

Literature review

Environmental factors related to Influenza A virus occurrence in wild birds

Soledad Ruiz P^{1,2}  M.Sc; Cecilia Baumberger^{1,2}  M.Sc; Pedro Jimenez-Bluhm¹  Ph.D;
Víctor Marambio^{1,2}  MV; Carla Salazar¹  MV; Christopher Hamilton-West^{1*}  Ph.D.

¹Universidad de Chile, Facultad de Ciencias Veterinarias y Pecuarias, Departamento de Medicina Preventiva animal, Unidad de Epidemiología. Av. Santa Rosa, 11735, La Pintana, Santiago, Chile.

²Universidad de Chile, Programa de Doctorado en Ciencias Silvoagropecuarias y Veterinarias, Campus Sur, Santiago, Chile.

*Correspondencia: christopher.hamilton@veterinaria.uchile.cl

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ABSTRACT

Research and interest in avian influenza virus have increased considerably in recent decades in response to highly pathogenic avian influenza outbreaks in poultry and its zoonotic potential. Wild waterfowl are the main reservoir of the virus, therefore studying the dynamics of influenza A virus (IAV) infection in these populations is essential in order to understand its potential persistence in the environment and transmission to poultry and humans. It has been identified that environmental factors (such as temperature, rainfall, vegetation and landscape characteristics, among others) can play an important role in the maintenance and dissemination of the virus in the areas of concentration of wild birds. However, studies that include ecological aspects of the virus and explore the interaction between the prevalence of IAV in wild birds and environmental factors remain scarce. This review summarizes research efforts that have been made to identify the environmental factors involved in the persistence and transmission of IAV in areas of wild bird concentration and how these factors may influence the prevalence of the virus in these populations, generating differences in the presentation of the infection among different geographical areas.

Keywords: Orthomyxovirus, bird disease, environment (*Source: MeSh*).

RESUMEN

La investigación y el interés por el virus influenza aviar han aumentado considerablemente en las últimas décadas en respuesta a los brotes de influenza aviar de alta patogenicidad en aves de corral y a su potencial zoonótico. Las aves silvestres acuáticas son el principal reservorio del virus en la naturaleza, por lo tanto, la comprensión de la dinámica de infección del virus influenza A (VIA) en estas poblaciones es fundamental para entender su potencial de persistencia en el ambiente y sus posibilidades de transmisión hacia aves domésticas y humanos. Se ha identificado que factores ambientales (como temperatura, precipitaciones, vegetación y características del paisaje, entre otros) pueden tener un importante rol en el mantenimiento y diseminación del virus en las zonas de concentración de aves silvestres. Sin embargo, los estudios que incluyen aspectos ecológicos

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del virus y que exploran la interacción entre la prevalencia del VIA en aves silvestres y el ambiente, continúan siendo escasos. En esta revisión se resumen los esfuerzos de investigación que se han realizado para identificar a los factores ambientales involucrados en la persistencia y transmisión del VIA en lugares de concentración de aves silvestres y cómo estos factores pueden incidir en la prevalencia del virus en estas poblaciones, generando diferencias en la presentación de la infección entre distintas zonas geográficas.

Palabras clave: Orthomyxovirus, enfermedad de las aves, medio ambiente (*Fuente: MeSh*).

INTRODUCTION

The influenza A virus (IAV) is considered a worldwide threat to both animal and public health, having caused the four largest human pandemics in the last hundred years (1): The "Spanish Influenza" in 1918 was one of the most destructive pandemics of humanity caused by a H1N1 subtype, the "Asian Influenza" in 1957 caused by an H2N2 subtype, the "Hong Kong Influenza" caused by a H3N2 subtype and the "Pandemic Influenza of 2009" which arose from an H1N1 subtype with a combination of genes from three different strains (avian H1N1, seasonal human H3N2 and swine H1N1 from North America and Asia) (2).

Since the beginning highly pathogenic avian influenza (HPAI) epidemic in 1997 caused by the H5N1 subtype in Hong Kong, more than 60 countries belonging to the 5 continents have been affected (Figure 1). In addition, the number of strains reported worldwide has increased alarmingly with the emergence of new HPAI variants H5N8 in East Asia and Europe, the H5N6 subtype in Asia and the introduction of an H5Nx virus of Eurasian origin in North America, all belonging to the new clade 2.3.4.4 (3). Furthermore, the emergence of new subtypes affecting humans (such as pandemic H1N1 and avian H7N9 introduced into the human population in Asia) highlights the need to address this disease from a comprehensive approach, understanding the ecological and environmental factors that affect host-pathogen interactions and that may influence virus presentation patterns.

