

# The Impact of New Epidemiological Information on a Risk Analysis for the Introduction of Avian Influenza Viruses in Imported Poultry Meat

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**SUMMARY.** New Zealand has never experienced an outbreak of avian influenza, and the Ministry of Agriculture and Forestry has long been wary of the possibility of introducing high-pathogenicity avian influenza (HPAI) viruses in imported goods. Besides the potential threat posed to poultry, there are concerns that introduced viruses might have negative effects on already endangered native avian species. Under the framework of the World Trade Organization, the sanitary and phytosanitary (SPS) agreement requires member countries to base their sanitary measures for imported animal products on the Office International des Epizooties (OIE) standard or on a scientific assessment of risk. This paper presents the New Zealand experience with assessing the risk of avian influenza viruses in imported chicken meat and considers how the assessment of risk has changed in recent years as a result of the advances in understanding of the disease. The currently accepted view that low-pathogenicity avian influenza (LPAI) viruses are widespread and that they mutate to virulence after introduction into poultry has important implications concerning the appropriate definition for avian influenza viruses of regulatory concern and has possible implications concerning the significance of viruses present in this country.

**RESUMEN.** Impacto de la nueva información epidemiológica sobre análisis de riesgo, para la introducción de virus de influenza aviar en carnes aviares importadas

Nueva Zelanda nunca ha experimentado un brote de influenza aviar y el Ministerio de Agricultura y Recursos Forestales ha estado preocupada de la posibilidad de introducción de virus de influenza aviar de alta patogenicidad a través de las importaciones. Además de la posible amenaza para la avicultura, existe la preocupación de que los virus introducidos puedan ejercer efectos negativos en las especies aviares nativas que se encuentran en peligro de extinción. De acuerdo con el marco de la Organización Mundial de Comercio, el acuerdo SPS requiere que los países miembros basen sus medidas sanitarias para productos animales importados de acuerdo con lo establecido por la Oficina Internacional de Epizootias (OIE), ó en una valoración científica del riesgo. Este trabajo presenta la experiencia de Nueva Zelanda en el análisis del riesgo de virus de influenza aviar en carne de pollo importada y considera cómo este análisis de riesgo ha cambiado en los años recientes como resultado de los avances en el conocimiento de la enfermedad. El enfoque actualmente aceptado de que los virus de influenza de baja patogenicidad están ampliamente diseminados y que mutan a virus muy virulentos después de su introducción en la avicultura, tiene implicaciones importantes concernientes a la definición apropiada de los virus con importancia en la regulación y tiene posibles implicaciones relacionadas con la importancia de los virus presentes en este país.

Key words: biosecurity, international trade, risk analysis, acceptable risk

Abbreviations: EU = European Union; HPAI = high-pathogenicity avian influenza; LPAI = low-pathogenicity avian influenza; MAF = Ministry of Agriculture and Forestry; OIE = Office International des Epizooties; SPS = sanitary and phytosanitary; WTO = World Trade Organization

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The World Trade Organization (WTO) framework of 60 agreements, annexes, decisions, and understandings is designed to provide an international forum that encourages free trade between member states by regulating and reducing tariffs on traded goods and services, protecting intellectual property rights, and providing a common mechanism for resolving trade disputes. One of the agreements under the WTO framework is the agreement on the application of sanitary and phytosanitary measures, commonly known as the SPS agreement. This agreement, which came into force on January 1, 1995, sets out basic rules for food safety and animal and plant health standards in international trade. An SPS measure is a standard that is applied to an internationally traded product, and such measures often result in certain restrictions on trade. The SPS agreement stipulates that SPS measures may be applied only to the extent necessary to protect human, animal, or plant health. However, governments may sometimes be pressured to go beyond what is needed for food safety and the protection of animal and plant health and to use SPS measures to shield domestic producers from economic competition. Safeguards that are not actually required for health reasons can be very effective protectionist devices, and because of their technical complexity they can be deceptive and difficult to challenge (19). Therefore, the key obligation on members under the SPS agreement is that measures must not be applied in a way that would constitute a disguised restriction on trade. Members may apply the SPS measures that conform to international standards or others that are based on sound scientific assessment of the risks. In the case of international trade in animals and animal products, the relevant international standards are the guidelines recommended by the Paris-based Office International des Epizooties (OIE).

