CHAPTER 2

LITERRATURE REVIEW

2.1 Avian influenza as a public health threatening

Highly pathogenic avian influenza (HPAI) is a highly contagious viral disease of domestic gallinaceous birds and is designed as a List A disease by the Office International des Epizooties (OIE)(2, 9, 20). List A disease are communicable diseases that have the potential for serious and rapid spread, irrespective of national border, which are the serious socioeconomic or public health importance and which are of major importance in the international trade of animals and animal products.

2.2 Avian influenza situation in Thailand

Avian influenza had not been reported in Thailand until 2004(18). But in late of 2003, many poultry farms in the Central and Northern Regions of Thailand had been reported with a sudden death of poultry. In the same period, there were reports of avian influenza A H5N1 in South Korea and following with Vietnam. In Thailand, Department of Livestock development (DLD), started to confirm the death of poultry. Cloacal swab from poultry throughout Thailand were taken to test of avian influenza and DLD announced the avian influenza outbreak in Thailand on 23 January 2004. The first case occurred in a layer farm in Songphynong district, Suphanbury province(18), thereafter the 149 reported outbreaks in poultry in 144 villages in 32 of the 76 provinces during the first report indicated that the virus had been widespread throughout the country(18) . DLD has initiated disease control and eradication follow the guideline of Office de International Epizooties, OIE, Initially all poultry, their products, feed, bedding, waste, and manure from infected flocks were destroyed immediately by the veterinary authorities. Culling infected birds in each flock was generally completed 1–2 days after the virus was confirmed by virus isolation. Meanwhile, a restriction on moving poultry and their products within a 5-km radius around the infected flocks was enforced by DLD inspectors in collaboration with local police, and control checkpoints were temporarily established in the areas. Moreover, infected premises and equipment were cleaned and disinfected. Although DLD used the extensive measure to control AI, the disease still occurred. In July 2004, the second wave of AI epidemic were reported, DLD developed control measures to enable quick action. When the mortality of poultry in any flock was more than 10% within a single day, all birds, their products, and other potentially contaminated materials had to be destroyed. Cloacal swabs of affected flocks were then collected for laboratory confirmation. Subsequently, neighboring flocks were destroyed immediately or quarantined until H5N1 laboratory confirmation. Upon a confirmative laboratory results, quarantined flocks were culled. Furthermore, movement of poultry and their products was restricted within a 1 to 5 km radius around the infected area. Unfortunately, there are report of AI outbreak indicate that the virus continues to circulate in the country. As 24 December 2006, Thailand has had 4 epidemic waves and the last detection was reported in July 2006.

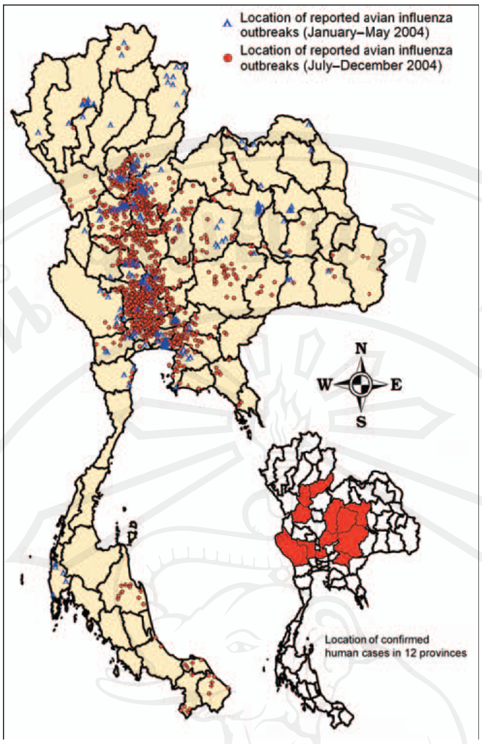


Figure1. Distribution of reported highly pathogenic avian influenza H5N1 outbreaks in villages in Thailand, January–December 2004(18)

2.2 National strategic plan of avian influenza control

For effective AI control, the National Committee on Avian Influenza has been established by government. The committee formulated the national strategic plan for avian influenza control in Thailand A.D.2005-2007(18). The strategic plan's targets for 3 years period are

1. Targets for the control of spread in poultry

1.1 No spread of avian influenza in industrial economic poultry within 2 years

1.2 Reduce the spread of the disease, so that avian influenza is not a problem with domestic poultry, fighting cocks, exotic birds and migratory birds within 3 years

1.3 No spread of avian influenza in other mammals within 2 years

2. Targets for the control of spread in humans

2.1 No spread from animals to humans within 2 years

2.2 Efficient pandemic preparedness within 2 years

There are 6 strategies in the National Strategic plan for Avian Influenza Control. (Figure2)

Strategic 1: Development of a disease free poultry management system. The objective is to enable poultry to be free from diseases and safe for consumption.

