A Pilot Project on Avian Flu

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INTRODUCTION

With the beginning of trans-border migration of birds from November, chances are there that the Avian Flu virus too flies into new areas. Is this the beginning of a pandemic? Nations are in a state of panic and scare as the virus threatens to melt borders and spread the wings of death. With the bird flu outbreak in Asia spreading to Europe, alarm bells have started ringing with the UN also asking for action. Thousands of ducks and chickens have been killed to curb the disease's spread. As human death toll continues to grow, many are concerned that the virus will mutate and trigger a human pandemic.

Humanity has been at the receiving end of many viral diseases since ages. Sudden emergency and reemergence of new viral diseases in human beings have surprised the medical scientists from time to time. "Avian influenza" or "Bird flu" by H5N1 epidemics is one such surprise (1). Bird flu is an infection caused by avian (bird) influenza (flu) viruses. These flu viruses occur naturally among birds. Wild birds worldwide carry the viruses in their intestines, but usually do not get sick from them. However, bird flu is very contagious among birds and can make some domesticated birds, including chickens, ducks and turkeys very sick and kill them (2). This disease was first identified in Italy more than 100 years ago (3).

Avian influenza is a highly contagious viral infection. A virus belonging to the family Orthomyxoviridae causes the disease. All commercial, domestic and wild birds species are susceptible to infection but disease outbreaks occur more frequently in chickens and turkeys. Avian influenza can cause up to 100% mortality in domestic fowls. Many species of waterfowls, especially geese, ducks and swans carry the virus but generally they show no signs of disease. (4)

But the subtle homoeopathic philosophy as well as vivo and vitro studies conducted in the past with clinical evidences indicate the efficacy in viral infectious diseases. However, it is felt imperative to establish scientifically that homoeopathic medicament do act curatively in combating this Avian Flu.

LITERATURE REVIEW :

Epidemiological / historical aspect:

Migratory ducks, geese, shorebirds and seabirds are among the known vectors for influenza A virus. When carried by birds, the virus can rapidly disperse across great distances. H5N1, a viral sub type recently discover in domestic poultry in Asia, is responsible for over 50 human deaths in 2004 and 2005. By geography, Alaska may be the prime site on the earth to monitor the emergency of new strains of avian influenza. Migratory birds from eastern and western hemispheres converge in Alaska each summer to nest. Strains of flu from different origins could mix, rearrange and mutate on the resting grounds (5).

Researchers believe that prolonged contact with infected birds or consumption of raw, infected chicken meat is required for the virus to jump to humans. But once it does make the jump, it appears to be lethal. H5N1 of today appears to be much more lethal than the strains from 5 years ago. The current out break has infected 55 humans in Asia and killed 42, a mortality rate of 76 percent (6).

It is now known that aquatic birds carry the full repertoire of genes of all influenza strains, including old human pandemic strains, and that the viruses do not cause any disease in them or undergo any mutational changes. Birds shed the viruses abundantly in feces, which contaminate lakes and ponds. In cold climates as in Canada, the viruses persists in such waters for long periods and can readily be isolated from them. Domestic birds like ducks can infected from wild birds and carry the infection to pigs, which may be an important link in the chain, as they are susceptible to infection by both human and Avian influenza strain. Recombination may take place in pigs and such hybrid strains may lead to human infection with potential pandemic spread. The postulated role of ducks and pigs in the development of new hybrids explains why pandemic strains tent to originate in China where millions of birds, pigs and people live closely together(7).

There were several serious out breaks of influenza in 20th century. The most famous (and the most lethal) was the Spanish flu pandemic (type A influenza, H1N1 strain), which lasted from 1918 to 1919, and is believed to have killed more people in total than World war I. Lesser flu pandemic included the 1957 Asian Flu (type A, H2N2 strain) and the 1968 Hong Kong Flu (typeA,H3N2 strain)(8).

- 1915 – 1919 : Wild water fowl captured between 1915 & 1919 were tested for Influenza A virus RNA. One bird captured in 1917 was infected with a virus of the same hemagglutinin (HA) sub type as that of the 1918 pandemic virus. This is more closely related to that of modern Avian virus than it is to pandemic virus, suggesting (i) there was little drift in avian sequences over the past 85 years and (ii) that the 1918 pandemic virus did not acquire its HA directly from a bird. (9)

- 1918 – Spanish Flu - caused 25 to 50 million deaths. In 1982 the antigenic sites of the HA of influenza A PR/ 85 which has sub type H1 strain that was isolated from humans in 1934 by studying the mutants which escape neutralization by antibody. Based on the sequence of hemagglutinin of 1918 Spanish influenza we can specify the extent of divergence of antigenic sites of the HA during the antigenic drift of the virus between 1918 and 1934. This result support hypothesis that the human 1918 pandemic originated from an avian virus of the H1 sub type that crossed the species barrier from birds to humans and adopted to humans, presumably by mutation and / or reassortment shortly before 1918. (8)

- 1957 – 1968 – H2N2 influenza A virus caused Asian pandemic of 1957 and disappeared from the human population 10 years later. The human H2 HAs that circulated in 1957 to 1968 form a separate phylogenetic lineage most closely related to Eurasian avian H2 HAs. We conclude that antigenetically conserved counterparts of the human Asian pandemic strain of 1957 continue to circulate in the avian reservoir and are coming into closure proximity to susceptible human population. (11)

- 1968 – Hong Kong flu pandemic of H3N2 virus (12).

- 1976 – Swine Flu in New Jersey (HswN1) in United states (8).

- 1977 – Russian flu of H1N1 virus (8).

- 1988 – There was an increased prevalence of H2 influenza viruses among wild ducks in North America, preceding the appearance of H2N2 viruses in domestic fowls. (11)

- 1994 – Mainland China – H9N2 avian virus were have circulated in domestic poultry. The present study analyzed 27 H9N2 avian influenza virus that were isolated from chickens & ducks from 1996 to 2002. (13).

- 1997 – H5N1 bird flu incident in Hong Kong in 1997 was considered to be an incipient pandemic situation, the chicken being the source of virus for humans. Prior to 1997 no particular virus sub type other than H4N6 would have been considered a candidate for pandemicity. The credible evidence for the candidacy is in order of

H5N1, H9N2, H6N1.(14) 18 persons were infected and six of them died. (10) Subsequently another avian virus H9N2 was directly transmitted from birds to humans in Hong Kong. Interestingly the genes encoding the internal proteins of the H9N2 virus are genetically highly related to those of H5N1 virus. (15)

- 1999 – Hong Kong and China – low pathogenetic avian influenza A H9N2 virus infection was confirmed in two children and resulted in uncomplicated influenza like illness. Both patients recovered. Poultry was the source of infection and the main mode of transmission was from bird to human (16).