#### **IMPORT RISK ANALYSIS: THE SCIENTIFIC MODEL**

The OIE *International Animal Health Code* recommends the following steps for import risk analysis:

- Hazard identification
- Risk assessment; comprising release assessment, exposure assessment, consequence assessment, and risk estimation
- Risk management

The risk analysis process as the Ministry of Agriculture and Forestry (MAF) in New Zealand

carry it out is illustrated in Fig. 1. In the hazard identification, the epidemiology or life history of each of the organisms of concern is examined so that a conclusion can be reached as to whether it should be regarded as a potential hazard in the context of the commodity under consideration. The release assessment evaluates in more detail each potential hazard in order to estimate the likelihood of the hazard being present in or on the commodity and the likelihood of persistence of the hazard during processing, storage, and transport. The release assessment thus provides an estimate of the likelihood of the hazard being associated with the commodity at the time of importation. The exposure assessment identifies biological pathways leading to exposure of susceptible hosts in New Zealand and estimates the likelihood that they will be exposed to the hazard. The consequence assessment describes the economic and health consequences associated with the exposure to the hazard, and the risk estimation step summarizes the preceding three assessments to enable a decision to be made as to whether sanitary measures are necessary. Finally, risk management is the formulation of sanitary measures that are considered appropriate for the identified hazards.

Underpinning the SPS agreement is an assumption that it is possible, through the application of rational analytical methods (scientific and economic), to objectively measure the levels of risk associated with proposed imports, to evaluate a number of options for risk management in terms of how much each option would reduce that risk, and to apply the measure or measures that delivered the correct (or appropriate) amount (or level) of protection (or risk reduction) in order to reduce the originally measured risk down to (but not below) a predetermined acceptable level.

Thus the appropriate level of protection is closely related to the acceptable level of risk. This relationship is illustrated in Fig. 2. In this hypothetical example, of the five measures available to manage the risk posed by the particular import, measure four delivers the appropriate level of protection. The outcome of such a purely rational and scientific process would achieve the SPS goal of transparent management of biosecurity risk without unnecessarily restricting trade. However, in order to implement the above approach, it is necessary not only to objectively assess the level of risk posed by a particular import proposal, but also to have established the acceptable level of risk for the disease agents of concern. Although the SPS agreement envisages such assessments to be quantitative, in practice this is rarely achievable with current methods.