Strategy 2: Disease surveillance and response during outbreaks. The objectives are to rapidly detect and control outbreaks of avian influenza in poultry and to closely follow up on the changes in the situation.

Strategy 3: Knowledge generation and management. The objective is to generate and manage knowledge, which can be used to efficiently solve problems of avian influenza.

Strategy 4: Capacity building of organizations and manpower.The objective is to strengthen capacity building of organizations and manpower working on surveillance and control at all levels.

Strategy 5: Create understanding and participation of the civil society and private sectors. The objective is to strengthen the roles of civil society and private sectors, in prevention and control of disease outbreaks.

Strategy 6: Develop sustainable integrated management systems and mechanisms. The objective is to create efficient and united mechanisms for the management of avian influenza problems.

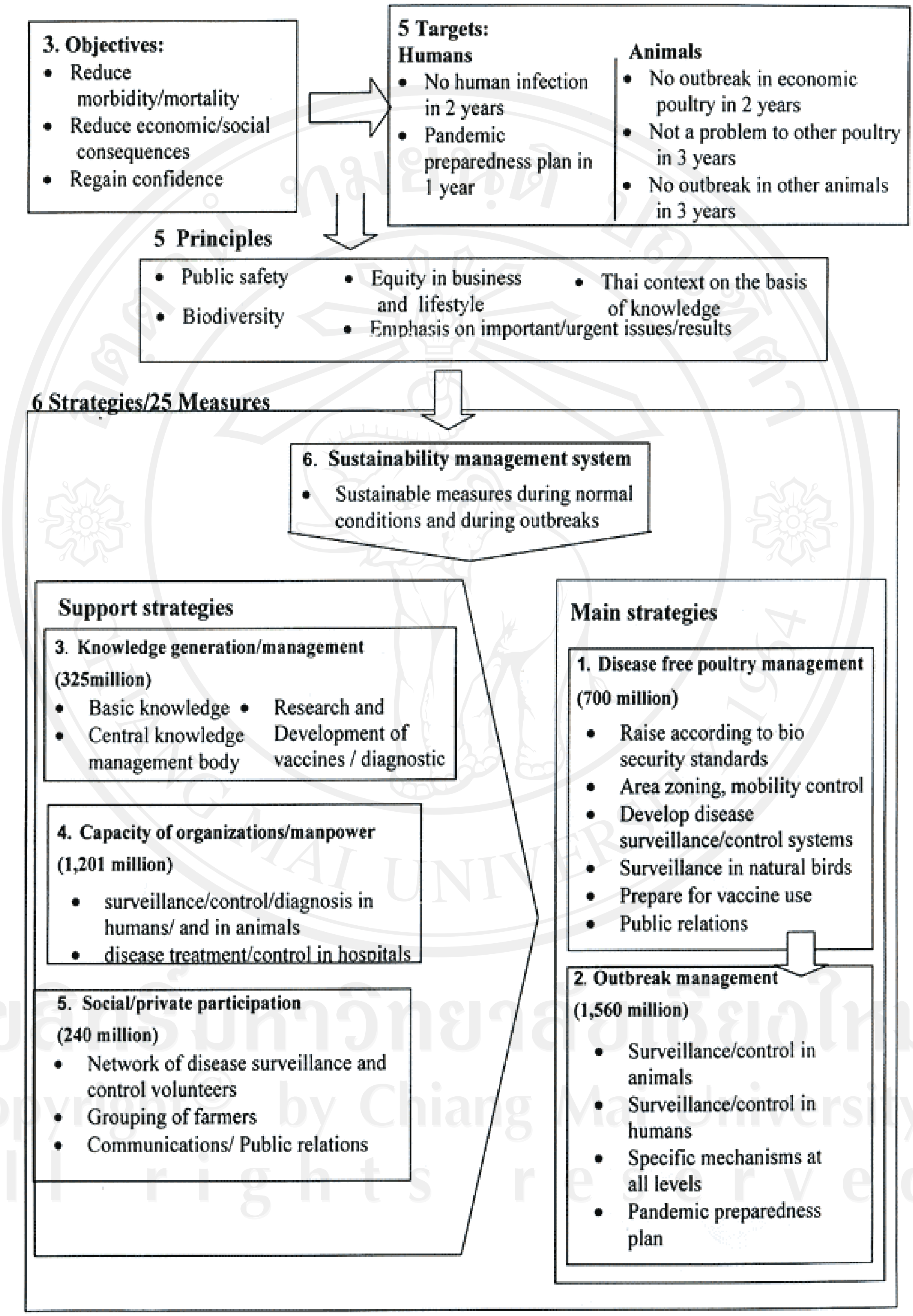


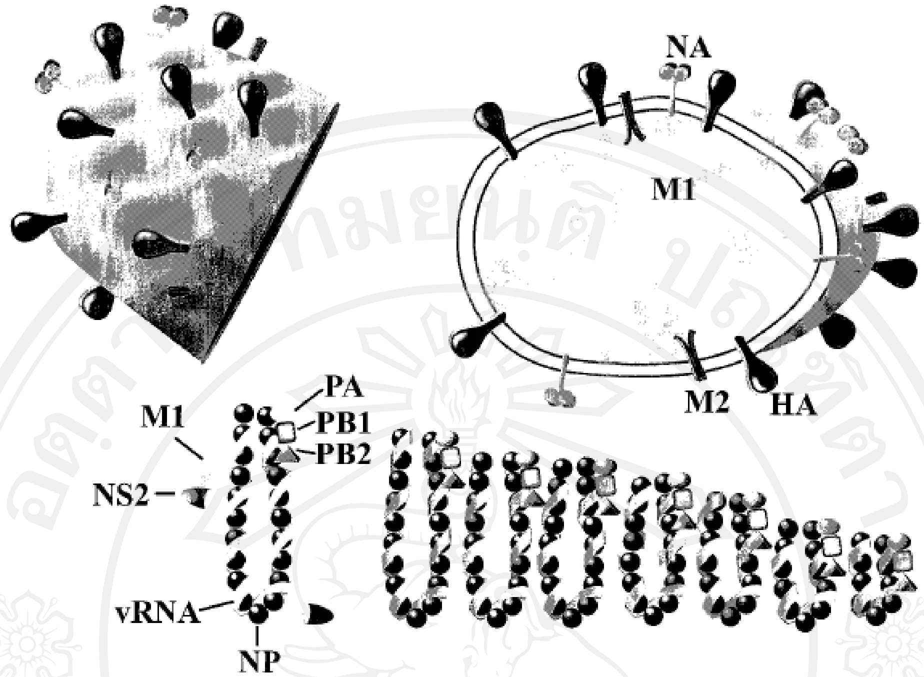
Figure 2. Summary of national strategic plan for AI control

2.3 Research and some studies

2.2.1 Cause of Avian influenza

Avian influenza is a viral disease of domestic gallinaceous birds. Influenza virus, which belongs to the Orthomyxoviridae family, consists of three types, A B and C based on antigenic differences in nucleoprotein (NP) and matrix (M1) and all avian influenza viruses are classified in type A(21). Further subtyping is based on the antigenicity of two surface glycoproteins, hemagglutinin (HA) and neuraminidase (NA). Currently, 16 HA and 9 NA subtypes have been identified among influenza A viruses. Type A influenza viruses can infect a wide variety of birds. However, the original reservoir of the avian influenza viruses is considered to be in wild waterfowl, gull and shorebirds.(11)