1999 to 2000 – Italy , a severe HPAI epidemic affected the country causing 413 out breaks, a total of about 16 million birds died or were stamped out. (17)

- 2001 (Oct) – Hanoi, Vietnam – specimens from 189 birds and 18 environmental samples were collected at 10 LBM (Live Bird Markets). Four influenza viruses of the H4N6, H5N2 and H9N3 were isolated from the healthy ducks. Two H5N1 viruses were isolated from healthy geese. (18).

- 2002 – Hong Kong, H5N1 occurred in chickens, gallinaceous poultry, waterfowl, greater flamingo (Phoenicopterus rubber), Little agret egretta garzetta, grey heron (Ardea cinerea), black headed gull (Larus ridibundus), feral pigeon (Columba livia), dead tree sparrow (Passer montanus). (19)

2002 – Oct – Italy, another LPAI virus of H7N3 sub type emerged and infected a total of 388 poultry holdings. (20)

- 2003 – Southern China, northern Vietnam, Laos and northern Myanmar - Severe acute respiratory syndrome (SARS) out broke. Avian influenza A (H5N1) also out broke in 2003 and continued to 2004. Human influenza A consists of many sub types of corona virus including the SARS virus and avian influenza H5N1. (21) H7N7 – Netherlands – An epidemic of high pathogenicity avian influenza (HPAI) of
virus sub type H7N7 occurred in the Netherlands in 2003 that affected 255 flocks and led to the culling of 30 million birds. (22)

2003 – Netherlands – an epidemic of HPAI occurred. (23)

2003 Dec – South Korea H5N1 – An unprecedented outbreak of H5N1 highly pathogenic avian influenza (HPAI) had been reported for poultry in 8 different Asian countries, including South Korea since Dec 2003. A phylogenetic analysis of the 8 viral genes showed that H5N1 poultry isolates from South Korea were of avian origin and contained the hemagglutinin and neuraminidase genes of the A / goose / Guangdong / 1 / 96 (Gs / Gd) lineage.(24)

- 2003-2004 – H5N1 in Asia. Outbreaks of highly pathogenic avian influenza A H5N1 among poultry were reported in Cambodia, China, Indonesia, Japan, Laos, South Korea, Thailand, and Vietnam. As of February 9, 2004 a total of 23 cases of laboratory confirmed H5N1 infections in humans resulting in 18 deaths had been reported in Thailand and Vietnam. (25)

H5N1 in Japan – Between the end of Dec 2003 and March 2004, four outbreaks of acute, highly transmissible and lethal disease occurred in birds in three prefectures separated by 150 to 450 Km, involving three chicken farms and a group of chickens raised as pets. The cause of each outbreak was an H5N1 influenza A virus – the first highly pathogenic virus to be isolated from the outbreaks in Japan since 1925. The H5N1 virus was also isolated from dead crows, apparently infected by contact with virus – contaminated material. (26)

- 2004 – British Colombia, Canada – an out break of highly pathogenic avian influenza H7N3 occurred in poultry. Surveillance identified 2 persons with confirmed avian influenza infection. Symptoms included conjunctivitis and mild influenza like illness. (27)

One typical fatal case of encephalitis in a child in southern Vietnam in 2004 was identified retrospectively as H5N1 influenza through testing of cerebrospinal fluid, fecal matter, and throat and serum samples.

Since January 2004 the WHO has reported human cases of Avian Influenza A (H5N1) in Asia, Africa, the Pasific, Europe and the Near East. (28)

- 2004 (Oct) – Thailand – Genome of Thai avian influenza virus A (H5N1) isolated from the epidemic during 2004. (29)

- 2005 – Notable findings of epidemiological investigations of human H5N1 cases in Vietnam during 2005 have suggested transmission of H5N1 viruses to at least two persons through consumption of uncooked duck blood. One possible instance of limited person-to-person transmission of H5N1 in Thailand has been reported. (30)

- 2006 – In early March 2006, Germany reported H5N1 infection in a stone marten (a weasel-like mammal). The Avian influenza A (H5N1) virus that emerged in Asia in 2003 continues to evolve and may adapt so that other mammals may be susceptible to infection as well. (31)
  In India the Avian influenza affected areas are Maharastra, Karnatak, Gujrat, and Kerla.

Distribution over last five years:

The number of outbreaks of avian influenza seems to be increasing – over the last five years outbreaks have been reported in Italy, Hong Kong, Chile, the Netherlands, South Korea, Vietnam, Japan, Thailand, Cambodia, Indonesia, Laos, China, Pakistan, United States of America, Canada, South Africa and Malaysia. (32)

AETIOPATHOGENESIS:

"Avian influenza" or "bird flu" is an infectious disease of birds caused by influenza A virus. Viruses of low pathogenicity can, after circulation for sometime in a poultry population, mutate into highly pathogenic viruses. To date of all out breaks of highly pathogenic form have been caused by influenza A / H5N1 virus, the only sub type that causes out breaks of severe disease in humans (33). The ability of the strain H5N1 to evade the body's defense mechanism by evading cytokines (the first line of defense against 'flu') may be responsible for the high pathogenicity of this particular strain. (34)

Genetics and morphology of virus:

Influenza A virus contains their genome in eight separate linear segments of negative sense RNA. Each segment contains a single gene, but some can be read twice at different starting point to create two distinct proteins. The segmented nature of the genome also allows for the exchange of entire genes between different viral strains when they cohabitate the same cell.

The eight genes are:

- HA gene encoding haemoagglutinin which produces about 500 copies.
- NA gene encoding neuraminidase which produces about 100 copies.
- NP gene encoding nucleoprotein. Influenza A, B, C are distinguished by their nucleoproteins.
- M gene encoding two matrix proteins (the M1 and the M2) by using different reading frames from the same RNA segment.
- NS gene encoding two distinct nonstructural proteins by using different frames from the same RNA segments.
- PA gene encoding an RNA polymerase
- PB1 gene encoding an RNA polymerase
- PB2 gene encoding an RNA polymerase

The genome segments have common terminal sequences, and the end of the RNA strands are partially complementary, allowing them to bond to each other by hydrogen bonds. After transcription from negative – sense to positive – sense RNA the +RNA strands get the cellular 5' cap added, allowing its processing as messenger RNA by ribosome. The +RNA strands also serve for synthesis of -RNA strands for new virions.

