



Emerging and re-emerging bacterial infections: A threat to effective health care delivery system in Africa

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Abstract

Since early 1900, the world have been faced with series of emerging and Re-emerging infectious diseases. The World Health Organization warned that infectious diseases are emerging at a rate that has not been seen before. To date, more than 40 infectious diseases have been discovered both belonging to bacteria and viruses. These agents are now considered as the main microbiological public health threat to an effective health care delivery system. With newer technologies and people traveling more frequently and far greater distances than in the past, the potential for emerging infectious diseases to spread rapidly and cause global epidemics is a major concern. The rapid spread of infectious diseases and their unpredictable consequences, in terms of human lives and economic losses, will require a change in our strategy, both at the clinical and the research level. Ultimately, the world need be ready to fight against infectious diseases affecting a huge number of people in different parts of the world. This new scenario will require rapid, inexpensive diagnostic systems, applicable anywhere in the world and preferably, without the need for specialized personnel. This review focus on bacterial emerging and re-emerging diseases and explore factors involved in their emergence, highlighting the major emerging bacterial pathogens of the last 50 years, Emerging Infections Priority Issues, Factors contributing to the emergence of infectious diseases, Prevention and control of Emerging Infectious Diseases as well as future prospects.

Keywords: bacterial pathogens, diagnostic systems, diseases, emerging and re-emerging infectious diseases, epidemics, health care delivery system, prevention and control

Introduction

In human history, numerous infectious diseases have emerged and re-emerged, causing a continuous threat to our public health systems due to limited experience in case management and lack of appropriate resources (Clemmons *et al.*, 2021) ^[37]. Many of these agents are zoonotic in origin and transmitted from animals to man either directly or via vectors. The reservoirs are often infected subclinically or asymptotically and the distribution of the diseases basically reflects the range and the population dynamics of their reservoir hosts (Bergwerff and Debast, 2021) ^[36]. The severe acute respiratory syndrome coronavirus (SARS-CoV) that emerged in China in early 2003, SARS-CoV-2 is considered a zoonosis, with bats suspected as the primary host species (Rabi'u *et al.*, 2020; Ijaz *et al.*, 2020; Rabi'u *et al.*, 2021) ^[41, 39, 40].

Many bacterial emerging and re-emerging diseases can be considered opportunistic infections. Increasing demands for protein necessitate increased levels of farming. Food can provide a vehicle for spread of pathogens from animals to humans. Contact with animals during farming, hunting, or by animal bites can increase transmission of diseases. Changing patterns of farming, life style, and transportation influence the dynamics of pathogen ecology. Pathogens are subjected to changes by many intrinsic and extrinsic factors (Klohe *et al.*, 2019) ^[42]. Mutation, recombination, selection, and deliberate manipulation can result in new traits acquired by pathogens and result in potential epidemic consequences (Uves, 2021) ^[14]. Re-emergence of diseases through opportunistic host switching is likely to continue as a major source of human infectious disease. Strategies to improve public health have focused on improved surveillance in regions of perceived high likelihood of disease (re-emergence). These strategies include improved detection of pathogens in reservoirs, early outbreak detection, broad-based research to identify factors that favour re-emergence, and effective control (i.e., quarantine and improved hygiene) (Bergwerff and Debast, 2021; Van-Zyl, 2021). ^[36, 16]

With the discovery of penicillin by Alexander Fleming in 1928 and scientific progress that followed during the 20th century, it was thought that bacterial diseases would be easily controlled (Clemmons *et al.*, 2021) ^[37].

However, since the 1950s, physicians have been faced with emerging and re-emerging infectious diseases (EIDs), which have brought significant public health and financial challenges. As an example, in 2010, specialists struggled with a mysterious clinical picture that associated a severe inflammatory syndrome with vascular events such as venous thromboembolisms or transient ischemic attacks (Patel *et al.*, 2018)^[5].

According to WHO Emerging infectious disease are previously identified diseases along with the newly discovered and unknown infectious agents that cause public health problems either locally or internationally (Klohe *et al.*, 2019)^[42].