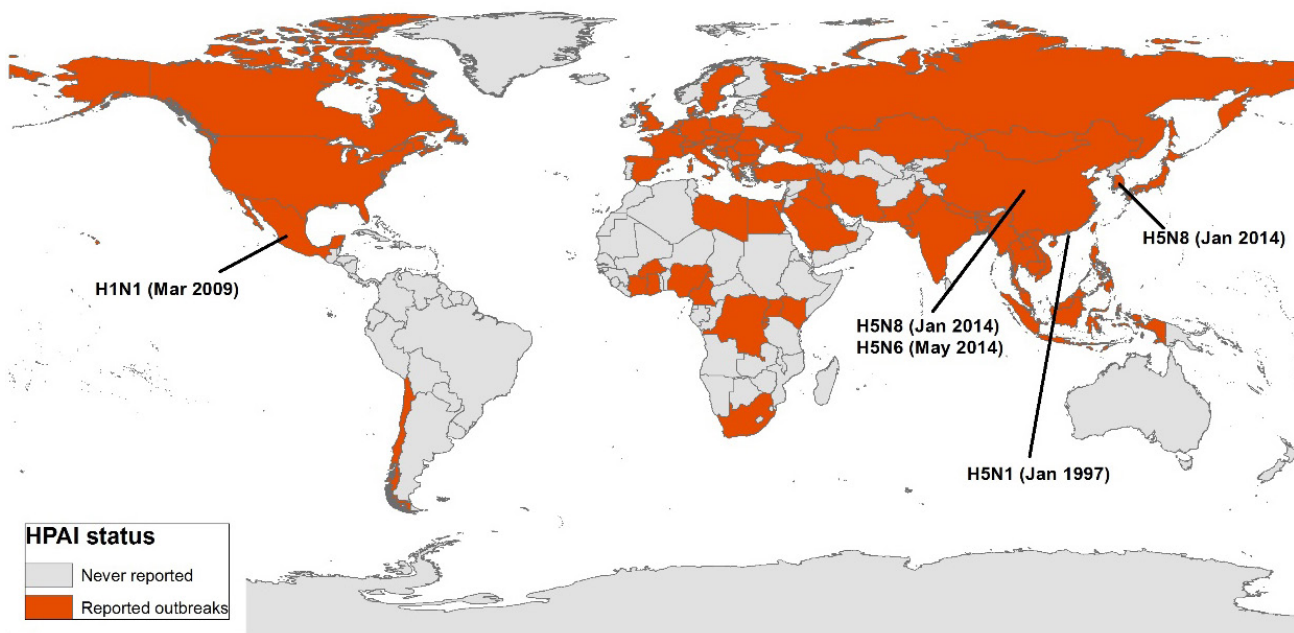


Figure 1. Countries affected by highly pathogenic avian influenza virus (IAAP) from 1997 to date and places of emergency of the main subtypes of influenza A virus.

The influenza virus can be classified in two groups according to its clinical presentation in poultry. HPAI viruses present multi-basic cleavage sites, replicating in multiple tissues causing systemic infection and high mortality. So far, only subtypes H5 and H7 have been associated with highly pathogenic presentations. On the other hand, low pathogenic avian influenza viruses (LPAI) present a monobasic cleavage site, therefore, they are restricted to replicate in respiratory and gastrointestinal tissues, causing a mild disease. However, it is described that LPAI strains may mutate to a HPAI strain after a period of circulation in poultry populations, causing severe disease with high mortality and morbidity (4).

Wild waterfowl have a key role in the IAV ecology because they are recognized as natural reservoirs of most of the subtypes described in the form of LPAI (5), having the potential to disseminate it when they migrate within and between continents, representing a risk for the emergence of HPAI outbreaks in domestic birds (6). Therefore, the epidemiology, prevalence and diversity of IAV are closely related to the behavior of these reservoir species, including their feeding, habitats and migratory patterns, among others (7). Environmental factors, such as temperature, rainfall, amount of vegetation and water characteristics, may also play a role in the maintenance and spread of the virus in areas of concentration of wild birds (8,9,10,11).