The RNA synthesis and its assembly with the nucleoprotein takes place in the cell nucleus, the synthesis of proteins takes place in the cytoplasm. The assembled virion cores leave the nucleus and migrate towards the cell membrane, with patches of viral transmembrane proteins [hemagglutinin (HA), neuraminidase (NA) and M2 proteins] and an underlying layer of M1 protein, and bud through these patches, releasing finished enveloped viruses into the extra cellular fluid. (35)

The hemagglutinin is a strain specific antigen and is capable of great variation. 16 distinct HA sub types, named H1 to H16 have been identified in avian influenza viruses. Neuraminidase has 9 different sub types, named N1 to N9. A unique feature of the influenza virus is its ability to undergo antigenic variation . It is highest in influenza virus type A.

The route of entry is the respiratory tract. The viral neuraminidase facilitates infection by reducing the viscosity of the mucus film lining the respiratory tract and exposing the cell surface receptors for virus absorption. The ciliated cells of the respiratory tract are the main sites of viral infection. These cells are damaged and shed, laying bare the basal cells in the trachea and bronchi. This renders the respiratory tract highly vulnerable to bacterial invasion. (36)

Environmental conditions have a marked effect on virus survival out side the bird. The avian influenza can survive for at least 35 days at 4^{o} C in manure. The virus can be isolated from lake water where water fowl are present. The virus can survive several days in carcasses at ambient temperature and up to 23 days if refrigerated. The virus can persists in poultry meat products but is eliminated by adequate heating / cooking. There are many strains of avian influenza virus, some of which cause no clinical signs while other can be devastating to susceptible birds. The virulent strains are referred to as highly pathogenic avian influenza. The highly pathogenic H5N1 is currently circulating in domestic poultry.

TRANSMISSION OF BIRD FLU:

Influenza A viruses have infected many different animals, including ducks, chickens, pigs, whales, horses and seals. However certain subtypes of influenza A viruses are specific to certain species, except for birds, which are hosts to all known subtypes of influenza A. subtypes that have caused wide spread illness in people either in past or currently are H3N2, H2N2, H1N1 and H1N2. H1N1 and H3N2 subtypes also have caused outbreaks in pigs and H7N7 and H3N8 viruses have caused outbreaks in horses. Influenza A viruses normally seen in one species sometimes can cross over and cause illness in another species. For example, until 1998, only H1N1viruses circulated widely in the U.S. pig population. However, in 1998, H3N2 viruses from humans were introduced into pig population and caused widespread disease among pigs. Most recently, H3N8 viruses from horses have crossed over and caused outbreaks in dogs. Avian influenza A viruses may be transmitted from animals to humans in two ways:

- Directly from birds or from avian virus-contaminated environment to people.
- Through an intermediate host, such as a pig (37).

Currently avian influenza or bird flu is only known to spread to human from contact with the feces or respiratory secretions of the infected birds. The bird flu virus does not pass from human to human. However influenza viruses survive by mutating constantly and if the bird flu virus mutates to a form that can be transmitted between humans the consequences could be catastrophic. (38)

Influenzas A viruses have eight separate gene segments. The segmented genome allows influenza A viruses from different species to mix and create a new influenza A virus if viruses from two different species infect the same person or animal. For example, if pig were infected with a human influenza A virus and an avian influenza A virus at the same time, the new replicating viruses could mix existing genetic information and produce a new virus that had most of the genes from the human virus, but a hemagglutinin and / or neuraminidase from the avian virus. The resulting new virus might then be able to infect humans and spread from person to person, but it would have surface proteins

(Hemagglutinin and / or Neuraminidase) not previously seen in influenza viruses that infect humans. This type of major change in the influenza A viruses is known as antigenic shift. Antigenic shift results when a new influenza A sub type to which most people have little no immune protection infect humans. If this new virus causes illness in people and can be transmitted easily from person to person, an influenza pandemic can occur. It is possible that the process of genetic reassortment could occur in a human who is co-infected with avian influenza A virus and a human strain of influenza A virus. (39)

WHO confirms human-to-human transmission of avian influenza strain H5N1. (40)

CLINICAL FEATURES:

They are very similar to that of the disease caused by other influenza viruses. Fever, malaise, myalgia, sore throat and cough are found in most of the patients while conjunctivitis is seen in some. Persistent high fever is a useful sign. Life threatening complications like viral pneumonia, respiratory distress syndrome and multi organ failure may result in the death of the patient. A patient is suspected to be suffering from avian influenza (bird flu) if he /she has any respiratory illness and has had recent direct or indirect contact by handling or by having taken care. Or by exposure to sick chickens or other birds. Besides the classical clinical presentations as described above, X-ray of the chest is useful in detecting early viral pneumonia. Specimens like naso-pharyngeal aspirate, sputum and serum from clinically suspected cases are subjected for laboratory investigations for further confirmation (41).

Sign and symptoms in birds:

1. Depression
2. Profuse watery diarrhoea
3. Reddening of legs
4. Laboured respiration
5. Blue and swollen combs
6. Respiratory signs of cold (42)

Signs and symptoms in Human being:

1. Fever
2. Headache
3. Myalgia
4. Sore throat
5. Dry cough
6. Sneezing
7. Congestion of nose
8. Redness of conjunctiva
9. Nausea / vomiting
10. Otitis media
11. Flushed face
12. Cyanosis
13. Coldness of extremities
14. Dyspnoea
15. Mottled extremities
16. Diffused rales
17. Signs of consolidation(43)

DIFFERENTIAL DIAGNOSIS:

Birds:

(i) Features of New Castle disease
(ii) Infections , laryngo tracheitis
(iii) Duck plague
(iv) Acute poisoning
(v) Acute fowl cholera
(vi) Bacterial cellulitis
(vii) Chronic respiratory diseases(44)

Human being :

(i) Early bacterial pneumonia
(ii) Severe streptococcal pharyngitis
(iii) Acute respiratory illness caused by any varieties of respiratory virus(45)

LABORATORY DIAGNOSIS: (BIRDS / HUMAN BEING)

1. Demonstration of the virus antigen by immunofluorescence by using specific monoclonal antibody and haemagglutination inhibition assay. (46)
2. Detection of influenza-specific RNA by reverse transcriptase-polymerase chain reaction (RT-PCR) is extremely sensitive.
3. Serological identification by measuring the specific antibodies by haemagglutination inhibition test.
4. Virus culture (47)

Treatment available at present

A simple way to reduce the risk of illness:

- Hand washing could be the key to avoid the common cold and influenza like the bird flu. In order to be effective hand should be washed with soap from 20 to 25 seconds. The three keys are soap, friction and water. Hand should be washed after going to rest room; before eating and preparing food; after helping a child to use the bathroom; after changing a diaper; after blowing the nose; after coughing or sneezing into the hands; after handling animals or animal waste; and before carrying out first-aid for an open cut or wound.
  In addition, to hand washing, eating right, getting enough sleep and exercising strengthen the immune system and fight sickness. (48)
- Wearing of masks and gloves by persons handling poultry.
- Cleaning kitchen surfaces and utensils before and after use.
- Cooking chicken till boiling temperature is reached.
- Controlling human traffic into poultries (49).