Re-emerging infectious disease are infectious agents that have been known for some time but had fallen to such low levels that they were no longer considered public health problems but are now showing upward trends in incidence or prevalence worldwide or have appeared in areas where they were not previously found (Marit, 2019)^[1]. About 60% of the re-emerging infectious diseases are of zoonotic origin and can both be viral, bacterial, fungal and protozoans etc. however this review will be limited to emerging and re-emerging infectious diseases of bacterial origin (CDC, 2019). There has been a worldwide explosion of infectious diseases: emerging diseases like the HIV/AIDS pandemic, or old diseases like cholera, tuberculosis, diphtheria, plague, yellow fever, dengue, or malaria. These re-emerging diseases are on the surge because of multiple factors: environmental changes, transformation of the ecosystems, the ongoing socio-economic degradation and the deterioration of the public health systems in many countries (Madigan and Martinko, 2006; Clemmons *et al.*, 2021)^[22, 37]. The emerging infectious diseases and their basic causes present a threat to the stability of the nations worldwide. The factors for the emergence/re-emergence of infectious diseases are complex and interrelated (Klohe *et al.*, 2019)^[42]. In the human history, numerous infectious diseases have emerged and re-emerged. Besides many others, the so-called 'exotic' agents in particular, are a threat to our public health systems due to our limited experience in the case management and due to the lack of appropriate resources. Many of these agents are zoonotic in origin and these are transmitted from animals to man either directly or via vectors. The reservoirs are often infected sub-clinically or asymptotically and the distribution of the diseases basically reflects the range and the population dynamics of their reservoir hosts (Lukjancenko *et al.*, 2010; WHO, 2010; Bergwerff and Debast, 2021; Issa *et al.*, 2021)^[21, 36, 46].

The Spread of the emerging and re-emerging infectious diseases

The emerging communicable diseases are those for which the incidence in humans has increased in the past decades or is threatening to increase in the near future. The re-emerging communicable diseases are those which are known and which reappear after a decline in their incidences. The term, 'emerging diseases', which is used interchangeably with the term, 'emerging infectious diseases', means 'the infections that newly appear in a population, or which have existed but are increasing in incidence or geographic range'. Over the past 3 decades, more than two thirds of the emerging infectious diseases have had an origin in animals (Daszak *et al.*, 2007; Rabiou *et al.*, 2022; Abdulfatai *et al.*, 2022).

Recent advances in basic scientific research, together with the development of molecular biology techniques, have not only improved infectious disease diagnosis, but have also provided relevant data about pathogenesis and epidemiology (Ogino *et al.*, 2019). As such, science offers the necessary tools for appropriate disease prevention and control. However, the progress made in this field over the past century is now facing a new challenge (Fernandez *et al.*, 2020). The available techniques for disease detection and treatment must be adapted to deal with global health problems (Clemmons *et al.*, 2021)^[37].

Meanwhile, the well-known diseases which were once thought to have been conquered, such as tuberculosis, plague, cholera, Dengue fever/Dengue haemorrhagic fever, yellow fever and diphtheria are re-emerging as public health threats in many countries, after a period of decline in their incidences. The spread of antimicrobial resistance is another emerging global public health issue. New pathogens and antimicrobial-resistant forms of the older pathogens continue to emerge, some with the potential for a rapid and a global spread, with high morbidity and mortality and these are of public health importance (Masalha *et al.*, 2010).

The infectious diseases have always afflicted mankind and they always will. New infectious diseases will emerge and old diseases will re-emerge as the microbes adapt to new hosts and new environments. To remain one step ahead of our pathogenic microbial foes, we must understand in detail how the pathogens interact with their hosts, and how biological, environmental, and social factors combine to allow pathogens to infect new organisms. Deciphering each step in the different processes by which microbes adapt to their new hosts, is critical to developing effective countermeasures to detect, prevent, and to treat infectious diseases (Klohe *et al.*, 2019)^[42].

