV- 2 and HPAI H5N1. Progress report IWC 2023 IWC SC Intersessional Correspondence Group on CDOC (Cetacean Diseases of Concern)

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WORKING PAPER

Emerging Pathogens in the Context of Marine Mammal Health

SARS-COV- 2 and HPAI H5N1

Progress report IWC 2023 IWC SC
Intersessional Correspondence Group on CDOC (Cetacean Diseases of Concern)

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ABSTRACT

Cetacean diseases of concern (CDOC) are a standing topic for E. Special disease primer sessions during 2020/2021 focused on known marine mammal pathogens such as *morbillivirus (CeMV), Herpes virus, Brucella ceti, and Toxoplasma gondii* that have been associated with morbidity and mortality in individual animals, but also have been implicated in UMEs. Recent emerging pathogens of concern include SARS-Cov2 and avian influenza. A primer session on SARS-Cov2 and implications from spillover into marine mammals was held during 2022. In response to the increasing evidence for Highly Pathogenic Avian Influenza (HPAI) spillover (natural infection) events in marine mammals in recent months the World Organization for Animal Health (WOAH) convened in March 2023 an ad hoc expert group to develop a Guidance Framework for HPAI outbreak management in marine mammals. Several members of the IWC CDOC intersessional working group are included in the WOAH working group as well as other experts at large. A final draft of the guidance document is expected by the end of May 2023.

KEYWORDS: CETACEAN DISEASES OF CONCERN; SARS-COV-2; HPAI H5N1 clade 2.3.4.4b; WOAH;

INTRODUCTION

SARS-COV-2 Update

Spill over (reverse zoonosis) of severe acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) to various animal species have occurred during the height of the pandemic as well as now. As of 2023, 699 natural infections (spillovers) have been confirmed in the Americas, Africa, Asia, and Europe into twenty-six mammals. The majority of spillovers have occurred in terrestrial mammals, with a few semi aquatic and aquatic mammals (mink, eurasian otter, fishing cat, hippopotamus, West indian manatee). The majority of cases occurred in animals under human care including domestic pets, but natural infections in commercial fur industry (e.g. mink) and free-ranging wildlife species with onward animal to animal transmission (e.g.white-tailed deer), have also occurred. On 7 March 2022, the Tripartite Organization FAO/ WHO/WOAH issued a joint statement on the prioritization of monitoring SARS-CoV-2 infection in wildlife and preventing the formation of animal reservoirs. Given the limited case material for aquatic and semi-aquatic species, health implications of Sars Cov2 with respect to morbidity and mortality in marine mammals remain difficult to judge, but both are part of the potential disease spectrum. That said, given the cumulative evidence for reverse zoonosis and our incomplete understanding of virus host range (see Audino et al. 2021; Li et al. 2022; Lean et al. 2022; 2023) surveillance of marine mammals under human care remains critical while virus circulation in humans remains ongoing. Furthermore, surveillance of stranded marine mammals and live animals during health assessments, especially coastal species, will provide a starting point to investigate epidemiological aspects of this novel viral agent within a marine environment. A recent stranding event of dolphins in New Zealand highlights marine mammal exposure pathways through waste water (Stocken pers. commun). Testing of wastewater has been used in evaluation of community cases in people in areas with lower resources to provide individual case evaluations. Briefly, buccal swabs of 3 dead animals tested positive for SARS-Cov2. Subsequent tests of blowhole swabs were not positive. Environmental cross contamination from waste water that had spilled into the coastal waters is considered the most parsimonious explanation. Buccal cavities of dolphins were likely exposed to the contaminated water while feeding. Though no spillover into dolphins occurred (animals were not the source of the SARS-Cov2 virus), it should be noted that false positives may be identified in stranded cetaceans due to environmental contamination, therefore additional pathology or internal testing should be done. In conclusion, though still considered a human disease, its potential for establishment of new terrestrial and aquatic animal host reservoirs, for viral adaptation etc. and for future spill backs clearly identifies it as a ONE-Health issue. (Banerjee et al. 2021; Clayton et al. 2022).