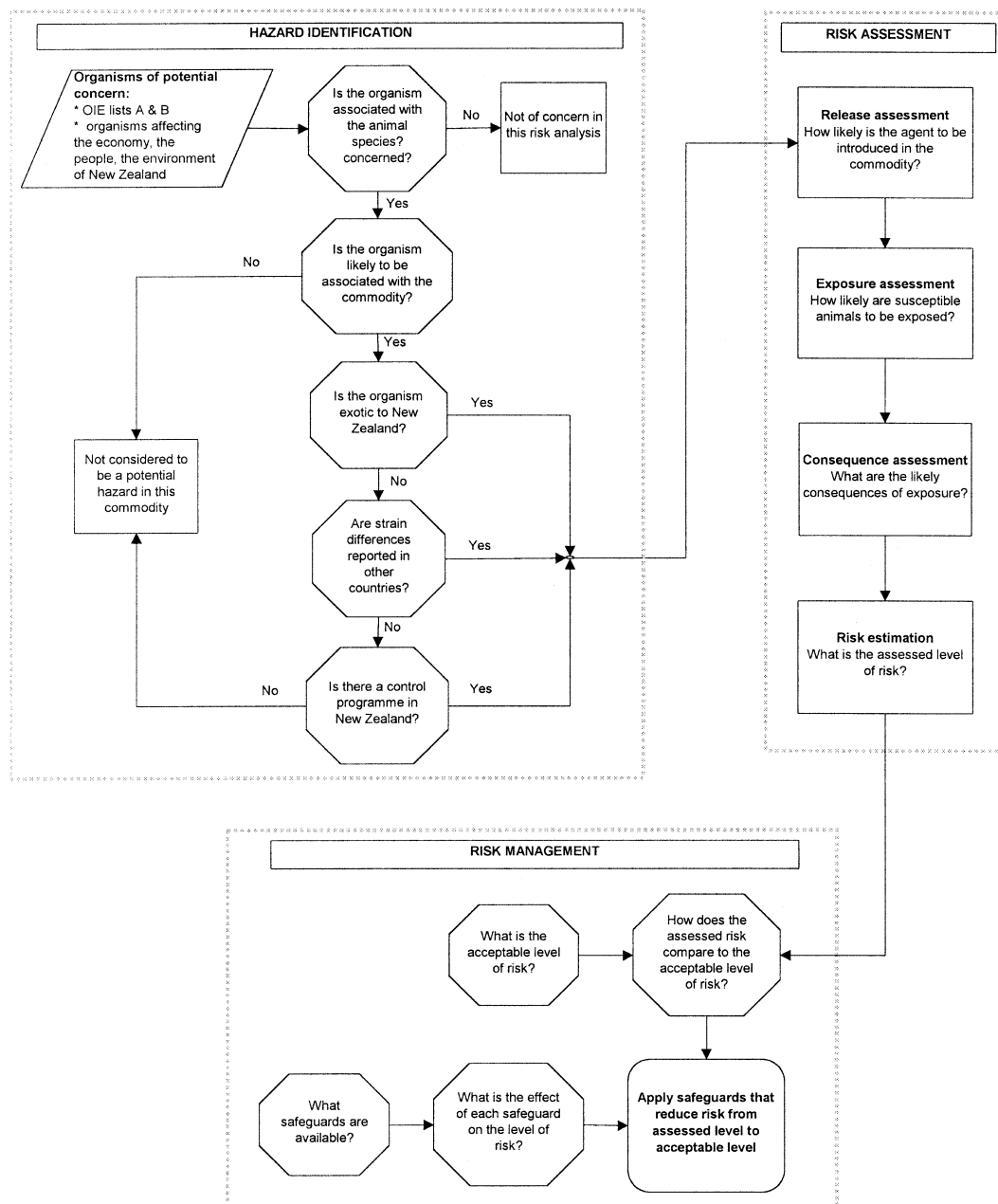


Fig. 1. The New Zealand Ministry of Agriculture and Fisheries risk analysis process.

**THE RISK OF AVIAN INFLUENZA VIRUSES IN IMPORTED CHICKEN MEAT**

The OIE *International Animal Health Code's* (13) chapter on high-pathogenicity avian influenza (HPAI) is the internationally agreed standard for this disease. When this chapter was written, the risk

management standard for Newcastle disease (ND) and HPAI were considered to be the same, so the chapter for HPAI refers to the standard in the ND chapter. Both chapters are under review by the OIE.

The first MAF risk analysis to address the issue of HPAI in chilled or frozen poultry meat was completed in 1991. That analysis concluded that

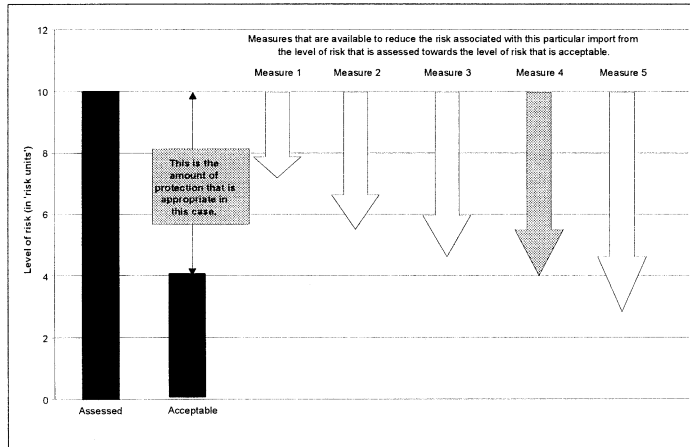


Fig. 2. Risk management and the relationship between the acceptable level of risk and the appropriate level of protection.

the risks justified the imposition of requirements for “fowl plague” area and flock freedom (10). Following the setting up of the World Trade Organization in 1995, a number of countries expressed an interest in exporting poultry meat to New Zealand. As a result of these enquiries and of negotiating the New Zealand/European Union Veterinary Agreement, in 1996 MAF initiated a specific import risk analysis for chicken meat (6). Although the avian influenza section of that analysis was based on the now outdated concept that HPAI viruses were distinct transmissible agents, either domestic or international stakeholders did not dispute the conclusions reached during the public consultation that followed (4).