The World Health Organization warned in its 2007 report that infectious diseases are emerging at a rate that has not been seen before. Since the 1970s, about 40 infectious diseases have been discovered this include SARS, Ebola, Avian flu, and Swine flu. With people traveling much more frequently and far greater distances than in the past, the potential for emerging infectious diseases to spread rapidly and cause global epidemics is a major concern (Moti *et al.*, 2018; Saka *et al.*, 2010).

The World Health Organization/Food and Agriculture Organization/World Organisation for Animal Health joint consultation on emerging zoonotic diseases, held in Geneva in 2004, defined an emerging zoonosis as "a pathogen that is newly recognized or newly evolved, or that has occurred previously but shows an increase in incidence or expansion in geographical, host or vector. Through continued alterations in human and animal demographics and environmental changes, new and recurring diseases are likely to continue to emerge. The

effects of zoonoses on human health and economies have recently been underscored by notable outbreaks such as those involving Nipah virus and severe acute respiratory syndrome (SARS) coronavirus (CoV). A recent retrospective study of 335 emerging infectious episodes over a 64-year period (1940–2004) emphasized the role of wildlife as a source of emerging infections. However, research efforts have typically been focused toward either humans or economically related species (Mbim *et al.*, 2016)^[25].

The frequency of these events increased substantially over the period of investigation. Such infections are now often perceived as agents of biologic warfare rather than infections with a long but insidious history in their appropriate ecologic niche. Why then are these infections becoming a serious public health concern? The answer is a complex multifactorial set of changing circumstances (McArthur, 2019)^[45]. To support the growing human population, we have an increasing demand for nutritional support, resulting in intensive agricultural practices, sometimes involving enormous numbers of animals, or multiple species farmed within the same region. These practices can facilitate infection to cross species barriers (Marit, 2019; Fernández *et al.*, 2020; Van-Zyl, 2021)^[38, 1, 16]. Additionally, we are witnessing increasing globalization, with persons, animals, and their products moving around the world. This movement enables unprecedented spread of infections at speeds that challenge the most stringent control mechanisms. Furthermore, continual encroachment of humans into natural habitats by population expansion or tourism brings humans into new ecologic environments and provides opportunity for novel zoonotic exposure (Klohe *et al.*, 2019)^[42]. Climatic changes have facilitated the expansion of compatible conditions for some disease vectors, remodelling dynamics for potentially new, emerging, and re-emerging zoonosis. In the next 2 decades, climate change will be the most serious issue that dominates re-emergence of pathogens into new regions. Climate change also effects evolution of pathogens, and where relevant, their vectors (Morikawa *et al.*, 2012; Clemmons *et al.*, 2021)^[26, 37].

Continual mutation and recombination events give rise to variants with altered levels of fitness to persist and spread. Changing ecologic circumstances and pathogen diversity can give rise to variants with altered pathogenic potential (Smith and Fratamico, 2018)^[44]. However, the host must not be ignored. Increased longevity and therapies for persons with diseases can modulate host susceptibility and concomitant infections and upset the evolving and dynamic infection balance (WHO, 2010; McArthur, 2019)^[45].