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Highly Pathogenic Avian Influenza (HPAI)

The current HPAI outbreak (2020 ongoing) is unprecedented in global extent and diversity of avian species being affected. H5N1 clade 2.3.4.4b is currently the dominant virus strain subtype circulating globally. In contrast to previous HPAI variants the latter strain has caused significant mortality in wild birds especially among waterfowl, raptors, corvids, gulls, seabirds and in terrestrial mammals (predators; scavengers). Infection of the brain is common among both avian and mammalian species with live animals exhibiting a range of neurological signs. Two UME's involving pinnipeds, (harbor seal (*Phoca vitulina*); gray seal (*Halichoerus grypus*); Southern sea lion (*Otaria flavescens*) in the Americas (USA; PERU) have been linked to infection with H5N1 clade 2.3.4.4b . Both UME's were concurrent with significant regional seabird mortality events (Puryear et al. 2023; Leguia et al. 2023). Additional single cases of infection with the same HPAI H5N1 clade confirmed were reported as of March 17, 2023 from Europe (UK;SWE) and the Americas (USA; Canada; Chile, Peru), and include several small cetacean species (Thorsson et al. 2023) (common dolphin (Tursiops truncatus); white-sided dolphin (Lagenorhynchus acutus);

harbor porpoise (Phocena Phocena); spiny porpoise (Burmeister porpoise, Phocoena spinipinnis); Chilean dolphin (Cephalorhynchus eutropia), a number of pinnipeds (gray seal; harbor seal; Southern sea lion; South american fur seal (Arctocephalus australis) and semi-aquatic mammals (marine (*Lontra felina)* and river otters (*Lontra canadensis; Lutra lutra*). Likely primary oral or inhalation exposure routes for affected aquatic mammals include environmental contamination, close contact between wild birds and marine mammals (pinnipedia) in haul-out areas, and scavenging on infected carrion. Survival of H5N1 virus pending tissue type and ambient temperature is prolonged (Yamamoto et al. 2017). Currently there is no evidence that mammal to mammal transmission has occurred, however the virus is rapidly evolving. In the past in the northeast US, low pathogenic avian influenza has been found in phocids and cetaceans associated with clusters or UMEs, however there is now strong evidence of pinniped to pinniped transmission and some strains have become endemic in the population. Therefore, a strong focus on tracking viral genome strains and animal disease is needed to inform whether animal to animal transmission is likely to occur. Direct contact transmission among pinnipeds is less likely thus far but cannot be ruled out as the viruses evolve.

World Organization for Animal Health

In response to the increasing evidence for HPAI spillover (natural infection) in marine mammals the World Organization for Animal Health (WOAH) convened during March 2023 an ad hoc expert group to develop a *Guidance framework for HPAI outbreak management in marine mammals*. Several members of the IWC CDOC intersessional working group are included in the WOAH working group as well as other experts at large. A final draft of the guidance document is expected by the end of May 2023. In the interim given the emerging nature of HPAI in non-avian species, and the many unknowns (transmission, pathogenesis, pathology, host susceptibility) thorough investigation of morbidity and mortality events (single, clustered, UME) in marine mammal species including those under human care is becoming more important. From a field response perspective, both clinical presentation and gross abnormalities on post-mortem examination are among the important gateway keepers to alert and raise suspicion regarding future potential HPAI cases in novel and known species (Table. 1). Standardized assessment of presenting symptoms in alive/moribund animals plus complete life history information, and succinct and complete description of gross abnormalities are required to inform our evolving knowledge base. Furthermore a detailed stranding history with associated spatial and temporal history of concurrent and prior events of HPAI (suspect/confirmed) in avian and non-avian species will be equally helpful. Finally neurologic signs in marine mammals are also a hallmark of infection with several other cetacean diseases of concern (Herpes virus, morbilli virus, toxoplasma gondii, brucella spp.) and marine biotoxins (domoic acid). Clinical samples collected from animals with neurological disease should be concurrently tested for HPAI and these CDOCs including SARS-COV2.