Few studies have investigated the ecological and environmental factors that affect the prevalence of the influenza virus in wild birds, mainly in the northern hemisphere (12,13,14,15) and in some regions of Africa (11,16,17).

The objective of this review is to summarize the research efforts that have been made to identify the main environmental factors that affect the persistence and transmission of the IAV in wild waterfowl and how these factors may influence the prevalence of the virus in these populations, generating differences in the presentation of the infection among different geographical areas.

Dynamics of LPAI virus infection in wild birds

In wild waterfowl, especially those belonging to the orders Anseriformes (ducks, geese, swans) and Charadriiformes (shorebirds, gulls, terns), all influenza virus subtypes described have been isolated, with the exception of subtypes H17N10 and H18N11, only described in bats to date (18).

In these natural hosts, the IAV replicates preferentially in the gastrointestinal tract, excreting in high concentrations through the faeces. Therefore, circulation of LPAI virus in wild bird populations depends on transmission between these reservoir species and susceptible hosts, mainly through the faecal-oral route (5). However, the prevalence and dynamics of LPAI virus infection in wild birds may vary depending on geographic location, season and bird species (7).

In North America and Europe, prevalence of IAV in waterfowl is greater when many birds of different ages and origins congregate at their breeding sites, and where there are also many immunologically naïve young individuals. In these areas, prevalence can reach 30% during late summer and early autumn, prior to migration, followed by a decline during winter (7,12). In contrast, in the southern hemisphere, although the dynamics of virus presentation has been scarcely studied, research in Australia and Africa has shown that there is no seasonality, suggesting that the factors influencing infection dynamics in southern hemisphere may differ from those in the northern hemisphere (11,19,20).

In tropical Africa, for example, the prevalence of IAV infection in wild birds is low but constant throughout the year (11,17) which could be explained by the fact that the breeding period of waterfowl is more extended than in the northern hemisphere, with immunologically immature individuals throughout the year, which could perpetuate the infection (11). This situation is different from that found in an IAV surveillance study of wild birds conducted in Chile between 2012 and 2015, where a difference in prevalence was observed between seasons, being greater during the summer/autumn months than in winter/spring (21).

Although these geographic differences can be attributed to factors related to hosts, such as: species present, feeding behavior, habitat use, migratory pattern, population size and seasonal congregation among others; environmental conditions and landscape structure in different geographic contexts can play a preponderant role in the dynamics of virus infection in these populations (11,22).

According to research carried out using mathematical models, the persistence of the virus in aquatic environments is fundamental for the maintenance and circulation of the virus in wild birds (23,23,24,25). This is because

infected birds eliminate large concentrations of virions to the environment through faeces, which can survive in water for long periods of time, maintaining the infection within the population through the faecal-oral transmission route (25). The importance of this transmission route may be influenced by population size. Thus, in large populations, where there is a greater density of individuals and a higher contact rate between them, transmission by direct contact may be more relevant than indirect (environmental) transmission. On the other hand, in small populations, environmental transmission plays a key role in maintaining the virus within the bird community (23).

Therefore, it is important to emphasize the role of the environment as a determining factor in the epidemiology of IAV in wild birds and the need for consideration of ecological and environmental factors in prevalence studies (25).

Persistence of influenza virus in aquatic environments

Among the environmental factors that influence the persistence and circulation of the influenza virus in aquatic ecosystems, both biotic and abiotic elements are included, and surface water plays a fundamental role (8). This has been demonstrated by numerous studies in which it has been determined that the virus can survive in water for long periods of time (Table 1).

Table 1. Persistence of influenza A virus in water according to various studies conducted.