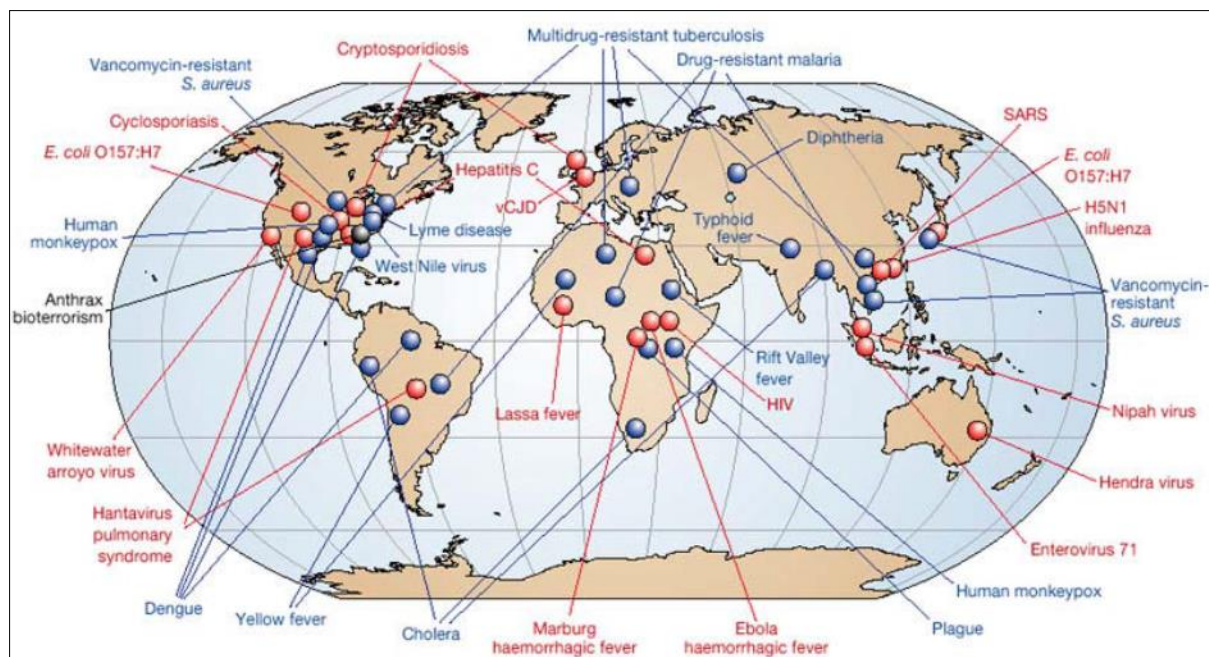


Fig 1: Examples of Recent Emerging Diseases Worldwide

Emerging and Re-emerging Bacterial Infections

The bacterial world is complex, dynamic and constantly evolving. Infectious agents reproduce rapidly, mutate frequently, cross the species barrier between animal hosts and humans and adapt with relative ease to their new environments. Because of these traits, infectious agents (bacteria) alter their epidemiology, their virulence, and their susceptibility to anti-infective drugs (Klohe *et al.*, 2019)^[42]. When bacterial disease is caused by a microbe that is newly identified and not known previously to infect humans, it is commonly called an emerging bacterial disease, or an emerging bacterial infection. When bacterial disease is caused by an infectious agent previously known to infect humans that has re-entered human populations or change epidemiology or susceptibility to anti-infective drugs is called a re-emerging bacterial infection (Sasseti and Rubin, 2007; McArthur, 2019)^[32, 45].

Bacteria are single celled organisms, microscopic in size (less than 1 μm to several μm in length) and lack a defined nucleus, belonging to the *Prokaryote* kingdom. Within the prokaryotic organisms. Four divisions are recognised, based upon cell wall characteristics (Ursula and Antoine, 2013)^[18].

Four divisions of Bacteria based on cell wall characteristics.

a. Division 1: *Gracilicutes*

Are Gram-negative type cell wall (contains Gram-negative bacteria)

b. Division 2: *Firmicutes*

Are Gram-positive type cell wall (contains Gram-positive bacteria).

c. Division 3: *Tenericutes*

This have no cell wall (contains class Mollicutes).

d. Division 4: *Mendosicutes*

These are Procaryotes with unusual walls, membrane lipids, ribosomes and RNA sequences (contains class Archaeobacteria).