Reported Cetacean Cases (as of April 24, 2023)

Avian influenza Americas (Canada)	mortality	White sided dolphin (!)	2022	H5N1
Avian influenza Americas (USA)	mortality	common bottlenose dolphin (1)	2022	H5N1
Avian influenza Europe (Sweden)	mortality	harbor porpoise (1)	2022	H5N1
Avian influenza Americas (canada)	mortality	harbor porpoise (1)	2022	H5
Avian influenza Americas (PERU)	mortality	dolphin (1)	2023	H5N1
Avian influenza Americas (Chile)*	mortality	chilean dolphin (2); spiny porpoise (2)	2023	H5N1
Avian influenza Europe (UK)	mortality	dolphin (2); harbor porposie (1)	2022/2023	H5N1

- Both cetacean species are endemic to South america. The Chilean dolphin (*Cephalorhynchus eutropia*) “ tonino” is a small protected cetacean species along the coasts of Chile.

Table. 1. Summary of HPAI associated clinical and gross pathologic observations in Mammals (terrestrial/aquatic). source: see references below note: cat and dog cases are from media; black bear media; purple Sea Lion; green Harbor Porpoise; red Harbor seal/Gray seal.

DATA	**Composite of HPAI associated OBSERVATIONS in Mammals (terrestrial/aquatic) source: see references below note: cat and dog cases are from media; black bear media; purple Sealion; green Harbor Porpoise; red Harbor seal/Gray seal**	NOTE: Harbor seal/Greyseal /sealion pathology not published; Note: Different observers -clinics/postmortem =Absence of evidence is not evidence of absence.;
Out of habitat	stranded, hauled out,	
Status	***alive, dead, moribund, euthanized***	
Carcass condition	fresh to autolized	
Predator scavenger clade	mesocarnivores; piscivorous; opportunistic feeders	
Species	red fox, bobcats, coyotes, grey foxes, fishers, raccoons, striped skunks, Virginia opossums, black bear, brown bear; Grizzly bear; Kodiak brown bear; mountain lion, stone marten, **eurasian otter, marine otter,** dogs, cats, mink, bush dogs; lynx, **harbor porpoise, *sealion, furseal,* common dolphin, atlantic white sided dolphin, *harbor seal, gray seal***	
Age class	mixed; possible demographic bias - juvenile, male	
Body condition index	poor to fair to good	
HPAI Confirmation	PCR/IHC	
HPAI VAriant	A/H5N1 lineage 2.3.4.4b (some mammalian adaptive mutations) e.g. mutation PB2-627K increases the replication of the virus in mammalian cell lines and at the mammalian temperature	
Samples	brain other tissues; oropharyngeal swabs; nasal swabs, rectal swabs	
ORGAN SYSTEM/BEHAVIOR	**CLINICAL PRESENTATION**	
Neurological symptoms	***seizures ,*** tremors , nystagmus, grimace; <30 minutes lip retraction, rapid opening and closing of mouth, skin twitching, head shaking; ***neurological***	

	signs (TBD)	
Respiratory symptoms	***dyspnoe; nasal discharge, respiratory signs (TBD)***	
Digestive symptoms	diarhea; vomiting; ***sialorrhea (drooling) salivation;*** foaming	
Ocular symptoms	ocular discharge; no response to sight stimuli (blindness), nystagmus	
Hearing & Smell	not responding to sound (Black bear), responded only slightly to smells of people (black bear)	
Touch Reception	loss of proprioreception	
Animal grooming/preening behavior	**data gap** (Two foxes had a shiny coat, and one fox (Oosterbeek) was covered with mud)	
Appetite	inappetence; showed no interest in water	
Posture/Motor Coordination	**swam in circles, was unable to right itself (drowned)** ***dissorientation; "stargazing" posture; ataxia,*** torticollis, circling, stumbling; crouching down with convex back and legs tucked under	
Reflexes	dimished swallowing reflex	
Responsiveness	inappropriate or lack of fear of humans; lethargy; fatigue/sleep; aggression; somnolent	
Withdrawal & Hiding beahvior	approaching and trying to get under cars (black bear)	
Animal communication	vocalization (moaning),	
Body temperature	fever	
Body mass	weight loss	
mortality		
PATHOLOGY_GROSS DESCRIPTION		
CNS	hemorrhage, congestion; congestion with hydrocephalus and malacia	
Sensory system	no lesions but behavior consistent with blindness reported	
Respiratory system	lung congestion, ***edema,*** failure to collapse, hemorrhage, and pleural effusion	
Cardiovascular system	Pericardial effusion, petechiae , and myocardial pallor	
Immune System	**data gap (on histopathology lesions)**	
Hepatobiliary system	pallor, congestion , enlargement , and hemorrhage , liver necrosis (Mountain lion)	