Materia Medica review:

1. **Belladonna**: Hot skin with inclination to perspire. Spasmodic cough aggravates headache.Sleepy but cannot sleep. Startling in sleep. Frequent sneezing, dryness of nose with frontal headache.Throat feels constricted, difficult deglutition worse of taking liquids. Nausea and vomiting, great thirst for cold water. Dreads drinking, uncontrollable vomiting. High feverish state burning pungent steaming heat with no thirst.

2. **Arsenicum alb.:** Sudden catarrh with threatening suffocation at night. Influenza in children with sudden onset & much prostration. Child looks as if it had been sick for a week. Profuse watery discharge from nose, corroding nostrils & making the upper lip sore, aggravation at night and after a meal. Great debility with spasmodic cough desire to vomit, with vomiting and expectoration of watery mucus, running eyes, excessive photophobia, inflamed eyes. Burning eyes, acrid lachrymation. Periodical burning pain in head, restlessness. Burning pain and anxiety at the pit of stomach. Vomiting after eating.

3. **Sulphur:** Constant heat on top of head. Burning ulceration on margin of lids. Chronic dry catarrh, dry scabs. Lips dry, bright red, burning. Drinks a lot eats a little.Difficult respiration, wants windows open. Dysponea in the middle of night. Frequent flushes of heat. Disgusting sweats.

4. **Calc .carb.**:Sense of weight on the top of head, much perspiration, wets the pillow. Dry nostrils, sore ulcerated. Lachrymation in open air. Takes cold at every change of weather.Dislike of fat and milk disagrees.Persistent sour taste. Scrofulous inflammation with mucopurulent otorrhoea. Swelling of tonsils.

5. **Nux vom.:** Nose stuffed especially at night. Acrid discharge with stuffed feeling. Rough scraped feeling of throat. Smarting dry sensation of inner canthi. Coryza fluent at day time, stuffed at night and outdoors.Nausea and vomiting with much retching. Wants to vomit but can not.

6.. **Pulsatilla:** Neuralgic pain, commencing in right temporal region with scalding lachrymation from affected side. Thick profuse yellow bland discharge. Itching burning in eyes. Aversion to warm food and drinks.Yellow and coated tongue. Vomiting of food eaten long before. Dry mouth without thirst.Dry cough in the evening and night, must sit up in the bed to get relief. Loose cough in the morning with copious mucoid expectoration.

7) **Mercurius:** Profuse burning ,acrid discharge from the eyes.Thick yellow discharge from ears .Nostrils raw,ulcerated.Coryza with sneezing,sore,raw and smarting sensation.Bluish red swelling of throat,constant desire to swallow.Putrid sore throat worse on right side. Intense thirst for cold drinks.

8) **Phosphorus:** Burning pains,chronic congestion of head. Brainfag with sensation of coldness in the occiput. Vomiting water thrown up as soon as it gets warm in the stomach.Throws up ingesta by the mouthfuls.Fan like motion of nostrils, foul imaginary odors. Chronic catarrh with small haemarrhages.

9) **Rhus tox. :** Heavy head, pain in forehead, proceeds backwards. Swollen, red oedematous eye. Profuse gush of hot, scalding tears . Sneezing coryza from getting wet.Nausea, vertigo and bloated abdomen after eating.Sore throat with swollen glands. Desire for milk, marked thirst. Chills with a dry cough and restlessness. Dry teasing cough from midnight till morning.

10. **Causticum:** Coryza with hoarseness. Burning rawness and soreness of the throat are the characteristic. Cough better by drinking cold water. Aversion to sweets, hoarseness with pain in chest. Restlessness at night, with tearing pain in joints and bones

11. **Natrum mur:** Headache from sunrise to sunset with paleface,nausea,vomiting periodical. Burning eyes, acrid lachrymation.Tears stream down the face on coughing. Violent fluent coryza followed by obstruction of nose, breathing very difficult. Infalliable for stopping a cold commencing with sneezing. Unquenchable thirst, sweats while eating. Coldness of body.

12. **Lycopodium:** Haedache over the eyes, throbbing headache after every paroxysms of cough, fluent coryza, stopped of nose, fan like motion of alae nasi, inflammation and dryness of throat with thirst, better by warm drinks, desire for sweet things, aversion to bread, chill between 3 to 4 p.m. followed by sweat, icy coldness of body with profuse foot sweat.

13. **Silicea:** Headache from fasting, better by wrapping up warmly. Profuse sweat on the head, offensive and extend to neck. Sneezing in the morning obstructed nose and anosmia, pricking as If a pin in the throat, Cold settles in the throat, parotid gland swollen, vomiting after drinking, disgust for meat and warm food, violent cough on lying down with thick yellow lumpy expectoration, cough and sore throat with expectoration of little granules like shot, which when broken smells very offensive.

14. **Sepia:** Chronic nasal catarrh,especially post nasal dropping of heavy,lumpy discharge must be hawked through the mouth. Nausea at smell and sight of food.Nausea in the morning before eating. Longing for vinegar, acids& pickles. Dyspnoea worse after sleep, better by rapid motion.Cough in the morning with profuse expectoration, tasting salty. Frequent flushes of heat, sweat from least motion.Feet cold and wet.

15. **Allium cepa:** Catarrh with epiphora. Smarting of eyes. violent sneezing with profuse bland lachrymation. Profuse acrid coryza, exocoriating upper lip. When coming into a warm room, must take a long breath then sneezing accordingly. Constant inclination to hack, immediately rising from bed in the morning, A violent sneezing fit. Dullness of eyes, aversion to light.

16. **Ammon carb.:** Burning water runs from nose in day time, dry coryza at night.Cough after mid night with tickling in larynx. Headache with chronic weakness of chest. Constant tingling of nose with disposition to sneeze. The least breath of cold air aggravates and brings on sneezing.

17. **Arsenicum hydr.**: Violent sneezing & such coldness of nose that it must be wrapped up in a warm cloth.Tickling up in the nose causes sneezing. Eyes yellow, deeply sunken, with broad blue circles, face pale, lips discoloured. Whispering, squeaking voice.