Study	Year	Country	Persistence of VIA according to different parameters			
			T°	pH	Salinity	Others
Webster <i>et al.</i>	1978	USA	- 4 days at 22°C - More than 30 days at 0°C	---	---	---
Stallknecht <i>et al.</i>	1990	USA	-100 days at 17°C -9 days at 28°C	-100 days at pH 8.2	-100 days at 0 parts per trillion (ppt) -9 days at 20 ppt	---
Brown <i>et al.</i>	2009	USA	More stable at low temperatures (<17°C)	More stable at a basic pH (7.4–8.2)	More stable between 0–20000 parts per million (ppm)	---
Nazir <i>et al.</i>	2010	Germany	-Days between 30 y 20°C -Weeks at 10°C - Months between 0 y -10°C	---	---	Distilled water: Longer persistence (up to 642 days) Normal saline solution: Less persistence (up to 321 days) Surface water: lowest persistence (up to 55 days)
Lebarbenchon <i>et al.</i>	2011	USA	Stable between 17 y 23°C	Stable at pH 7.2	---	---
Keeler <i>et al.</i>	2013	USA	All viruses were tested at 17°C	---	---	Distilled water: Longer persistence (more than 80 days) Filtered surface water: Less persistence (up to 60 days) Intact surface water: lowest persistence (less than 20 days)
Keeler <i>et al.</i>	2014	USA	High viability at low temperatures (<17°C)	Stable between 7.0- 8.5	Stable at 0.5 ppt	Stable at low ammonia concentrations (<0.5 mg/L)

In 1978, Webster et al (26) published the first information related to IAV persistence in aquatic environments using an A/Duck/Memphis/546/74 (H3N2) virus, proving that it can remain infective in lake waters for up to 4 days at 22°C and more than 30 days at 0°C. Subsequent studies, conducted under laboratory conditions, have shown that the persistence of the virus in water can vary widely depending on the viral strain and the characteristics of the water (temperature, pH and salinity) (9,27).

These studies, using a modified distilled water model, determined that low temperatures (4 to 17°C), neutral to basic pH (7.0-8.5) and low salinity (<20000 ppm) favour the persistence of the IAV in water, while acidic conditions (pH <6.6), high temperatures (>32°C) and high salinity (>25000 ppm) significantly reduce it. Subsequently, Lebarbenchon et al (28) found similar results when evaluating two viral subtypes (H4N6 and H3N8) isolated from ducks in the United States.

Both subtypes persisted for several months in distilled water at constant temperatures (between 17 and 23°C) and at neutral pH. Another study by Nazir et al (29), evaluated the persistence of three LPAI virus strains (H4N6, H5N1, and H6N8) under different temperatures and in waters with different physicochemical properties (distilled water, normal saline, and surface water obtained from Constance Lake). Virus persistence was greater in distilled water, followed by normal saline water. Virus strains had a lower persistence in surface water. In addition, results showed that virus survival time was inversely proportional to temperature, remaining infectious for a few days at temperatures between 20 and 30°C and for months at temperatures between -10 and 0°C. This situation is consistent with that reported by Keeler et al (30), where the persistence of the virus was greater in distilled water (more than 80 days) and notably less in intact surface water (less than 20 days).

It is important to note that all the above studies were performed under laboratory conditions, using modified distilled water to obtain different physicochemical parameters. A study that more closely replicate natural water bodies properties was performed by Keeler et al (31). In this study, surface water samples collected from 38 waterfowl habitats in the United States were used to evaluate the persistence of different virus subtypes. Results agree to those described above and also demonstrating that

low concentrations of ammonia (<0.5 mg/L) favor the persistence of the virus. Shoham et al (32), also evaluated the persistence of several IAV subtypes in artificially frozen environmental water, most of which were stable over a year at -30 and -20°C, suggesting that arctic regions could represent an important environmental reservoir of the virus for wild bird populations.

However, since there are other variables in natural water bodies that can interact with those mentioned above, it is important to implement future studies under field conditions, considering factors such as: temperature variations between day and night; water flow and depth; UV exposure; turbidity; adherence of IAV to organic and inorganic substrates present in the water; and biological diversity (bacteria, biofilms, filtering organisms and other invertebrates) among others (8,33). Biological diversity has been considered relevant in some studies, since it has been determined that the biotic community present in the water would have an important role in the concentration and/or inactivation of the virus in the environment (34).

Effect of environmental factors on IAV prevalence in wild birds.

Empirical research on environmental and ecological factors that influence the dynamics of IAV presentation in wild birds is still in full development (10,11,13,14). Studies conducted so far agree on those factors that could have an important role on the prevalence of IAV in ecosystems, within which abiotic elements are described, such as rainfall and temperature; biotics, such as bird species present and amount of vegetation; and anthropogenic factors, such as land use and type of land cover (15,19,22).

