Anthropogenic factors responsible for emerging and re-emerging infectious diseases

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This article discusses about the ecology of various emerging infectious diseases and the factors that influence their emergence. In an endemic state of an infectious disease, the determinants responsible are pathogen, host, vector and environment. But for the past 2–3 decades, the most important factor responsible for a disease to emerge or become an epidemic has been human intervention by progress in science and technology. Therefore, this article discusses with examples how progress in science and technology or human intervention can be included as the fifth determinant in an emerging epidemic disease.

Keywords: Anthropogenic factors, infectious diseases, emergence and re-emergence, scientific progress.

The term emerging infectious diseases (EID) was first used in the late 20th century. It has been widely used from 1970 onwards after a large number of human infectious disease outbreaks occurred, e.g. Lyme disease, AIDS and antibiotic-resistant microbial infections. Thereafter, increased publication and funding for surveillance lead to this term to be used regularly to represent these new diseases.

The definition of the term ‘emerging’ was given in 1981 by Krause and Lederberg as ‘emerging diseases are those that have recently increased in incidence, impact, geographic distribution or host range (e.g. Lyme disease, TB, West Nile virus, Nipah virus), that are caused by pathogens that have recently evolved (e.g. new strains of influenza virus, drug resistant strains of malaria), that are newly discovered (e.g. Hendra virus) or are diseases that have recently changed their clinical presentation (e.g. hantavirus pulmonary syndrome)’. The time-span which the term ‘recent’ represents may vary, but to eliminate this ambiguity most authors and scientists agree on the time-frame to be 2–3 decades. ‘Reemerging diseases are a subclass of emerging diseases that historically occurred at significant levels but which became less significant and only recently have increased in incidence’.

The term ‘emerging disease’ has a fairly broad definition and in general, the following can be included to the above points:

- A known agent or its close relative occurring in a new species.
- A previously unknown agent detected for the first time.

Every infectious disease is an emerging infectious disease until it establishes itself as an endemic disease over a period of time. What makes a disease appear or increase in incidence are the factors or determinants of an infectious emerging disease. Historically, the first emerging infectious diseases occurred with people moving across Pleistocene land bridges and later because of domestication of animals and living in close dense regions; and so with that came small pox, measles and influenza.

This article discusses about the ecology of various emerging infectious diseases, and the factors that influence their emergence. For the ease of classification and comprehension, the ecology of emerging infectious diseases can be classified as follows: ecology of emerging livestock and poultry diseases; ecology of emerging pet and companion animal diseases; ecology of wildlife diseases and ecology of zoonotic diseases. This classification causes confusion as factors tend to overlap amongst all the emerging infectious diseases. Factors attributed to the emergence cannot be segregated based on the host species population as they are common among various species populations. It was found better to classify the ecology of emerging infectious diseases based on the determinants of a disease. In an endemic state of an infectious disease, the determinants responsible are pathogen, host, vector and environment. But for the past 2–3 decades the most important factor responsible for a disease to emerge or become an epidemic has been due to human intervention by progress in science and technology. Therefore this article discusses with examples how ‘progress in science and technology’ or ‘human intervention’ can be included as the fifth determinant in an emerging epidemic disease.

When the emerging diseases are classified based on the major factors responsible for their emergence, it is evident that human activity plays a major role.

Pathogen characteristics
- Evolution/selection pressure
- Mutation
- Immune pressure

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Exponential growth in the human population has increased the food demand all over the world. Large areas are being converted to agricultural land. Waterlogging in paddy fields forms the focus for Japanese encephalitis as the clear water facilitates multiplication of the vector culex. In the Malaysian peninsula a new, highly contagious respiratory and neurological disease of pigs was reported during 1998–1999. A novel paramyxovirus, distinct from Hendra virus, was isolated from both porcine and human victims and was named Nipah virus. Epidemiological and serological investigations revealed that the virus is a commensal in fruit bats of genus Pteropus and the fruit bat is the natural host and reservoir of the virus. The reasons for emergence of the disease in 1998 were extensive deforestation in the peninsula, habitat destruction of the bats and the newly developed fruit orchards which caused the bats to enter farms. Intensive pig farming was also on the rise during the decade which facilitated the virus to be transmitted to pigs and then across different species.