The following discussion constitutes a review of the risks posed by avian influenza viruses in line with the OIE methodology and in the light of relevant new epidemiological information that was not considered in MAF’s original risk analysis and that might impact on future definitions of HPAI.

**Hazard identification.** It has long been recognized that wild birds constitute the principal reservoir for avian influenza viruses that infect domestic birds, and the role of waterfowl in particular is well documented. However, it has always been difficult to define HPAI viruses in a way that distinguishes them from avian influenza viruses in general.

In the 1980s it was recognized that HPAI viruses were only associated with the H5 and H7 subtypes, and that viruses of low pathogenicity could become fully pathogenic following a single or multiple point

mutations. The molecular basis for pathogenicity was shown to be the presence of multiple basic amino acids and the cleavage site of the hemagglutinin, and it was considered that amino acid sequencing of the cleavage sites of H5 and H7 subtype viruses of low virulence *in vivo* should enable identification of viruses that have the capacity, following mutation, to become highly pathogenic in poultry (12).

More recently it has become generally accepted that influenza viruses of low pathogenicity occur naturally in wild birds and that mutation to virulence occurs after such viruses are introduced into poultry flocks (1). Mutations may involve the insertion of basic amino acids at the hemagglutinin cleavage site due to a transcription fault, and it is assumed that this occurs more commonly in AI viruses while replicating in chickens or turkeys than in free living birds. However, there could also be nucleotide substitution rather than insertion or insertions without repeating nucleotides (2).

This change in understanding presents problems identifying the exact hazard for the purposes of a risk assessment. The OIE and European Union (EU) definitions of HPAI were formulated over 10 years ago, and it might be more appropriate to include precursor viruses if they could be identified. However, although several model systems have been developed in an attempt to predict emergence of HPAI viruses from H5 or H7 viruses, the predictability of such systems appears to be limited (18), so it may be more practical to consider all H5 and H7 viruses as potential hazards. The redefinition of

AI for regulatory purposes would allow the application of measures to limit the spread of low-pathogenicity avian influenza (LPAI) viruses of H5 and H7 subtype to poultry in order to limit the likelihood of a mutational event occurring (2). This change in definition would require the focus of the surveillance program to shift from confirmation of the cause of disease to the detection of subclinical infection.

**Risk assessment—release assessment.**

The likelihood of avian influenza viruses being on or in imported meat would depend primarily on the likelihood of birds being viremic when slaughtered. In addition, considering that infected birds may excrete large volumes of virus in feces, the likelihood of contamination of the carcass during processing and the likelihood of survival of the virus is relevant.

Influenza viruses are most stable at pH 7–8 (8). They are not very stable below pH 6, and the ultimate pH of poultry muscle is between 5.7 and 5.9 (10). However, since infectivity is retained for several weeks at 4 C, for months at –20 C, and for years at –40 C (7), if the commodity did contain the virus it could be expected to survive processing and storage.

Although the MAF risk analysis (6) concluded that there was a remote likelihood that birds would be viremic when slaughtered, that related only to HPAI viruses. It is difficult to estimate that likelihood with regard to H5 and H7 viruses in general, but it is reasonable to assume that the likelihood would be higher.

**Risk assessment—exposure assessment.**

Since the spread of avian influenza viruses between flocks is predominantly by mechanical transfer of infected feces (1), it was considered that the primary transmission of introduced viruses would be by the oral route. However, as influenza viruses are inactivated by heating for 15 min at 56 C or for 5 min at 60 C (7), they would not survive cooking. Therefore, in order for contaminated imported chicken meat to be able to infect birds, it would be necessary for raw infected carcasses or scraps to be fed, and the MAF risk analysis concluded that this was unlikely to occur apart from in household garbage fed to backyard poultry.