Urinary system	kidney congestion and cortical hemorrhage	
Body cavities	hemoperitoneum & hemothorax	
Reproductive system	**data gap**	
Digestive system	congestion, hemorrhage, and loose feces, pancreatitis	
Skeletal muscle system	petechial haemorrhages in the muscles	
Integumentary system	petechial hemorhages subcutaneous tissue	
Trauma	road traffic accident;	
Co-Infection	rare (viral co-infection) including adenovirus, parvovirus, rabies, parasites common	

Fig.1-3. Maps by the FAO (Jan 01 22 - Mar 27, 2023 wild birds), the Japanese Ministry of Agriculture. Fisheries and Forestry (MAFF) (wild birds & mammals 2023), and USGS (USA) (cumulative HPAI detection in the Americas 2021-2023).

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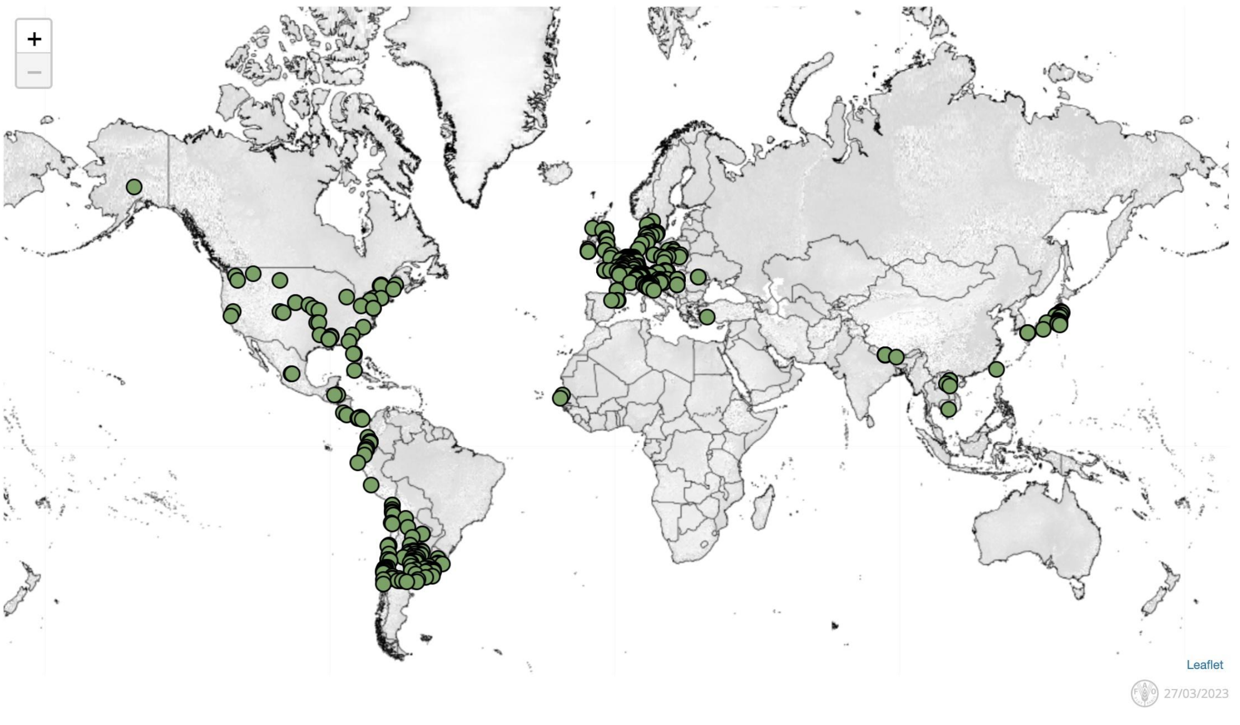

