Monitoring project on human avian influenza (AI) infections in contact with AI-infected animals

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON54806

Source
ToetsingOnline

Brief title
Study on avian virus in humans

Condition

- Viral infectious disorders
- Respiratory tract infections

Synonym
Avian influenza, birdflu

Research involving
Human

Sponsors and support

Primary sponsor: RIVM
Source(s) of monetary or material Support: Ministerie van VWS en/of RIVM

Intervention

Keyword: avian influenza, prepandemic phase, transmission

Outcome measures

Primary outcome

Contact investigation into human AI infections in incidental and prolonged

contact with AI-infected animals:

• Prevalence of asymptomatic AI infections.

• Incidence of asymptomatic AI infections.

• Transmission risks and route of avian influenza virus.

• The course of antibody titres over time.

Secondary outcome

Does not apply

Study description

Background summary

Since autumn 2021, there have been ongoing outbreaks of highly pathogenic avian influenza virus (HPAI) A(H5N1) clade 2.3.4.4b among poultry and wild birds worldwide and also in the Netherlands. This is a different variant of the A(H5N1) virus than the variant that has been circulating in China and Southeast Asia for several years and has led to infection in several hundred people there, often with serious illness and regularly leading to death. The current A(H5N1) clade 2.3.4.4b is now circulating worldwide and also in China.
To prevent transmission to other poultry farms, infected poultry are culled by the NVWA. To date, these mainly concern separate introductions and transmission between farms appears to be very limited. While contamination of poultry farms during previous seasons was geographically strongly correlated with waterfowl-dense areas and was limited to certain types of poultry farms, both the geographical distribution and the diversity of infected poultry farm types are currently increasing. Outbreaks also occur all year round and are no longer seasonal. This ongoing transmission is likely due to contamination via infected wild birds. Wild birds with HPAI are reported very frequently, often resulting

in significant mortality. In Spain, a mink farm was recently infected with the virus, whereby mink-to-mink transmission cannot be ruled out (Agüero et al., 2023).
Seven human cases of HPAI A(H5N1) 2.3.4.4b viruses have been reported worldwide. (WHO data as of December 21, 2022). These viruses belong to the same clade A(H5N1) viruses that have recently been detected in poultry and wild birds in the Netherlands. It is a worrying fact that in several countries, including the Netherlands, wild mammals are regularly infected with these clade A(H5N1) viruses and adaptation mutations in the virus for replication in mammalian cells are found, as is also the case with the previously mentioned kept minks. This means that the risk of transmission from bird to human and the development of the human-adapted A(H5N1) virus is estimated more realistically. In the Netherlands, 27 infected wild mammals, including many foxes, were found in 2021 and 2022. An estimated 600 infected and mostly dead sea lions have recently been found in Peru. More than 100 infected mammals from more than 10 species have been found in the US.

Problem/challenge
Adaptation of the HPAI A(H5N1) virus to infection and multiplication in mammalian cells allows effective transmission to humans. The risk of infection with HPAI A(H5N1) is greatest for people with a high degree of (unprotected) exposure to infected animals. When the virus mutates to efficient human-adapted infection and virus replication or reassortment of an HPAI A(H5N1) with a human seasonal influenza virus occurs, effective human-to-human transmission may become possible, posing a risk to public health. It is therefore important to detect possible infections with HPAI A(H5N1) in humans in good time. Currently, passive monitoring only takes place of exposed persons who develop respiratory complaints, but not of exposed persons without complaints. It is not known how many people develop respiratory complaints after exposure to HPAI virus (including A(H5Nx) and (A(H7Nx)). In the context of passive monitoring, there is urgent advice to persons who develop respiratory complaints after exposure to infected poultry to have themselves tested for HPAI virus infection (LCI Avian Influenza scenario, Appendix 4, 2022). Among those who have had themselves tested (until 2021 a few people annually, in 2022 41 people, in 2023 (t /m April 15) one person) no HPAI virus has been detected so far. As mentioned, it is not known which part of the total number of exposed persons develops respiratory complaints and subsequently undergoes testing.

Study objective

In addition to the aforementioned passive monitoring of high-risk persons with respiratory complaints after exposure to HPAI, this project aims to set up active monitoring (exclusion diagnosis) in high-risk persons without respiratory complaints in order to gain a better insight into possible transmission of the HPAI virus (including A(H5Nx), (A(H7Nx)) to humans, following the advice of the Expert Council-Zoonoses of 9th of May 2022.

Study design

Persons from the target group are advised to collect a throat and nose swab and a finger prick blood as soon as possible after exposure to proven infected animals and to send these to RIVM together with a self-completed collection form. It is important that the throat and nasal swab are taken under hygienic conditions, i.e. not immediately after work at the infected company, but only after showering and putting on clean clothes and in the home. The collection form will include questions about demographic data, possible complaints and symptoms and the degree and type of exposure to infected poultry. RIVM/IDS will perform influenza virus diagnostics with PCR on the submitted swabs: generic influenza virus type A and B detection and subtyping H1pdm09, H3 and H5. Based on the results, it is determined whether there is a probable infection with HPAI H5 virus. This is the case with a positive influenza A and H5 PCR. In the event of a positive influenza A PCR and subtype negative for H1pdm09, H3 and H5, depending on the viral load, additional testing is first done and a repeat sample may be requested (via the GGD) to determine which subtype of virus is involved. In both cases, the virus is sequenced and the sample is cultured for definitive laboratory diagnosis. The diagnostics will be performed twice a week and will be included in the routine of regular influenza surveillance.
The finger blood is only used as a reference serum in case of a positive laboratory diagnosis for H5 (or other HPAI virus).

Study burden and risks

This research is of primary public health importance and has no direct benefit to the individual participant. Participants are asked to complete one short questionnaire. In addition, the participants are asked to take a throat and nasal swab and to take some blood by means of a finger prick.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Persons exposed to avian influenza infected animals or humans

Exclusion criteria

- no informed consent
- child younger than 1 year

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting

Start date (anticipated):	26-06-2009
Enrollment:	1000
Type:	Actual

Ethics review

Approved WMO Date:	13-02-2007
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	12-05-2009
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-02-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-12-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-12-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-12-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-03-2020

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-03-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-04-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-05-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-05-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-09-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-12-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-02-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-07-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-02-2024

Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 25872
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL13529.041.06
OMON	NL-OMON25872
OMON	NL-OMON29654