Increase in Japanese encephalitis incidence in India during 1970 to 1980 can be attributed to increase in agriculture, adoption of rice cultivation and establishment of large, modern pig farms during that time. Leptospirosis has increased in India during the past 20 years due to increased farming and inadequate rodent control.

**Antibiotic abuse**

Prolonged overuse of antibiotics in food animals for therapeutic purposes has resulted in many organisms becoming resistant to antibiotics. Antibiotics are used in livestock and poultry for therapeutic, metaphylactic, prophylactic and subtherapeutic reasons, thereby flooding both animals and environment with antibiotics. In India, the following organisms have become resistant to antibiotics and are causing reemergence and concern. *Yersinia pestis* has been reported to be resistant to streptomycin, tetracycline, chloramphenicol and sulfonamides; *Staphylococcus aureus* to methicillin and vancomycin; *Neisseria gonorrhoeae* to penicillinase-producing, ceftriaxone; meningococci to sulphonamides, cefotaxime and ceftriaxone; *Salmonella typhi* and *S. paratyphi A* to chloramphenicol, ampicillin, cotrimoxazole and fluoroquinolone and *Shigella* to azithromycin, ceftriaxone and ciprofloxacin.

**Bioterrorism**

Bioterrorism has been suspected in quite a few incidences, but biological attack to the US in 2001 is an incidence that can be documented as bioterrorism. *Bacillus anthracis* spores were intentionally distributed through the postal system causing 22 cases of anthrax, including five deaths. The outbreak was reported in Columbia, Florida, New Jersey, and New York.

**Blood transfusion**

In 1997, transfusion-transmitted virus (TTV) of the Circoviridae family was discovered as the cause of some cases of hepatitis, transmitted by infected blood donations. The prevalence of TTV antibodies in various populations is under test and has been found to be variable.

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**Host characteristics**
- Naïve population
- Immune suppression
- Increase in host population

**Environmental changes**
- Climatic changes
  - (a) Global warming
  - (b) Rainfall
- Natural calamities

**Vector characteristics**
- Migration
- Increase in vector population
- Vector range
- Vector competence
- Change in vector behaviour

**Progress in science and technology**
- Agriculture and intensive production
- Antibiotic abuse
- Bioterrorism
- Blood transfusion
- Breakdown in public health measures
- Change in eating habits
- Change in food processing
- Change in storage techniques
- Deforestation
- Exotic pet-keeping
- Good documentation/research
- Improved diagnostic techniques
- Improved monitoring and surveillance
- Mass food processing
- Mixed farming
- Occupational exposure
- Recreational activities
- Reforestation
- Road construction
- Trade and transportation
- Travel and tourism
- Urbanization
- War
- Water control projects
- Xenobiotic transplantation
**Breakdown in public health measures**

Cholera has recently been causing panic in South America and Africa. The rapid spread of cholera in South America may have been caused by recent reductions in chlorine levels used to treat water supplies. The US outbreak of waterborne *Cryptosporidium* infection in Milwaukee, Wisconsin in the spring of 1993, with over 400,000 estimated cases, was in part due to a nonfunctioning water filtration plant; similar deficiencies in water purification have been found in other cities in the US. The plague outbreak in Maharashtra and Gujarat, India in 1994 was attributed to lack of proper sanitation and garbage disposal, as well as increase in rodent population.

**Change in eating habits**

Culture, tradition, religion and geographical location govern the range of food we are exposed to, how they are cooked, the ingredients added, etc. and therefore will also govern the parasites that we are exposed to. Pork (*Toxoplasma gondii*, *Taenia solium* and *Trichinella* spp.) is shunned by Jews, orthodox Christians and Muslims. Cattle (*Taenia saginata*) are considered holy and not consumed by the Hindus. Animals that some cultures consider companion, work, wild or domestic are viewed by others as important sources of protein; guinea-pigs, horses (*Trichinella spiralis*), dogs (*Leptospirosis*, *Cryptosporidiosis*) and a range of wildlife species are consumed by many people. Tourism, immigration and exposure via the media have increased popularity of different kinds of food and have broadened people’s eating habits. The rapid transport and cold storage facilities enable the survival of parasites in food as well as surface contaminants.