Orthomyxovirus virions are pleomorphic, 80-120 nanometers in their dimension. Virions consist of an envelope with large peplomers surrounding eight helically symmetrical nucleocapsid segments of different size. Genomic segments have a loop at one end and consist of a molecule of viral RNA enclosed within a capsid composed of helically arranged nucleoprotein (NP). Associated with the RNA are three proteins that make up the vial RNA polymerase (PB1, PM2, and NA). Virion envelopes are lined by the matrix protein (M1) and are spanned by the small number of ion channels composed of tetramers of the second matrix protein, M2. The genome in eight, seven, and six segments consists of liner negative-sense, single stranded RNA.(19)



The figure 3: The structure of avian influenza virus(5)

Influenza A viruses binds to cell surface sialyloligosaccharides with specificities that vary according to the host species and origin. Human viruses preferentially bind to oligosaccharides containing N-acetylneuraminic acid α2,6-galactose (NeuAcα2,6Gal), while avian viruses bind to NeuAcα2,3Gal. Furthermore, the swine has been the leading contender for the role of intermediate host for influenza A viruses. This susceptibility is due to the presence of both α2,3- and α2,6-galactose sialic acid linkages in cells lining the trachea which can result in modification of the receptor binding specificities of avian influenza viruses from α2,3 to α2,6 linkage(5, 19).