However, if exotic influenza viruses were to become established in backyard poultry flocks by infected meat scraps, further spread might be possible by a number of routes, primarily via human activities. Whether it would be possible for free living birds to become infected as a result of eating feed destined for backyard chickens or by being in close association with such chickens is not known.

A critical question from the New Zealand perspective is whether native bird species (some of which are highly endangered) might be exposed to viruses introduced in this way. Such exposure might be possible by certain native bird species coming into direct contact with poultry flocks, or it might be indirect with other free-living birds acting as intermediaries. Evaluating the likelihood of such exposure is extremely difficult.

**Risk assessment—consequence assessment.**

If HPAI viruses were introduced into backyard poultry flocks, the effects on those flocks would be significant. Spread to other poultry flocks would be likely, perhaps including commercial flocks, in which very serious losses could be expected. Even in the absence of spread to commercial flocks, if HPAI were detected in this country, as a list A disease it would be reported to the OIE within 24 hr of diagnosis, and this would have an immediate effect on exports of hatching eggs and day-old chicks, which are currently valued at \$7 million *per annum* and are expanding rapidly (T. Parker, pers. comm.).

There are several difficulties associated with assessing the consequences of introduction of LPAI viruses. First, although LPAI infections in poultry usually produce subclinical or mild disease, severe clinical signs may occur if LPAI infection is associated with *Escherichia coli* or *Pasteurella multocida* infections (2). Second, if a new H5 or H7 LPAI virus were introduced and became established in poultry in this country, then the consequences of subsequent mutation to virulence could be severe. Third, the potential effect of influenza viruses in general on endangered native birds in this country is unknown.

**Risk assessment—risk estimation.** There is considerable uncertainty surrounding both the likelihood of AI viruses being present in the imported commodity and the likelihood of any such virus resulting in infections in avian species in New Zealand. However, there is no doubt that the consequences of an outbreak of avian influenza would be severe, even if the virus were to have no effect on endangered native birds. In such low-probability high-impact events, there are significant difficulties associated with the assessment of risk, but the uncertainty and the potentially severe consequences are considered sufficient to warrant the imposition of measures to manage the risk of introduction of influenza viruses in poultry meat.

**Risk management.** In 1999, the MAF risk analysis concluded that the risks associated with the importation of chicken meat were adequately dealt

with by adopting the guidelines recommended in the OIE code. Those safeguards referred to country/zone/establishment freedom from HPAI. However, in view of the possibility of a redefinition of HPAI as any H5 or H7 viruses (2), that conclusion may require revisiting, in which case safeguards may need to focus on defining the status of broiler flocks in terms of H5 and H7 viruses.

### THE SIGNIFICANCE OF ENDEMIC INFLUENZA VIRUSES IN WILD BIRDS IN NEW ZEALAND

**Surveillance for avian influenza viruses in New Zealand.** Although avian influenza has never been diagnosed in poultry in New Zealand, a number of nonpathogenic viruses have been isolated from wild ducks. In 1976 16 influenza viruses (four H4N6, two H1N3, one H11N3) were isolated from ducks, but the gulls, terns, and shearwaters surveyed were negative (5). Surveys of wild ducks were carried out in 1989, 1990, and 1997 (3,15,16). No viruses were isolated from the 1989 survey, and only two AI viruses were isolated from the 1990 survey (one H6N4, one H4N6). In the 1997 survey, six avian influenza viruses were isolated, of which four were H4N6 and two were H5N2. Moreover, more than 30% of 335 duck serum samples were antibody positive for avian influenza viruses (17).

These survey results suggest that avian influenza infections in wild ducks are not uncommon. Furthermore the isolation of H5N2 viruses raises the possibility that HPAI outbreaks might occur in this country if an endemic duck virus were to be introduced into poultry flocks, with subsequent mutation to virulence. However, predicting such a mutation event with any confidence is currently not possible. Although the best predictor of mutability for H5 LPAI viruses is the presence of three or more basic amino acids at the hemagglutinin cleavage site (18), and although the amino acid sequence of the New Zealand H5N2 virus (17) suggests that it has a low probability of mutating to HPAI, there is considerable uncertainty surrounding such negative predictions.