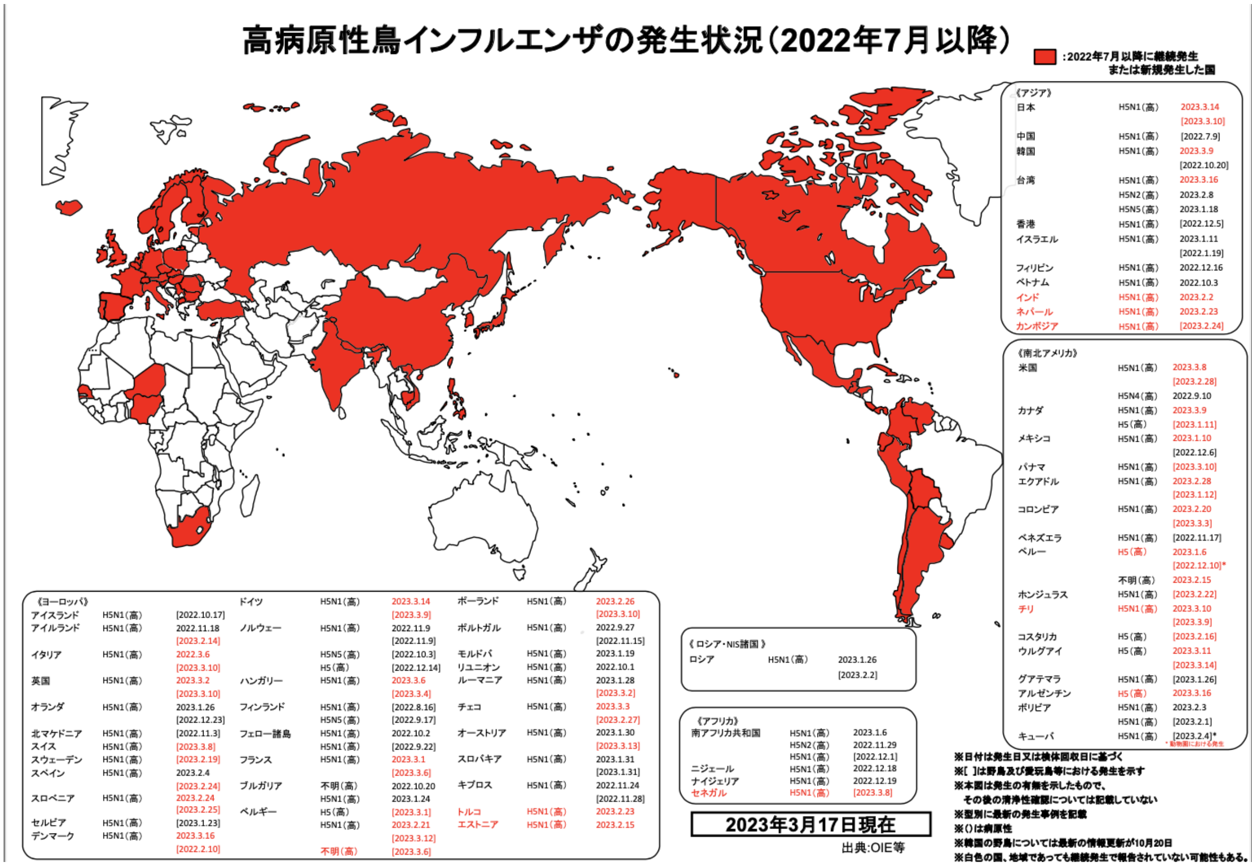
高病原性鳥インフルエンザの発生状況（2022年7月以降）
:2022年7月以降に継続発生
または新規発生した国
《アジア》
日本 H5N1（高） 2023.3.14
[2023.3.10]
中国 H5N1（高） [2022.7.9]
韓国 H5N1（高） 2023.3.9
[2022.10.20]
台湾 H5N1（高） 2023.3.16
H5N2（高） 2023.2.8
H5N5（高） 2023.1.18
香港 H5N1（高） [2022.12.5]
イスラエル H5N1（高） 2023.1.11
[2022.1.19]
フィリピン H5N1（高） 2022.12.16
ベトナム H5N1（高） 2022.10.3
インド H5N1（高） 2023.2.2
ネパール H5N1（高） 2023.2.23
カンボジア H5N1（高） [2023.2.24]
《南北アメリカ》
米国 H5N1（高） 2023.3.8
[2023.2.28]
H5N4（高） 2022.9.10
カナダ H5N1（高） 2023.3.9
H5（高） [2023.1.11]
メキシコ H5N1（高） 2023.1.10
[2022.12.6]
パナマ H5N1（高） [2023.3.10]
エクアドル H5N1（高） 2023.2.28
[2023.1.12]
コロンビア H5N1（高） 2023.2.20
[2023.3.3]
ベネズエラ H5N1（高） [2022.11.17]
ペルー H5（高） 2023.1.6
[2022.12.10]*
不明（高） 2023.2.15
ホンジュラス H5N1（高） [2023.2.22]
チリ H5N1（高） 2023.3.10
[2023.3.9]
コスタリカ H5（高） [2023.2.16]
ウルグアイ H5（高） 2023.3.11
[2023.3.14]
グアテマラ H5N1（高） [2023.1.26]