Anisakiosis has been reported in European countries and USA, where the parasite was not seen earlier. The exposure to Japanese food and Sushi has introduced raw fish food to these populations, who otherwise do not have the practice of raw fish delicacies and would not have been exposed to the parasite. Also the practice and knowledge about raw fish preparation is less in countries that have been recently introduced to it.

Bushmeat (primate meat and brain) is a multibillion dollar business with huge urban demand. The demand is recently being easily met due to facilitated access to primate habitats by logging roads in Africa. The consumption of bushmeat has been reported to be 1–3.4 million tonnes and 67–164 million kg in Central Africa and the Amazon Basin respectively. People consuming and merely being in contact with fresh non-human primate bushmeat have been infected with simian foamy virus. Human T-lymphotropic viruses 3 and 4 have been found in persons who hunt, butcher, or keep monkeys or apes as pets in southern Cameroon. Several outbreaks of Ebola virus in western Africa have been associated with consumption of bushmeat, mainly chimpanzees that were found dead.

**Change in food processing**

Bovine spongiform encephalopathy (BSE) is a fatal neurological disease of cattle that first came to attention in November 1986 in the UK. Between November 1986 and May 1996, approximately 160,000 cases were reported. Epidemiologic studies suggested that the source of disease was cattle feed prepared from carcasses of dead ruminants. The disease had not appeared till 1986 as the temperature of rendering process for preparing cattle feed was decreased during 1981–1982. By May 1996, BSE had been reported from 10 countries and areas outside the UK. Feeding processed ruminant carcass to ruminants is forced cannibalism to a herbivore by humans, thereby giving an opportunity to the organism to emerge, which in otherwise natural conditions would never be able to do so.

**Change in storage techniques**

In 1955, the first human case of a serious intestinal granulomatous disease caused by larvae of *Anisakis* spp. was diagnosed in The Netherlands. The ascарoid nematode of marine mammals and fishes was never reported in human beings till 1955. The disease occurred after ‘improved’ icing procedure on herring fishing boat (especially the use of ice containing antibiotics) was implemented. Hence fish spoilage was retarded so that herring and other fish formerly gutted promptly at sea were now gutted ashore after their landing. The infective larvae of *Anisakis*, normally present only in the gut of the fish, reacted to the death of their host burrowing into the muscularate. From here, humans who consumed the infected raw fish meat or lightly cooked would get infected with this nematode, causing an anaphylactic reaction.

**Deforestation**

In 1957, Kyasanur forest disease was restricted to 300 square miles in Shimoga district, Karnataka, South India. This tickborne disease occurs in a predominantly evergreen rainforest with clearings for rice cultivation and human habitation. In 1983, a major epidemic occurred during which several monkeys died, 1555 humans were infected and 150 humans died. The outbreak occurred in previously undisturbed forest where some 400 ha was felled to establish a cashew tree plantation. As many as 1000 human infections occur each year, and this number has increased in the past 5 years. Such a zoonosis is a good example of deforestation and agricultural development leading to human habitat expansion into natural foci of a viral infection.
Leishmaniasis (kala-azar) is caused by the protozoan *Leishmania* spp. and transmitted by phlebotomine sandflies. In Latin America, parts of the thick dense forests were interspersed with only few farmlands. With growth of the fox population, an excellent reservoir host of visceral leishmaniasis, kala-azar has increased and the sylvatic leishmaniasis vector sandflies have become peridomestic. In mountainous coffee-growing regions of Latin America, leishmaniasis became a serious problem due to the high multiplication of phlebotomine sandfly population. The vector growth is speculated to be due to the favourable large shade trees and sugar from the ripe coffee fruit.

In the Amazon basin, Para State in Brazil, prevalence of leishmaniasis increased when the forests were felled to grow pines and gmelina for paper industry. The spiny rat, reservoir host for cutaneous leishmaniasis increased in number by adapting to the changed environment and facilitated in the transmission and maintenance of the disease.