Influenza A viruses infecting avian species can be divided into distinct groups on the basis of their ability to cause disease in chicken. The very virulent viruses now termed highly pathogenic avian influenza (HPAI), in which mortality may be as high as 100% in poultry. These viruses have been restricted to subtype H5 and H7, although not all viruses of this subtype cause HPAI. All other viruses cause a much milder, primarily respiratory disease designated as low pathogenic avian influenza (LPAI)(5).

Host of avian influenza virus, mode of transmission and clinical signs

Many domestic and wild avian species are infected with avian influenza viruses. These include chickens, turkey, ducks, guinea fowl, domestic geese, quail, pleasant partridge, gulls, shorebirds, sea birds, and emu. Among domestic avian species turkey and chicken are the most frequently involved in the outbreak of influenza. Ducks and geese are susceptible species to infection with all avian influenza viruses but only some very virulent viruses produce clinical disease. The virus is commonly isolated from these species in endemic area. Waterfowl are considered to be the potential major source of the virus for epidemic in poultry(5).

Infected birds excrete virus from the respiratory tract, conjunctiva, and feces; thus the modes of transmission including both direct contact between infected birds and susceptible birds and indirect contact including aerosol (droplets) or exposure to virus-contaminated. Since infected birds can excrete high level of virus in their feces, spread is readily accomplished by contaminated with fecal material, e.g., feed, water, equipment, cages, and delivery vehicle. The virus re readily transported to other areas by contaminated people and equipment, movement of infected birds, or live birds market(5).

The clinical signs of highly pathogenic avian influenza are severe and result in high mortality rates in many species of birds, especially in domestic fowl. Wild birds, water fowl, goose and duck may not be susceptible to clinical signs but play important role in carrier for the virus(4, 5, 11).

In peracute case the animal may died without clinical sign. The clinical signs are acute respiratory disease with significant declines in feed and water consumption and egg production, watery diarrhea, swollen and congested conjunctiva with occasional hemorrhage, diffuse hemorrhage between hocks and feet, nasal and ocular discharge, coughing/sneezing, incoordination, nervous signs such as paralysis. Visceral lesions included petechial hemorrhage of various serosal and mucosal surfaces particularly the mucosal surface of the proventiculus near the junction with the gizzard. The pancrease often had blotchy light yellow and dark areas along its length, severe kidney swollen, sometimes with urate deposit in tubules. Ovary may be hemorrhagic or degenerated with darkened areas of necrosis and peritoneal cavity often filled with yolk from rupture ova(5).

Impact on public health

Besides the mechanism of antigenic drift avian influenza virus has ability to change more drastically and virus can transmit directly from human to human. Because people had no immunity to the new subtype, result in high infection rate, as there have pandemic of influenza at least three times. The first reported was "Spanish flu" in 1918, an estimated 40-50 million people died during the outbreak. The pandemics that began in 1957 and 1968 killed 1-4 million people each (13).

During the first documented outbreak of human infections with H5N1, which occurred in Hong Kong in 1997, the 18 human cased were reported and six of whom died. Extensive studies of human cases determined that direct contact with diseased poultry was the source of infection (17). Although chicken-to- human transmission had been identified as the initial source of human infection, whether H5N1 could be efficiently transmitted from human to human was a source of concern, because this would have indicated that another influenza pandemic was likely to emerge. A case-control study of 15 patients hospitalized for influenza A (H5N1) virus was conducted by Katz in 1999 to seek the serologic antibody response to the avian H5N1 virus in these infected individuals and to investigate the possibility of human-to-human transmission of the virus to assess its pandemic potential. The result demonstrated that 6 0f 51 household contacts, 1 of 26 tour-group numbers, and 0 of 47 coworkers exposed to H5N1-infected persons tested positive for H5 antibody(15). The results suggest that human-to-human transmission might have occurred though close physical contact with H5N1 patients. For this reason, we have to eradicate H5N1 from Thailand. The key to success is the effective surveillance system in animal to reduce the risk of human infection by detects the infected animals in outbreak area in shortest time, to eliminate the source of infection of human.

Avian influenza control measures in Thailand

Because avian influenza is clearly become a serious threat to human life as well as to economics. The primary aim of an early and rapid response to HPAI is to contain the disease before it spread and eliminate it. The strategies include:

1. Stamping out, this involves quarantine and slaughter of infected and exposed poultry on infected premises and sanitary disposal of destroyed poultry and contaminated poultry products. The objective of HPAI eradication by stamping out is to remove the source of infection.

2. Quarantine and movement control on poultry, poultry products and other things in control areas to prevent spread of infection.
3. Vaccination. As now there was no AI vaccine approved for use in Thailand, due to argument in safety, efficacy, and public health concerns in the use of vaccine(18).