アルゼンチン H5（高） 2023.3.16
ボリビア H5N1（高） 2023.2.3
H5N1（高） [2023.2.1]
キューバ H5N1（高） [2023.2.4]*
*動物園における発生
《ヨーロッパ》
アイスランド H5N1（高） [2022.10.17]
アイルランド H5N1（高） 2022.11.18
[2023.2.14]
イタリア H5N1（高） 2022.3.6
[2023.3.10]
英国 H5N1（高） 2023.3.2
[2023.3.10]
オランダ H5N1（高） 2023.1.26
[2022.12.23]
北マケドニア H5N1（高） [2022.11.3]
スイス H5N1（高） [2023.3.8]
スウェーデン H5N1（高） [2023.2.19]
スペイン H5N1（高） 2023.2.4
[2023.2.24]
スロベニア H5N1（高） 2023.2.24
[2023.2.25]
セルビア H5N1（高） [2023.1.23]
デンマーク H5N1（高） 2023.3.16
[2022.2.10]
ドイツ H5N1（高） 2023.3.14
[2023.3.9]
ノルウェー H5N1（高） 2022.11.9
[2022.11.9]
H5N5（高） [2022.10.3]
H5（高） [2022.12.14]
ハンガリー H5N1（高） 2023.3.6
[2023.3.4]
フィンランド H5N1（高） [2022.8.16]
H5N5（高） [2022.9.17]
フェロー諸島 H5N1（高） 2022.10.2
H5N1（高） [2022.9.22]
フランス H5N1（高） 2023.3.1
[2023.3.6]
ブルガリア 不明（高） 2022.10.20
H5N1（高） 2023.1.24
ベルギー H5（高） [2023.3.1]
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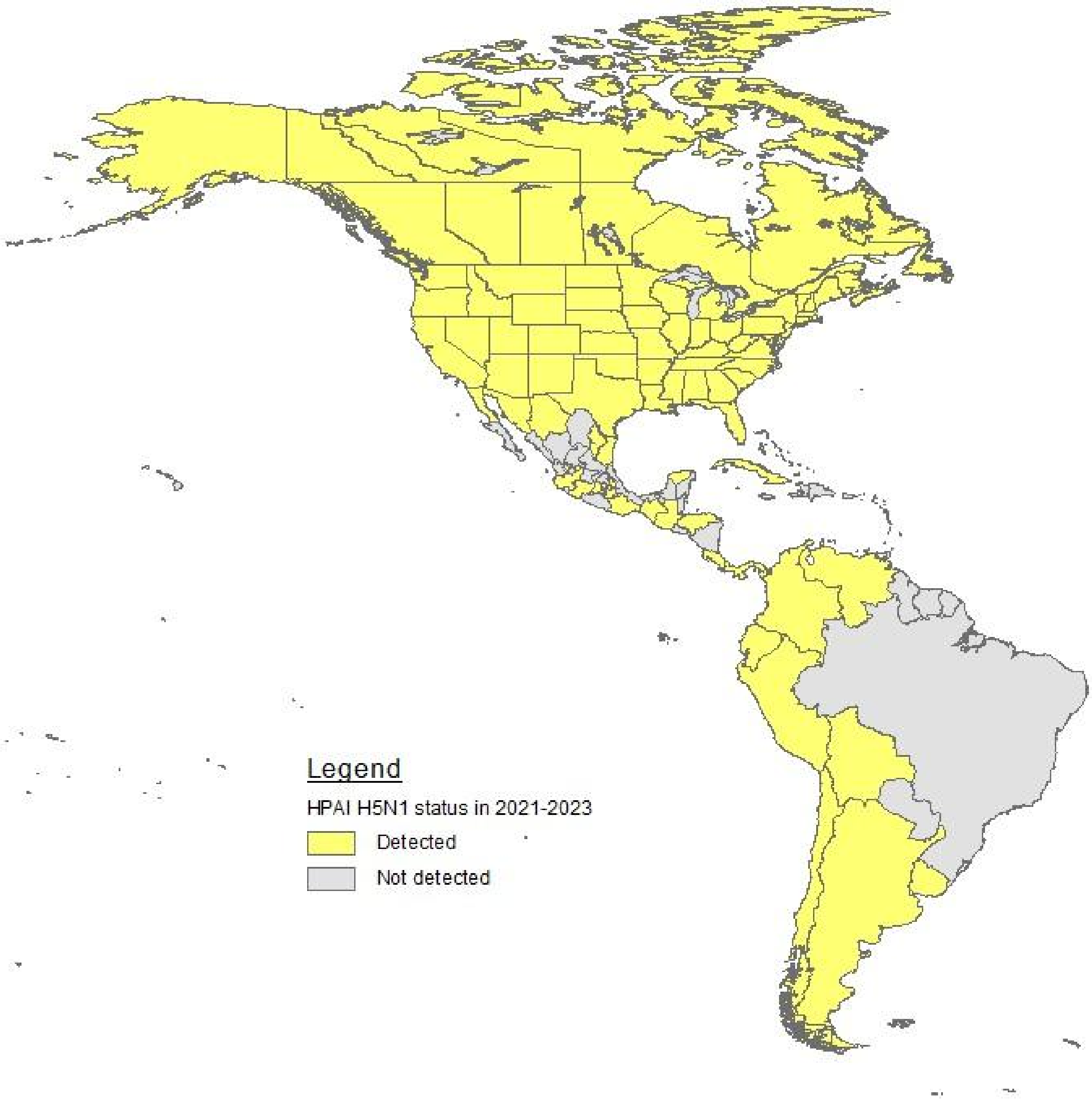