**Exotic pet-keeping**

Exotic pets have been a source of infection from endemic regions to very rare or new regions. An outbreak of monkey pox in the US (71 cases) was traced back to infected prairie dogs that had been transported with African rodents imported from Ghana. Similarly, an outbreak caused by *Francisella tularensis* type B occurred among wild-caught, commercially traded prairie dogs. African pygmy hedgehogs have been implicated in human salmonellosis cases and ringworm infections along with chin-chillas in the US. Correlation has been found with salmonella infection in children and handling a reptile or owning an iguana. Marmosets (*Callithrix jacchus jacchus*) caused rabies of a new variant in eight people in Ceará, Brazil, from 1991 through 1998. In 1999, encephalitis was diagnosed in an Egyptian rousette bat (*Rousettus aegyptiacus*) that had been imported from Belgium and sold in a pet shop in southwestern France. The pet bat was infected with a Lagos bat *Lyssavirus* and resulted in the infection of 120 exposed persons.

**Good documentation/research**

Advances in diagnostic technology can also lead to recognition of agents that are already widespread. Due to years of good documentation and recordkeeping, the human herpesvirus 6 (HHV-6) was recently identified as the cause of roseola (*Exantherma subitum*), a common childhood disease. Another example is the bacterium *Helicobacter pylori*, which was only recently identified as one of the probable causes of gastric ulcers and some cancers.

**Improved diagnostic techniques**

Eosinophilic enteritis caused by *Ancylostoma caninum* in human beings was reported positive in 233 patients complaining about abdominal pain and with or without eosinophilia from Queensland, Australia, when tested using a specifically developed ELISA and Western Blot techniques in 1998. The disease was diagnosed in 33–100 patients a year till 1988. The increase in the number of cases of ancylostomiasis reported is attributed to the improved sensitivity of diagnostic techniques over the years.

**Improved monitoring and surveillance**

After BSE spread across Europe from the UK, stringent monitoring and surveillance was followed in Italy for BSE by screening brains of slaughtered cattle for prions as a routine procedure. Over 1.6 million brains were tested in 2004, where 103 cases of a new prion causing a distinctly different type of spongiform encephalopathy called bovine amyloidotic spongiform encephalopathy (BASE) was discovered. The new BASE prion differs by a fewer sugars.

**Mass food processing and distribution**

Industry food preparation and mass food distribution of food products may lead to large outbreaks of foodborne diseases. An outbreak of salmonellosis resulted in illness in around 250,000 people in USA in 1985 due to contaminated milk. Similarly, a widespread outbreak of *Salmonella* occurred in 1994, when ice cream premix was transported in tanker trucks that had not been thoroughly sanitized after transporting raw liquid egg. In 1982 *Escherichia coli* O157:H7 was first recognized as a human pathogen when two outbreaks in the US were associated with consumption of undercooked hamburgers from a fast-food restaurant chain.

**Mixed farming**

Avian influenza virus has been reported to spread through birds and mammals, including pigs and horses. Mixed farming or transfer of farm waste to other farms can facilitate the emergence of a new variant of a virus. For example, feeding faecal material from ducks to fish that are used as food for pigs has been postulated to cause avian influenza to emerge in pig farms. More directly, the practice of raising pigs under chicken houses or feeding pigs untreated garbage or the carcasses of dead birds can also cause the virus to spread to pigs or cause a new variant to emerge as reported in Pennsylvania in 1982 (ref. 20).

**Occupational exposure**

Marburg virus, related to Ebola virus, was first detected in 1967 in a laboratory in Marburg, Germany, when peo-
ple working with infected green monkey tissue from Uganda also became infected and died. Thirty one people were infected resulting in seven deaths. The virus was hence named Marburg virus after the place of outbreak. In 2005, an outbreak of Marburg virus disease occurred in Angola21. Health-care workers experience high exposure to blood-borne viruses resulting in 16,000 hepatitis C, 66,000 hepatitis B and around 5000 HIV cases annually in the Rural North Indian health care setting22.