18. **Arsenicum iod.:** Frequent sneezing. Severe coryza with catarrhal tendency. Pungent irritation about nose & eyes and watering secretion.Puffiness of lower lids, face, thick, white tongue

19. **Arum triph**.: Acrid fluent coryza and much sneezing, aggravation at night.Nose moist and still feels stopped up.Tickling cough from mucus in trachea; lassitude and low spirits.;discharge excoriating both nostrils and upper lip..

20. **Chelidonium:** Shortness of breath & tighness of chest.Drawing in nape & occiput. Photophobia. Lachrymation, nose, tongue, throat, dry mouth or thirstless. No appetite, delirium, mostly at night. Lethargy which followed through the day

21. **Dulcamara**:This is one of our best remedies in the acute forms; the eyes are suffused, the throat is sore and the cough hurts because of the muscular soreness. If brought on by damp, cold changes in the weather, so much the surer is Dulcamaralis indicated.

22. **Eupatorium perf.:** This remedy has much soreness and aching of the entire body. Hoarseness and cough, with great soreness of the larynx and upper respiratoy tract. Coryza with thirst, and drinking causes vomiting. The cough is a very shattering one, hurts the head and chest, and as in Drosera, the patient holds the chest with the hands The back bone pain are characterstic of the remedy. Add to this bilious derangement.

23. **Gelsimium:** This remedy corrospends to the commencement of the trouble, when the patient is weak, tired and aches throughout the body.It removes speedily the intense aching and muscular soreness.There is constant chilliness and the patient hugs the fire. An extensive experience with this remedy in the great Epidemic of 1918 proved its usefulness simple cases are rapidly cured.

24. **Phellandrium:** Hoarseness with roughness in throat; dry cough, with shortness of breath, stitches in chest and oppression; great thirst, loss of appetite, sleepiness on account of cough;small black spots like petechiae disappearing without desquamation urging to urinate, with scanty emission and violent burning after micturition;urine pale and watery, almost greenish.

25. **Phytolacca:** Influenza with derangement of the digestive organs;thin watery discharge from the nose, which increased until the nose became stuffed; inability to breathe through the nostrils, difficulty in swallowing; dry cough, hacking exicited by tickling in larynx and dryness of pharynx; hearts action weak.

26. **Sabadilla:** Violent spasmodic sneezing and lachrymation on going to open air; fluent coryza, dullness of head; gray dingy color of skin; dull cough, with vomiting and spitting of blood, especially when lying down.Throat feels as if constricted by a string; red spots in face and chest.

27. **Senega**: Constant tickling and burning in larynx and throat with danger of suffocation when lying down; walls of chest sensitive or painful when touched or when he sneezes; copious expectoration of tough mucus; relief from outdoor exercise, but aggravates on walking fast.

28. **Silphium lanc**: Scraping-tickling irritation of fauces and throat, nausea, faint feeling sense of soreness in epigastrium; constant hawking and scraping to throw off thin viscid mucus; constant sneezing, followed by discharge of limpid acrid mucus from the nose, with expectoration of yellow mucus.

29. **Sticta pulm:** Excessive dryness of the nasal mucosa, painful with inability to breathe through the nose, worse in the afternoon and better in the fresh air, in the morning hours being nearly free from distress; dull heavy pressure in the forehead and root of nose; depression of the whole system.

30. **Spigellia:** Influenza accompanied by facial neuralgia; fluent coryza, with dry heat and no thirst; headache, with hoarseness and anxiety about the heart; dry hard cough at night, with dysponea, worse when bending backward.

31. **Tuberculinum:** Tuberculinum is an excellent prevention of recurring attacks in those who have annual attacks. (50, 51,52)

REPERTORIAL REVIEW:

Human being

Symptoms	**Repertorial rubric**
1) Fever	Fever- heat in general
2)Headache	Head- pain
3)Rhinitis	Nose- inflammation
4)Dry cough	Cough-dry
5)Sore throat	Throat- pain- sore
6)Redness of eyes	Eye- discolouration- redness
7)Burning of eyes	Eye- pain- burning

8)Vomiting	Stomach- vomiting
9)Otitis media	Ear- inflammation
10)Flushed face	Face- discolouration,- red- excitement
11)Hot dry skin	Skin- dry- hot
12)Diaphoresis	Perspiration- profuse
13)Cyanosis	Generals- cyanosis
14)Dysponea	Respiration- difficult
15)Mottled skin	Skin –discolouration- mottled
15)Cold extremities	Extermities- coldness
16)Congested nose	Nose- congestion

Birds

	Symptoms	**Repertorial rubric**
1.	Dullness	Mind-Dullness
2.	Diarrhoea	Rectum- diarrhoea
3.	Profuse stool	Stool- profuse
4.	Watery diarrhoea	Stool – Watery
5.	Reddened legs	Extremities –discoloration-red-legs
6.	Catarrhal discharge	Nose-catarrh
7.	Sneezing	Nose-Sneezing
8.	Nose obstruction	Nose- obstruction

Methodology (for mathematical model)

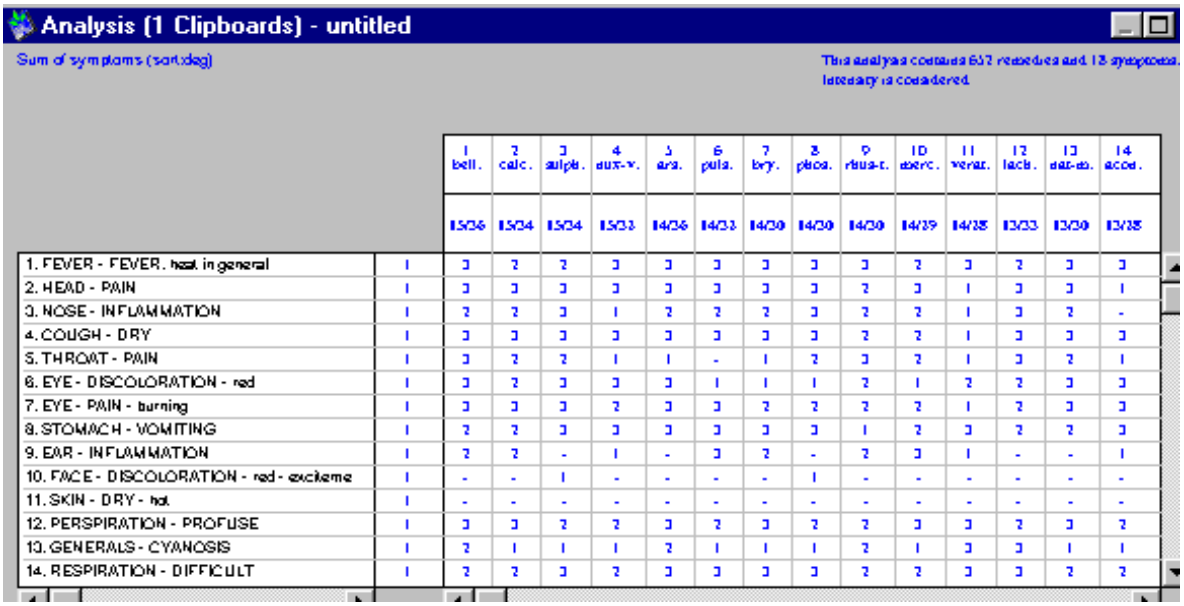
Aim - To ascertain the preventive and curative medicine for Avian Flu .