[2023.3.12]
不明（高） [2023.3.6]
ポーランド H5N1（高） 2023.2.26
[2023.3.10]
ポルトガル H5N1（高） 2022.9.27
[2022.11.15]
モルドバ H5N1（高） 2023.1.19
リユニオン H5N1（高） 2022.10.1
ルーマニア H5N1（高） 2023.1.28
[2023.3.2]
チェコ H5N1（高） 2023.3.3
[2023.2.27]
オーストリア H5N1（高） 2023.1.30
[2023.3.13]
スロバキア H5N1（高） 2023.1.31
[2023.1.31]
キプロス H5N1（高） 2022.11.24
[2022.11.28]
トルコ H5N1（高） 2023.2.23
エストニア H5N1（高） 2023.2.15
《ロシア・NIS諸国》
ロシア H5N1（高） 2023.1.26
[2023.2.2]
《アフリカ》
南アフリカ共和国 H5N1（高） 2023.1.6
H5N2（高） 2022.11.29
H5N1（高） [2022.12.1]
ニジェール H5N1（高） 2022.12.18
ナイジェリア H5N1（高） 2022.12.19
セネガル H5N1（高） [2023.3.8]
2023年3月17日現在
出典:OIE等
※日付は発生日又は検体回収日に基づく
※[ ]は野鳥及び愛玩鳥等における発生を示す
※本図は発生の有無を示したもので、
その後の清浄性確認については記載していない
※型別に最新の発生事例を記載
※()は病原性
※韓国の野鳥については最新の情報更新が10月20日
※白色の国、地域であっても継続発生で報告されていない可能性もある。


Legend
HPAI H5N1 status in 2021-2023
Detected
Not detected

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