Temperature, rainfall and vegetative cover measured by the Normalized Differential Vegetation Index (NDVI) have been identified as key environmental factors related to the occurrence of HPAI H5N1 outbreaks in Europe (10). The NDVI is the most widely used index for remote detection of vegetation, which estimates the amount of photosynthetic mass from the intensity of radiation from certain bands of the electromagnetic spectrum emitted by vegetation. Elevated NDVI values, low precipitation and an increase in minimum temperatures during the cold season were shown to be related to outbreaks of HPAI. An increase in NDVI in combination with an increase in minimum temperatures during the winter provides greater

food availability and shelter for birds in cold seasons, increasing bird congregation and viral spread (10).

Something similar was observed in Africa and the Middle East, where the occurrence of HPAI H5N1 has been associated with high levels of NDVI, indicating that the spatial distribution of HPAI H5N1 cases in these areas would be related to specific environmental characteristics, generating an "environmental fingerprint" for the presentation of the virus (35).

Research in North America also indicates temperature as an important factor influencing LPAI virus prevalence in wild birds, associating a higher probability of infection with lower temperatures (15,36,37). This situation is consistent with a predictive model carried out by Herrick *et al* (38), where temperature and precipitation were identified as important predictors for IAV outbreaks in wild birds. Regions with low annual precipitation and low temperatures were indicated as the primary environmental niche for IAV outbreaks in wild birds, emphasizing the importance of boreal regions in the epidemiology of the virus. In Mediterranean climate regions, low temperatures and low rainfall have also been associated with a higher prevalence of IAVs in wild birds (13).

Conversely, research in Australia and tropical regions of Africa indicates that temperature would not have a major influence on IAV prevalence in wild birds, suggesting that there are other factors influencing virus presentation in these regions (11,16,19). Gaidet *et al* (11) used a set of wetland data from 15 African countries to assess the influence of a wide range of ecological factors on IAV prevalence in wild birds. This study found that variations in prevalence were related to host ecological factors rather than temperature conditions, being positively associated with the arrival of migrant birds from Eurasia and with the density of birds in wetlands.

Climate variables (temperature and humidity), on the other hand, were poorly related to prevalence. This differs from that found in boreal regions, since Afro-tropical regions are characterized by temperatures greater than or equal to 20°C throughout the year, which is not favourable for the maintenance of the virus in the environment, suggesting that in these areas transmission by direct contact would have greater relevance than environmental

transmission for the maintenance of infection in populations (16).

These results are similar to others found on the African continent, where an increase in prevalence was related to the arrival season of migrant birds (17,39). In addition, Fuller *et al* (39) also determined that rainy seasons would be associated with an increase in the prevalence of IAVs in wetlands in Central Africa. This is probably due to two mechanisms: [1] that rainfall triggers an increase in food availability and hence a greater abundance of birds and [2] that the onset of the rainy season coincides with the onset of the bird breeding period, favouring congregation at sites by increasing the rate of contact.

Based on these results, authors suggest that rainfall determines a breeding opportunity, influencing the age structure within the population (greater number of juveniles), which affects the dynamics of infection of the IAV (39). This is consistent with the findings of Van Dijk *et al* (12), who demonstrated that the peak prevalence of IAV in collared ducks (*Anas platyrhynchos*) in the Netherlands was associated with an increase in susceptible young individuals during late summer/early autumn. This time coincides with the time of arrival of migrants, providing strong evidence of the role that migratory birds would have as disseminators in seasonal epizootics of LPAI viruses in wild birds.

In a study conducted in south-eastern Australia (19), the prevalence of IAVs in wild duck faeces samples and their relationship to biotic (number of birds) and abiotic (climatic variables) factors was assessed. These results also demonstrated a positive effect of rainfall on prevalence, both immediately and in the long term as a result of the southern child oscillation phenomenon (ENSO). Temperature, unlike in the northern hemisphere, did not have a significant effect on the data, nor did the number of birds present at the time of sampling, indicating that the dynamics of the IAV is not simply a function of the number of birds in the wetland, but a combination of many factors involved.