Recreational activities

Water recreational activities like swimming in public pools, interactive fountain or water canals have caused outbreaks of giardiasis, cryptosporidiasis and schistosomiasis in many states in USA, especially during summer, which is a suitable time of the year for outdoor water activities and optimum temperature for the survival of the organism23. During World War II several airforce training bases were built in the deserts of San Joaquin Valley, Arizona, USA. Many soldiers started showing signs of illness beginning with respiratory problems. The disease was found to be coccidioidomycosis and exposure to the pathogen was due to the Indian burial sites that were around the valley. Recreational activity and sometimes just driving through the valley have caused disease in people24.

Reforestation

Deforestation is conversion of forest land to agricultural land and is a well-known cause for humans and animals to be exposed to emerging infectious pathogens. It is interesting to note that the reverse, i.e. reforestation also caused emergence of an infectious disease. The deer population is northern states of USA had decreased drastically due to uninhibited hunting and deforestation. Therefore, reforestation measures were taken up and the deer population increased. Along with deer population and its ectoparasite *Ixodes scapularis* ticks also increased. Simultaneously, an increase in *Borreliaburgdorferi* was reported15.

Road construction

The construction of new roads provides access for human, livestock, vector and parasite populations. Roads facilitate acceleration of crop farming, ranching, logging, mining, commercial development, tourism, building of dams, hydroelectric plants and new settlements. Construction of roads in previously inaccessible forested areas can lead to erosion and may create ponds by blocking the flow of streams. The ponds then serve as breeding grounds. By providing access to forested and newly deforested areas, non-immune, non-protected populations, such as construction workers, loggers, miners, tourists and conservationists are exposed to indigenous and newly arrived vectors and their parasites. Further, these visiting human populations bring with them and introduce parasites to vectors and settlers along the forested/deforested interface. Establishment of animal conservation and rehabilitation centres, national parks and wildlife reserves, which is facilitated by new access roads, increases the association between humans and animals, as do zoos, aquaria and seaworlds, industrial animal production, non-traditional agriculture, aquaculture, free-ranging/farmed game species and hunting18.

Travel and tourism

Adventure travel is the largest growing segment of the leisure travel industry; growth rate has been 10% per year since 1985 (Adventure Travel Society, pers. commun.). This type of travel increases the risk of tourists participating in activities such as safaris, tours, adventure sports and extreme travel contact pathogens uncommon in industrialized countries. The most commonly encountered rickettsial infection in travel medicine is African tick bite fever, caused by *Rickettsia africane* and transmitted in rural sub-Saharan Africa by ungulate ticks of the *Amblyomma* genus. Most patients are infected during wild game safaris and bush walks15.

Trade and transportation

Chikungunya was endemic only to Kenya till 1940. The disease was then reported in Lamu in 2004, affecting 13,500 people. The occurrence of the disease in these islands near Madagaskar was due to movement of goods through ships. The disease was reported in Réunion in 40,000 people by January 2006. The trade and shipment of goods to and from India, African islands and Nigeria resulted in the virus entering India which had a dense naïve population to cause an epidemic in the country from March 2005 to 2009 affecting more than 1.35 million people25.

Animals imported for commercial trade are a substantial risk of infectious disease emergence in human beings as in the case of the monkeypox outbreak in 2003, where 71 humans were infected in USA with monkey pox from prairie dogs which were housed with newly shipped African Gambian giant rats26.

Transportation vehicles can serve as mechanical vectors for the dispersion of pathogen or vectors. It is well known that one of the vectors of dengue fever, *Aedes albopictus*, was introduced into the US from Asia via automobile tires on ships coming from Asia. The tires contained pools of water, which provided the vectors with...
ideal conditions for survival and replication. This has potentially serious consequences for the US, since the possibility exists that dengue can be introduced into even temperate areas of the country once the vector is present. 

**Urbanization**

People in some urban localities in Europe were estimated to be at a greater risk of being exposed to *Echinococcus multilocularis* because red foxes, the primary sylvatic reservoir of the parasite were reported to scavenge around human dwellings as concentrated resources influence host migration into urban landscapes and therefore increase species contact rates, including contact between humans and wildlife hosts. 