Methods - A diagnostic criterion was determined by taking clinical features such as
Fever, Headache, Myalgia, Sore throat, Dry cough, Sneezing, Congestion of nose, Redness of conjunctiva, Nausea / vomiting, Otitis media, Flushed face, Cyanosis, Coldness of extremities, Dyspnoea, Mottled extremities, Diffused rales, Signs of consolidation.
Above symptoms were repertorised with the help of RADAR & HOMPATH soft ware

Results of mathematical model (53)

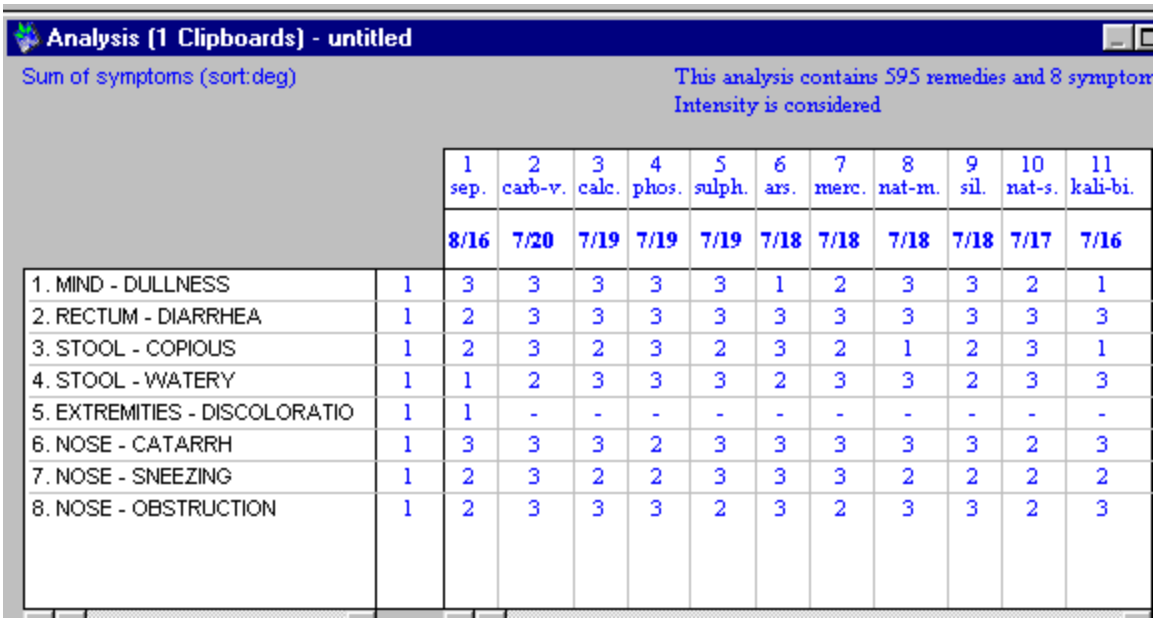
RADAR

HUMAN BEING



		1 bell. 15/36	2 calc. 15/34	3 sulph. 15/34	4 nux-v. 15/33	5 ars. 14/36	6 puls. 14/33	7 bry. 14/30	8 phos. 14/30	9 rhus-t. 14/30	10 merc. 14/29	11 verat. 14/35	12 lach. 13/33	13 nat-m. 13/30	14 acon. 13/35
1. FEVER - FEVER, heat in general	1	3	2	2	3	3	3	3	3	3	2	3	2	3	3
2. HEAD - PAIN	1	3	3	3	3	3	3	3	3	2	3	1	3	3	1
3. NOSE - INFLAMMATION	1	2	2	3	1	2	2	2	3	2	2	1	3	2	-
4. COUGH - DRY	1	3	3	3	3	3	3	3	3	2	2	1	3	3	3
5. THROAT - PAIN	1	3	2	2	1	1	-	1	2	3	2	1	3	2	1
6. EYE - DISCOLORATION - red	1	3	2	3	3	3	1	1	1	2	1	2	2	3	3
7. EYE - PAIN - burning	1	3	3	3	2	3	3	2	2	2	2	1	2	3	3
8. STOMACH - VOMITING	1	2	2	3	3	3	3	3	3	1	2	3	2	2	3
9. EAR - INFLAMMATION	1	2	2	-	1	-	3	2	-	2	3	1	-	-	1
10. FACE - DISCOLORATION - red - eczema	1	-	-	1	-	-	-	-	1	-	-	-	-	-	-
11. SKIN - DRY - hot	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
12. PERSPIRATION - PROFUSE	1	3	3	2	2	3	2	3	2	2	3	3	2	3	2
13. GENERALS - CYANOSIS	1	2	1	1	1	2	1	1	1	2	1	3	3	1	1
14. RESPIRATION - DIFFICULT	1	2	2	3	2	3	3	3	3	2	2	3	3	2	2