Another investigation under field conditions corresponds to a study carry on in Spain in which the influence of various environmental factors (climatic conditions, density and diversity of birds, physical-chemical properties of water and

vegetation structure) on the dynamics of IAV in various wetlands was evaluated (13). In this study, explanatory variables were grouped into factors. Results determined that the combination of spatial and temporal variables (sampling location, year and sampling period) may mostly explain the variation in IAV prevalence over the study period (36.8%), followed by meteorological variables (21.5%) and finally the combination of the composition of the wild bird community (Anseriformes density and species richness) with the vegetation structure (21.1%).

Although these results are similar to those found in other regions of the northern hemisphere, it is important to note that none of the variables included in the factor "physical-chemical characteristics of water" were retained in the final model, probably because under field conditions there are other variables such as the effect of dilution and other biotic factors, which could have been potentially more important than the degree of variation of the physical properties evaluated (8).

Anthropogenic factors related to agricultural land use have also been indicated as important factors affecting IAV presentation. Studies have already determined that there is a strong association between HPAI H5N1 outbreaks and rice-intensive areas in Asia, due to a large congregation of domestic ducks foraging in rice paddies, corresponding to a critical factor in the persistence and spread of HPAI on that continent (40,41,42). Something similar was found in Madagascar, where serological data of poultry were combined with environmental factors obtained by remote sensing.

In this study, LPAI virus seroprevalence was higher on farms adjacent to rice fields and wetlands than on those surrounded by savanna landscape, reaffirming the role of ecosystems composed of rice fields and high densities of ducks in the epidemiology of the virus (43). In the same way, the use of agricultural land close to wetlands would favor the aggregation of wild birds in search of food, increasing the rate of contact between individuals, creating ideal conditions for the transmission of the virus (10). This was previously determined in a study conducted in the United States in which a spatial risk map of IAV in wild birds showed that the amount of land cultivated in each county had a significant relationship with the prevalence of IAV found in birds (36).

In addition, land use change resulting from intensive agriculture has led to fragmentation and loss of wetlands, altering wild bird populations. Many bird populations have decreased, while others have adapted to landscapes altered by humans, causing a greater density of birds in the sites, stress and proximity to domestic birds, favouring the transmission of the virus within flocks and between different species (44).

In addition, climate change also plays an important role in causing significant alterations in the ecology of the IAV. An increase in temperatures could potentially affect bird migration patterns, creating new species assemblages and new opportunities for viral transport and reassortment of viral genes (45). In addition, climate change could modify the survival of the virus in the environment. Water temperature and its physicochemical characteristics (pH and salinity) may also be altered, resulting in increased viral persistence, pathogenicity and transmissibility (44,45).

However, research models that include the interaction of several variables (such as, survival of the virus in the environment, change in land use, existence of smaller wetlands, greater density of birds and increased contact rates, among others) are needed in order to predict the impacts of climate change on the ecology of IAV (44,45). Improved understanding of climatic influences on virus ecology will be critical to improve IAV prevention and surveillance strategies at the global level.

In conclusion, despite the considerable effort made worldwide for the surveillance of VIA in wild birds, the existing information about the ecology of the virus and the environmental factors that favor its presentation in these populations, remains very scarce.

Research has focused primarily on the identification and characterization of subtypes, focusing on survival and viral transmission under laboratory conditions or through mathematical models. However, few studies have delved into relationship between the pattern of occurrence and environmental factors under field conditions. In addition, this empirical knowledge is derived mainly from studies conducted in the northern hemisphere and in some regions of Africa, therefore, it could not be extrapolated directly to regions of the southern hemisphere, where there are differences in the hosts, in climatic factors and the seasonality.

To date, there are no studies in South America that explore ecological and environmental factors related to the presentation of IAVs in wild birds, despite the fact that a wide diversity of subtypes circulating in the region have been described, both of North American origin and lineages that are unique to South America (21,46,47,48). Therefore, it would be interesting to generate information regarding the dynamics of virus presentation and the environmental factors involved at the local level. For this, it is necessary to improve field level research and conduct prevalence studies that include ecological and environmental factors in different

geographical contexts. This would better assess the risk associated with virus transmission from wildlife reservoirs to domestic animals, improve surveillance programs, and direct sampling efforts to habitats and seasons that are more favourable for viral maintenance and transmission.

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