**War**

Dengue fever is an old disease, but in the past 25 years the disease has been reported in large numbers and across many countries. The disease was reported before the year 2000 in less than 100,000 individuals across less than 10 countries. In 2000, the disease has been reported in around 500,000 individuals across 60 countries. The reason for global pandemic can be attributed partly to major demographic and societal changes that have occurred since World War II. During the war, both the virus and the principal urban mosquito vector became widely distributed in the urban centres of Southeast Asia. The War caused a slack in economic development and negligence towards planned urbanization and mosquito control. In addition, the advent of modern airplane travel and the increased movement of people, many of them infected and incubating Dengue virus facilitated the spread of the disease across the globe. 

Contagious bovine pleuropneumonia was not detected in Tanzania till it spread across the country. Once it had been detected, the Tanzanian veterinary services found it difficult to control the disease due to lack of resources and due to political fragmentation. Botswana and Zambian veterinary services were able to control the disease, while civil war-stricken southern Angola was not able to keep the disease under check. 

Rinderpest has still not been eradicated in many countries due to lack of funds, as these countries have to prioritize their finances to more basic human necessities. Somalia and southern Sudan remain endemic to Rinderpest as two civil wars have drained out their resources. 

**Water control projects**

The appearance of Gnathostomiasis in Culiacan, Mexico was reported to coincide with the custom of eating raw freshwater fish in the form of ceviche or callos, that had begun 20 years earlier, shortly after the construction of three nearby dams and the formation of lakes that produce 700 ± 900 tonnes of freshwater fish annually. Freshwater fish were apparently introduced into Sinaloa from other lakes in Mexico, including Temascal, which had been shown to be endemic for gnathostomiasis. Since no cases of gnathostomiasis had been reported in Mexico before 1970, mass production and commercial distribution of tilapia has been implicated as the most likely explanation for the findings. 

Construction of water reservoirs and dams in eastern India showed a significance rise of *Visceral leishmaniasis* in Bangladesh and West Bengal as the water bodies served as habitat for the multiplication of sandflies. 

**Xenobiotic transplantation**

Four people died after receiving organs from a donor who had died of subarachnoid haemorrhage caused by suspected drug abuse. The patient had nausea, vomiting and difficulty while swallowing before his death. Further investigation by Arkansas Health Department, US, following the death of the organ recipients revealed that the donor was bit by a bat and the clinical signs were caused by rabies and not the suspected drug-induced subarachnoid hemorrhage. Similarly, three out of six recipients died in Germany (two received a cornea each (avascular) and the other had protective antibody titre from vaccination) following organ transplantation from a German woman who died of drug abuse. The clinical signs were attributed to toxic psychosis, her exposure to rabies was not identified even after investigation. In another incident two recipients died of rabies when they received organs from a donor who was declared brain dead after an automobile accident in USA. It is evident from these cases that xenobiotic transmission of rabies is possible. 

In August 2002, four recipients of organs were admitted to hospitals near their homes with encephalitis and febrile illness. A few weeks later they died and the autopsy concluded that they had died of West Nile virus infection. It was found that all the patients had received organs from the same donor. A detailed retrospective study revealed that the donor was admitted to the hospital with no clinical signs correlating with encephalitis, but had received blood transfusion a day before his death in the hospital from a donor who had febrile signs and was later found positive for West Nile virus infection. This case demonstrates the emergence of an infectious disease through blood transfusion and organ transplantation. 

**Conclusion**

This article highlights human interference with nature and disruption of ecology leading to the spread of infectious diseases to regions and species previously unseen. Scientific progress has been demonstrated here clearly to
be a two-sided coin; increasing efficiency of work, improving standard of living and decreasing in world hunger, but simultaneously having negative effects like high population, species eradication, global warming, lifestyle disorders and emergence of infectious diseases. There is an urgent need for the global community to understand that mankind has gone need beyond and is now greedy to satisfy his wants. If we learn to live with minimal needs, respect the ecosystem and adapt sustainability, then we can decrease deforestation, road constructions to virgin lands, urbanization, trade and transport, fuel burning, fuel digging, mass food production, intensive and mixed farming, antibiotic abuse, war, etc. Therefore, also making it easier for monitoring and surveillance of the population and maintaining effective public health measures.


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