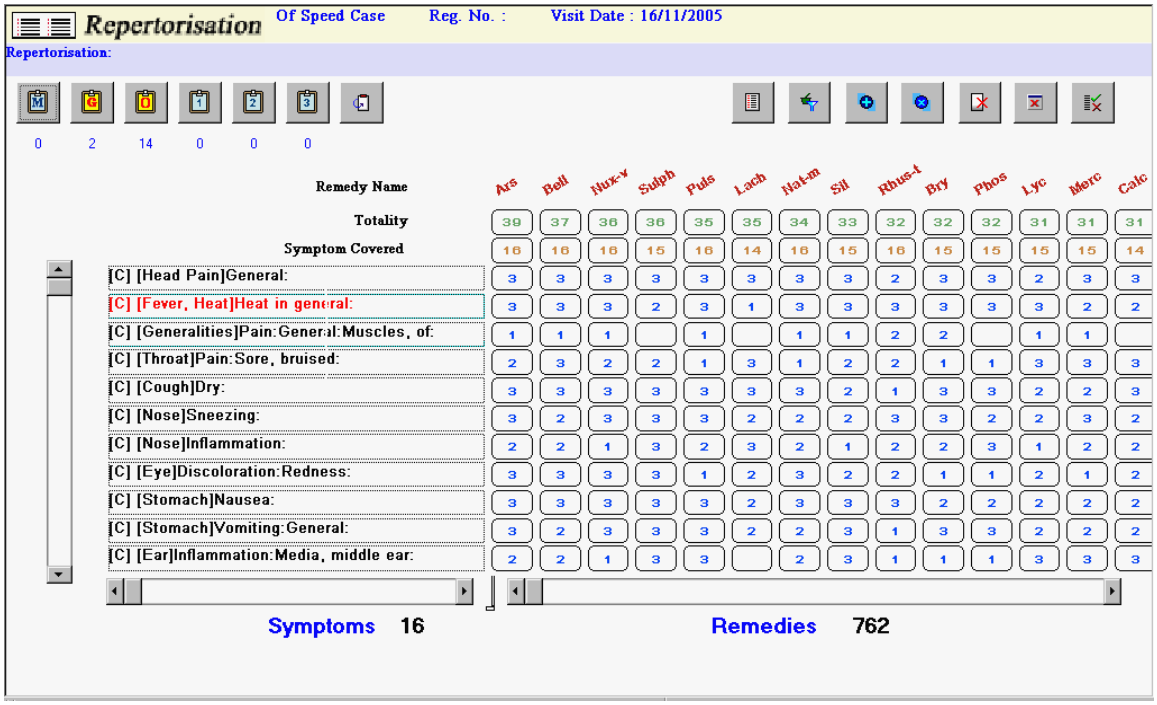
BIRDS



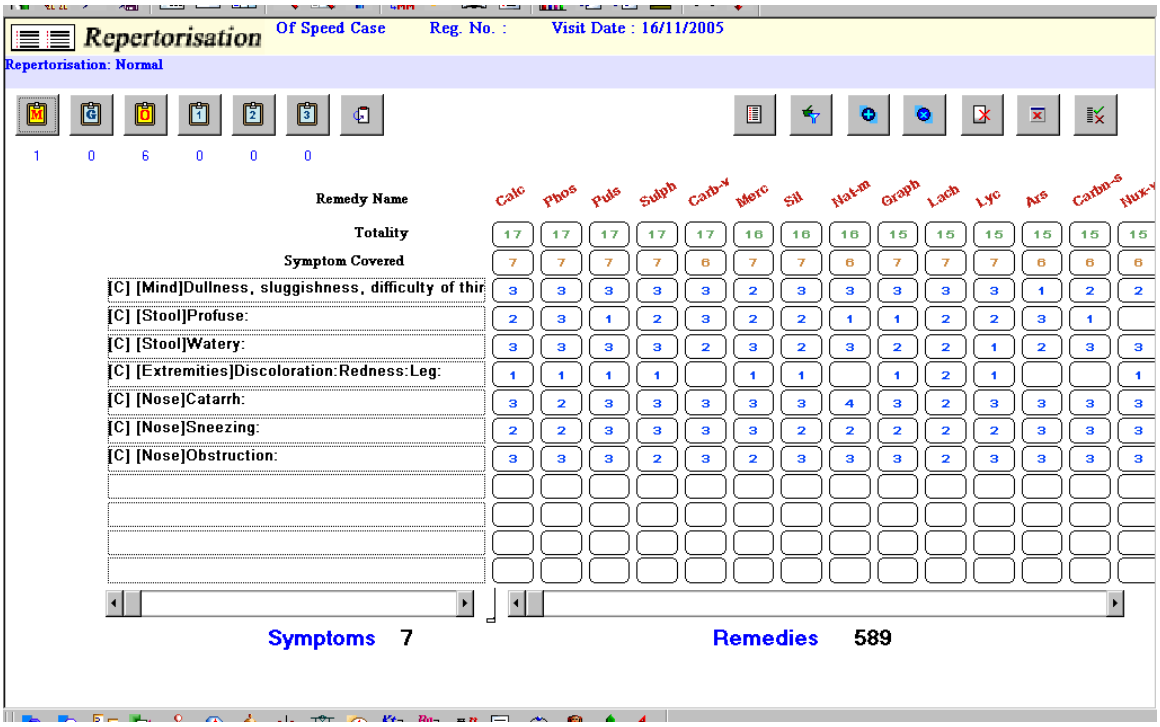
		1 sep. 8/16	2 carb-v. 7/20	3 calc. 7/19	4 phos. 7/19	5 sulph. 7/19	6 ars. 7/18	7 merc. 7/18	8 nat-m. 7/18	9 sil. 7/18	10 nat-s. 7/17	11 kali-bi. 7/16
1. MIND - DULLNESS	1	3	3	3	3	3	1	2	3	3	2	1
2. RECTUM - DIARRHEA	1	2	3	3	3	3	3	3	3	3	3	3
3. STOOL - COPIOUS	1	2	3	2	3	2	3	2	1	2	3	1
4. STOOL - WATERY	1	1	2	3	3	3	2	3	3	2	3	3
5. EXTREMITIES - DISCOLORATIO	1	1	-	-	-	-	-	-	-	-	-	-
6. NOSE - CATARRH	1	3	3	3	2	3	3	3	3	3	2	3
7. NOSE - SNEEZING	1	2	3	2	2	3	3	3	2	2	2	2
8. NOSE - OBSTRUCTION	1	2	3	3	3	2	3	2	3	3	2	3

HOMPATH

HUMAN BEING



BIRDS



Proposed Methodology

Aims / Objectives

1) To determine the efficacy of the drugs evolved through mathematical model (Repertorisation) for preventive and curative aspect of Avian Flu either in single or in serial or in combined form.
   a. To ascertain the suitable potency(s)
   b. To determine the effective dose(s)
   c. To find out the repetition schedule(s)
   d. To find out the most effective therapeutic option(s)

Research Protocol

Methods

- **Target groups**

  a. Domesticated / Commercial birds
  b. Human being of globe

- The experiment is to be "Randomized double blind control trail". It is to be of multicentric.
- Route of administration of drug will be oral
- A standardized case recording format will be adopted for documentation of data & follow up will be done periodically, which is as follows