After slaughter and decontamination procedures have been completed the premises must be left without susceptible animals for a period of time, determined by the estimating survival time of the pathogen in the environment. Restocking should not be place until at least 21 days after cleaning and disinfection has been complete. After repopulation, monitoring should be continuous through the sampling of dead birds or collecting the sample from birds in the flock to determine re-infection has occurred(11).

Laboratory testing for avian influenza

There are many laboratory testing technique for diagnosis of HPAI disease but the standard diagnostic method for official control propose recommended by OIE are:

1. Identification of the virus: suspension in antibiotic solution of tracheal and cloacal swab (or feces) taken from live birds and pooled sample of organs from dead birds, are inoculated into the allantoic cavity of 9-11-day-old embryonated fowl egg. The egg are incubated at 35-37 C for 3-7 days. The allantoic fluid or any eggs containing dead or dying embryos as they arise are tested for the presence of heamagglutininating activity. The presence of influenza A virus can be confirmed by an immunodiffusion test between concentrated virus and an antiserum to the nucleocapsid or matrix antigens,

both of which are common to all influenza A virus. Samples from poultry to Identification of AIV are taken from dead birds should include intestinal contents (farces) or cloacal and oropharyngeal swabs. Samples from trachea, lung, air sacs, spleen, kidney, brain, liver and heart may also be collected ether separately as a pool. Samples from live birds should include both tracheal and cloacal swabs. The sample will be maintained refrigerated at all times and submitted to a laboratory as soon as possible or within 24-48 hours. (FAO)

2. Subtyping the virus. The method recommend by OIE involve the use of highly specific antisera, prepare in an animal giving minimum nonspecific reaction (e.g. goat) directed against the H and N subtype.
3. Serological test. Agar gel immunodiffusion test are used to detect antibodies to AI antigen Hemagglutination Inhibition tests and Enzyme-linked immonosorbent assays have also been used in diagnostic laboratory.

Surveillance and information system for avian influenza

The key of success in handling avian influenza is early detection(11). If the disease can be detected very early in the phase of epidemic development, the possibility exists that it can be arrested and eliminated before it actually inflicts damage. Early detection presupposes that there is a surveillance system in place that will bring infection to light when it first seen, for this reason, surveillance is the primary key to effective disease management.

For avian influenza, the objectives of surveillance include:

1. To detect clinical disease and infection

2. To understand the epidemiology and ecology of AI to help to design effective control program for poultry production system
3. To assess the temporal and spatial patterns and thereby to improve the effectiveness of control measures
4. To understand the evolution of avian influenza virus
5. To help to define and control of risks to human health
6. To monitor for antigenic drift in AI viruses
7. To maintain the viability of subsistence level poultry production and help assure food security
8. To demonstrate freedom from disease in a country
9. To assess the efficacy of vaccination (where used)

The set the surveillance system requires understanding of the behavior and ecology of influenza viruses.

Surveillance comprises both active and passive methods. Active surveillance is based on specific targeted investigation of at-risk populations for evidence of infection that may be detecting exposure to the agent (antibody detection by serology) or the presence of agent (virus or antigen detection). The methods used must be modified according to the epidemiology of the diseases (10).

The role of Geographic Information System in disease control and prevention

In recent year geographic information system (GIS) have been widely used in veterinary medicine especially in the filed of epidemiology. Definition of GIS was explained by Elther (12), GIS is an automated system for the input, storage, analysis and output (viewing) of spatial distribution.

GIS consists of five components for input, storage, manipulation and output of geographical data. The five components are hardware, software, peopleware, procedure, and data. They are used as tools for analysis, modeling, and decision-making.

Figure 4: The components of Geographic information System

The main advantage of GIS is not just to see disease distribution geographically, but also that an animal disease can be viewed against other information, for example, rainfall maps, vegetation maps, and so on. The disease presence can then be related to other factors and more easily appreciated visually. Many researches showed the advantages of GIS for animal disease control. Ehlers et. al. use the GIS for the analysis and management of avian influenza in Italy during 1999-2000 epidemic, it can be used for analyzing epidemiological risk and managing emergency measures in epidemics and applied to actual avian influenza during outbreak(12).

From AI epidemic in Thailand resulted in massive slaughter of over 26 millions poultry. It should be noted that Thailand was previously free form AI outbreak. Epidemiological studies result is necessary to assist in decision making and planning for outbreak management, particularly the epidemiology of avian influenza outbreak in northern Thailand and establish avian influenza surveillance system.