**The likelihood of new viruses being introduced by migratory birds.** Although in the northern hemisphere HPAI in poultry is associated with migratory water birds, especially ducks, banding studies show that wild ducks in New Zealand (whether endemic or introduced) are not migratory, and there is no evidence that Palaeartic ducks reach New Zealand (11). There are

several possible alternative explanations for the presence of avian influenza viruses in this country. The gray duck (*Anas superciliosa*), a native of Australia and New Guinea, introduced itself to New Zealand in 1957, and the species has since become abundant in this country (9). In addition, a small number of vagrant Australian ducks appear in New Zealand every year, and it is possible that influenza viruses might be introduced by such natural events. However, it is also possible that the currently endemic avian influenza viruses were introduced inadvertently as a result of the many deliberate releases of mallard ducks (*Anas platyrhynchos*) in New Zealand over the last 125 years (British stock via Australia from 1870s onwards, and American stock from 1940s up to about 1960) (9).

The majority of birds migrating to this country are shorebirds of the family Scolopacidae (sandpipers and allies) in the order Charadriiformes. These birds breed in the arctic regions of Europe, Asia, and North America, and they migrate south for the boreal winter. The most numerous species that migrate to New Zealand are bar-tailed godwit (*Limosa lapponica*), lesser knot (*Calidris canutus*), ruddy turnstone (*Arenaria interpres*), curlew sandpiper (*Calidris ferruginea*), red-necked stint (*Calidris ruficollis*), and pacific golden plover (*Pluvialis fulva*) (9). The 1997 survey of wild birds carried out by MAF included 26 lesser knots and one bar-tailed godwit, but no influenza viruses were isolated from any of these birds (16). For migratory waders to be shedding influenza viruses when they arrive in New Zealand, they would have to either become infected prior to migration and to continue shedding throughout migration or become infected somewhere along the migratory route. Although the migratory routes of these birds are usually not completely understood, migration typically involves long nonstop flights over the west Pacific Ocean between only a few staging areas such as in the Gulf of Carpentaria, where large numbers of birds from different flight groups congregate (14).

Because of the intestinal nature of avian influenza infections in waterfowl, large quantities of virus are excreted in feces, and ducks have been shown to excrete the virus for as long as 30 days. In North America, up to 60% of juvenile ducks may be infected just prior to migration, but once migration begins the infection rate falls markedly. Although virus may be isolated from untreated lake water just before migration, the water does not retain infectious virus after the birds left, suggesting that the viruses may survive for only short periods in the environment (8). Therefore there is probably

limited opportunity for migratory birds to pick up influenza virus infections during migration, but it is possible that this could happen at staging grounds, so the likelihood of new viruses being introduced in the future cannot be ruled out.

## DISCUSSION

The assessment of the risks posed by avian influenza viruses in imported poultry meat is surrounded by uncertainty, as a result of which the analytical approach to risk analysis implied by the SPS agreement is currently untenable. As a consequence of critical gaps in information, the level of assessed risk cannot be expressed quantitatively. Furthermore, determining the level of protection to be applied in the case of a particular proposed import requires making a comparison between the assessed risk and the level of risk that is acceptable to society. This presents unique and intractable difficulties to biosecurity agencies. When the consequences of failure are potentially high, and when national icons such as endangered native birds may be at stake, the public perception of risk is driven by the uncertainty. Although the only acceptable outcome to this country with regard to avian influenza is "no outbreaks," it is widely accepted that "zero risk" is unattainable.

With regard to avian influenza, two events are of concern to MAF: 1) the mutation to virulence of the endemic H5 subtype virus and 2) the introduction of new viruses, either existing HPAI viruses or LPAI viruses that may mutate to virulence. While the former concern must be addressed by New Zealand's surveillance and disease control policies, the latter is an issue for import risk analysis.

The current definition of HPAI was developed to enable the characterization of viruses that are isolated from outbreaks of severe clinical disease. However, in view of the current understanding that such outbreaks occur as a result of the mutation of LPAI viruses after they are introduced into poultry flocks, the current definition is inappropriate for import risk analysis. Since the potential consequences of introduction of LPAI viruses are so difficult to predict, particularly since specific LPAI viruses that may mutate to HPAI cannot be accurately identified, it may be necessary to redefine avian influenza of regulatory concern as all H5 and H7 viruses.

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