REVIEW

Poultry food products—a source of avian influenza virus transmission to humans?

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Abstract

Global human mobility and intercontinental connectivity, expansion of livestock production and encroachment of wildlife habitats by invasive agricultural land use contribute to shape the complexity of influenza epidemiology. The OneHealth approach integrates these and further elements into considerations to improve disease control and prevention. Food of animal origin for human consumption is another integral aspect; if produced from infected livestock such items may act as vehicles of spread of animal pathogens, and, in case of zoonotic agents, as a potential human health hazard. Notifiable zoonotic avian influenza viruses (AIV) have become entrenched in poultry populations in several Asian and northern African countries since 2003. Highly pathogenic (HP) AIV (e.g. H5N1) cause extensive poultry mortality and severe economic losses. HPAIV and low pathogenic AIV (e.g. H7N9) with zoonotic propensities pose risks for human health. More than 1500 human cases of AIV infection have been reported, mainly from regions with endemically infected poultry. Intense human exposure to AIV-infected poultry, e.g. during rearing, slaughtering or processing of poultry, is a major risk factor for acquiring AIV infection. In contrast, human infections through consumption of AIV-contaminated food have not been substantiated. Heating poultry products according to kitchen standards (core temperatures $\geq$70°C, $\geq$10 s) rapidly inactivates AIV infectivity and renders fully cooked products safe. Nevertheless, concerted efforts must ensure that poultry products potentially contaminated with zoonotic AIV do not reach the food chain. Stringent and sustained OneHealth measures are required to better control and eventually eradicate, HPAIV from endemic regions.

Keywords: Avian, food safety, heat treatment, influenza, OneHealth, transspecies transmission, zoonosis

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Introduction

There is a constantly increasing demand to provide food, including high-quality animal proteins, for an ever-growing human population [1]. As an 'entrepreneurial response' towards these demands an immense increase in industrialized livestock production has occurred particularly in the last two decades [2]. Poultry offers highly economical feed-use efficiency rates associated with very low carbon costs, which explains the sharp rise in global poultry production particularly in South East Asia [3]. Poultry rearing is also very well suited to village-level and even family-level production, most notably in low-resource regions. However, altered and intensified poultry production and trading practices also enhance the risks for acquisition and spread of infectious diseases not only imposing negative effects on animal health but also with possible impact on food safety and human health. Food safety comprises all measures and facets of producing and handling food items that are dedicated to prevent illness resulting from consumption [4].

Along with the intensification of poultry production an increase in outbreaks of avian influenza viruses (AIV) in poultry has occurred [5,6]. Although avian influenza continues to primarily be an issue concerning poultry health, certain AIV strains

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show a propensity to also infect mammalian hosts, including humans. Therefore, AIV-infected poultry flocks may carry zoonotic risks, and public health awareness towards zoonotic AIV infections has increased steadily [7]. An increasing rate of human AIV infection with a lethal outcome has been observed, notably after 2003. Up to November 2015, WHO has registered 844 confirmed cases in humans of infection with highly pathogenic (HP) AIV H5N1 and 681 cases in humans due to H7N9 AIV showing case fatality ratios of 53% and 40%, respectively [8,9]. Consequently, concerns were raised about the threat to humans from poultry viruses, the safety of food products derived from poultry, and the pandemic potential of zoonotic AIVs like H5N1 and H7N9.

AIV pathobiology

Avian influenza viruses are members of the influenza A virus genus in the *Orthomyxoviridae* family containing eight segments of single-stranded genomic RNA of negative polarity. Based on genetic and antigenic differences of their two major membrane glycoproteins, 16 haemagglutinin (H) and nine neuraminidase (N) subtypes are currently known in AIV. In their natural hosts, aquatic wild birds of the orders Anseriformes and Charadriiformes, AIV induce acute, in most cases mild and self-limiting, infections of the epithelium of respiratory and gastrointestinal tracts. Infections are usually clinically inconspicuous [10]. Virus excretion mainly occurs through the oropharyngeal and cloacal routes, resulting in transmission not only by direct contact with infected hosts but also indirectly through contaminated feeding grounds and surface waters [11]. In surface waters, AIV can retain infectivity for more than 6 months under favourable environmental conditions (low temperature and salinity, neutral to slightly alkaline pH values), which may contribute to the sustained endemic transmission of these viruses in their natural host populations [12,13].

In contrast to galliform poultry, domestic waterfowl are considered susceptible to most of the AIV subtypes circulating among aquatic wild birds. Productive infection of chickens and turkeys often requires adaptation by the virus [14,15]. In general, AIV infection in poultry causes only mild, inconspicuous clinical signs, although a substantial drop in egg production might ensue. Such AIV infections in poultry are referred to as low pathogenic (LP) AIV. However, in the case of concurrent infections with bacterial/parasitic opportunistic pathogens and/or adverse environmental conditions (e.g. high ambient temperatures) some LPAIV infections can exacerbate and, depending on poultry species and age of hosts, cause substantial morbidity and mortality. The widespread LPAIV infections by subtype H9N2 in turkeys and chickens cause considerable economic losses. LPAIV of subtypes H5 and H7 can spontaneously mutate into HPAIV, which cause extensive mortality in poultry and, often to a much lesser extent, in domestic waterfowl and wild birds [10]. Hence, all infections of poultry with H5 or H7 AIV (both LPAIV and HPAIV) are notifiable to the veterinary authorities. Likewise, the occurrence of HPAIV in wild birds is notifiable. Notification regulations apply to national laws; directives 94/2005/EC and 437/2006/EC provide the legal framework in the European Union regarding all measures related to combat notifiable AIV. All outbreaks of notifiable AIV have to be reported by the national authorities to the World Organization for Animal Health (OIE) [16].

In contrast to epithelial infections caused by LPAIV, HPAIV induce systemic infections affecting the whole organism with various organs. HPAIV replication causes high titres of infectious virus in internal organs (e.g. liver, heart) and also in muscle [10,17]. Accordingly, feline and mustelid predators became infected with HPAIV and diseased when consuming infected birds [18,19]. Likewise, the reproductive tract is affected during HPAIV infection [20] and infectious virus is excreted in yolk (ovary infection) and albumen (oviduct infection) and can also be found on the egg shell [21]. However, laying activity of infected poultry ceases rapidly after HPAIV infection and egg shells from infected layers are often malformed. In addition, feather cones of HPAIV-infected poultry and wild birds harbour infectious virus [22]. Although viraemic spread of LPAIV has also been described [23], these viruses are to a large extent replication-incompetent outside the gastrointestinal and respiratory tissues. In these cases infectivity titres, e.g. in muscle or liver tissues, will be very low. Recently, some LPAIV strains of the H10 subtype have been shown to be able to replicate in kidneys of infected chickens [24]. It should be noted in this context that due to the avian anatomy, remnants of kidney and lung tissues usually remain in poultry carcasses in the course of industrial, modern slaughtering processes.

AIV as zoonotic agents

Accidental transmission of AIV from infected birds to mammals occurs sporadically. In rare events, new stable influenza lineages may evolve from transspecies transmission events as documented for viral lineages of avian origin circulating in swine, horse, marine mammals and humans [7]. Since 1959 more than 1500 human AIV infections have been confirmed, with a lethal outcome in about 48% [25,26]. The majority of these cases were observed from 2003 onwards and were mainly caused by the Asian origin HPAIV H5N1 and by an LPAIV of subtype H7N9 that circulates in China [27,28]. Apart from subtypes H5 and H7 sporadic infections with H6, H9 and H10 viruses of

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