Case Recording Format

I) Particulars

Name
Address
Age
Sex
Occupation

II) Presenting Complaints

Location	Sensation	Modalities	Concomitants / Associated Features / Extension / Unexpected features
	Fever		
Head	Headache		
Muscles	Myalgia		
Throat	Sore throat		
Chest	Dry cough		
Nose	Sneezing		
Nose	Congestion		
Conjunctiva	Redness		
Stomach	Nausea / vomiting		
Ear	Otitis media		

	Flushed face
	Cyanosis
Extremities	Coldness of extremities
Respiration	Dyspnoea
Extremities	Mottled
Chest	Diffused rales
Chest	signs of consolidation

III) Laboratory Investigations

Tests	Results
a) Viral culture	
b) Polymerase Chain reaction	
C) Immune fluroscent Assay	

Diagnostic Criteria

For documenting the results following inclusion and exclusion criteria will be applied

1. **Inclusion Criteria**

Birds

(A) Clinical Features

I) Depression
II) Profuse watery diarrhea
III) Reddening of the legs
IV) Laboured respiration
V) Blue & swollen combs
VI) Respiratory sign of cold

(B) Laboratory Diagnosis

i) Viral culture
ii) Polymerase chain reaction
iii) Immune fluroscent Assay

Human being

(A) Clinical features

i) Fever
ii) Headache
iii) Myalgia
iv) Sore throat
v) Dry cough
vi) Sneezing
vii) Congestion of nose
viii) Redness of conjuctiva
ix) Nausea/ vomiting
x) Otitis media

xi) Flushed face
xii) Cyanosis
xiii) Coldness of extremities
xiv) Dyspnoea
xv) Mottled extremities
xvi) Diffused rales
xvii) Signs of consolidation

(B) Laboratory Diagnosis:

i) Viral culture
ii) Polymerase Chain reaction
iii) Immuno flouroscence assay

2. Exclusion criteria

Birds

i) Features of New castle disease
ii) Infectious Laryngo tracheitis
iii) Duck plague
iv) Acute poisoning

Diseases that can cause swelling of combs wattles includes

i) Acute Fowl cholera
ii) Bacterial cellulites
iii) Chronic respiratory diseases

Human being

i) Early bacterial pneumonia
ii) Severe streptococcal pharyngitis
iii) Acute respiratory illness caused by any varieties of respiratory virus

Different Therapeutic Drug Options

(Preventive / Curative purposes)

To find out most effective drug(s) for preventive and curative purposes of Avian Flu an unbiased trial will be undertaken with the drugs evolved as drug of choice from mathematical model study which are delineated below:

I) **Single Drug** (A single drug will be given at one time and waiting for the change)

Human being

a. Belladonna
b. Calc. carb.
c. Sulphur
d. Pulsatilla
e. Ars. alb.
f. Nux. vom.

Bird

a. Phos.
b. Ars. alb.
c. Carbo veg.
d. Nat. mur.
e. Calc. carb.
f. Belladonna

II) **Multiple Drugs in Serial (Both for Bird / Human being) [Drugs will be given serially at specific time gap]**

Options are:

a. Belladonna → Calc. carb. → Tuberculinum
b. Belladonna → Sulphur. → Tuberculinum
c. Ars. alb . → Calc. carb. → Tuberculinum
d. Rhus. tox → Pulsatilla → Sulphur

III) **Combined drugs [A group drugs will be mixed to prepare a compound with a new name]**

a)	b)	c)
Belladonna	Ars. hydro	Nux vom.
Calc. carb.	Rhus. tox	Pulsatilla
Tuberculinum	Sulphur	Belladonna
Pulsatilla	Bry. Alb.	Ars. alb.
Rhus. tox	Belladonna	Calc. carb.
Ars. alb.	Nux. vom	Sulphur
--------	Phelandrium	Silphinum lanc
--------	----------	Dulcamara

Various potency options - **To ascertain the most effective potency various potencies will be tried. A comprehensive type should be as follows**

i) **Single medicine**

a. - 30
b. - 200
c. - 1M

ii) **Multiple drugs in serial**

a. - 30
b. - 200
c. - 1M

iii) **Combination of drugs**

a. - 3x
b. - 6x
c. - 30

Different dosages options : **It is also necessary to determine what should be the amount needs to be prescribed for which various doses will be tried. A detail account is furnished below:**

i) **Single medicine**

	Adult	**Children**
a)	4 Globules (glb. No -20)	- 2 globules
b)	½ drop	- ¼ drop
c)	1 drop	- ½ drop

ii) **Multiple drugs in serial**

Adult		**Children**
a)	4 Globules (glb. No -20)	- 2 globules
b)	½ drop	- ¼ drop
c)	1 drop	- ½ drop

iii) **Combination of drugs**

For human being

Adult		**Children**
a)	1 drop each	- ½ drop
b)	5 drop	- 2½ drop
c)	10 drop	- 5 drop

For birds

Adult		**Young**
a)	½ drop)	- ¼ drop
b)	1 drop	- ½ drop
c)	2 drop	- 1 drop

Different repetition schedule - To fix the repetition schedule in different types of therapeutic options following classification and category will be tried

i) Single medicine
   a. One dose only
   b. One dose daily for three days
   c. Two dosages daily for three days

Repetition after 15 days / 1 month / 3 month / 1 year

ii) Multiple drugs in serial
   a. One dose from each drug consecutively
   b. One dose from each day for three days
   c. Two dosages from each day continuously one after another

Repetition after 15 days / 1 month / 3 month / 1 year

iii) Combination of drugs
   a. One dose daily for three days
   b. Two dose daily for three days

   Repetition after 15 days / 1 month / 3 month / 1 year

Different age groups – **For documentation of the efficacy of different therapeutic options on different age groups following classification will be used**

Birds – Young
Adult

Human being - Children
Adults

Results will be documented as per following **Parameters**

i) **Positive response**
- Complete disappearance of sign & symptoms with negative pathological findings

ii) **Negative response**
- No improvement of signs / symptoms along with pathological symptoms
- **Dropped out** - Did not stick to therapy.

Finally results will be evaluated with statistical tools

Expected Results

1. Out of different therapeutic options the most effective therapeutic procedure needed for combacting Avian Flu will be determined.
2. Most effective potency (ies), dose(s), repetition schedule(s), will be determined.
3. Which age group(s) is amenable to homoeopathic medicament will be ascertained.
4. Which strain is better amenable to the therapy will be unfurled.

Conclusion / Recommendations

1) The drug(s) evolved after clinical trial can be used as preventive and curative purposes for preventing / controlling. Avian Flu both for Avian and homosapiens.
2) As the stains are very often undergoing mutation the research should be a continued process to unveil the role of Homoeopathic medicament at different epoch of time.

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