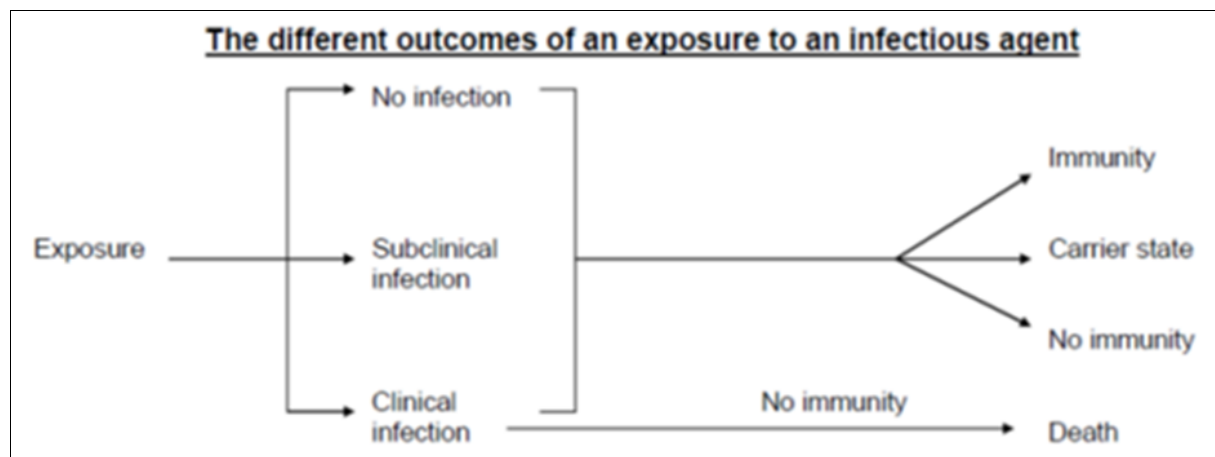
The taxonomy of bacteria has undergone considerable revision during the past two decades. The basic unit of bacterial classification is the species, which may be defined as a collection of strains that have many features in common, differing in these features from other groups of strains.

Bacterial Diseases

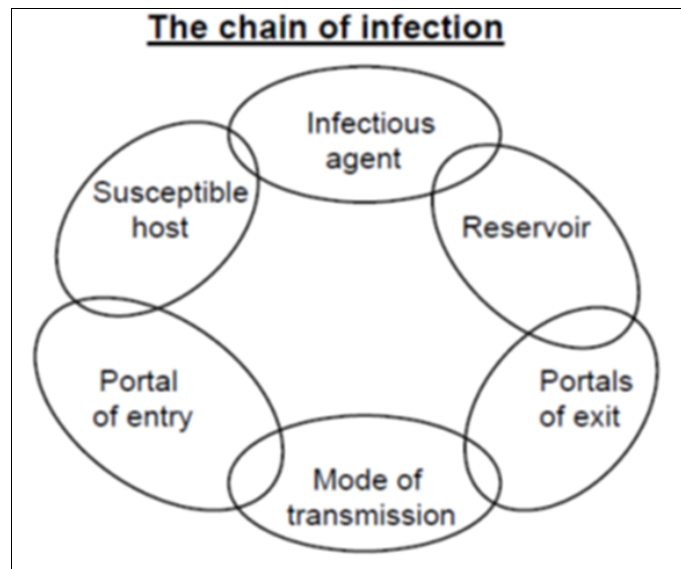
Bacterial diseases remain of major economic and public health importance. Diseases increase mortality rates, decrease body mass gain, decrease egg production, and increase medication costs. In recent years, public health concerns for food borne bacterial infections and antibiotic resistant strains increased causing major political issues in several countries. The following highlights key developments in the field of emerging and re-emerging bacterial diseases. Worldwide the new emerging bacterial diseases are Amyloid Arthropathy and *Ornithobacterium rhinotracheale* infections. In addition, avian mycoplasmosis, erysipelas, Necrotic Enteritis and chlamydiosis appear to be making a comeback (Omitola and Taylor-Robinson, 2020)^[43]. Finally, reports during recent years reveal *Salmonella* (especially *S. enteritidis*) and *Campylobacter* sp. are the most common causes of human food borne bacterial diseases linked to poultry products. These diseases are explained below

1. Amyloid Arthropathy

In 1992, a clinically unknown joint disease was identified in heavy breed layers in The Netherlands and France. Clinical symptoms were growth retardation, generalized amyloidosis and amyloid arthropathy. Laboratory investigations resulted in isolation of *Enterococcus faecalis* (*E. faecalis*) and a reovirus. A single type of heavy breed layers were affected regardless of being reared in cages or on the floor. No seasonal variability was observed. Brown replacement pullets were the most frequently involved from 1996 and 1997 in The Netherlands. The major pathogen identified from the joints of affected animals was *E. faecalis*. Amyloid arthropathy was also observed sporadically in broiler breeders and *Staphylococcus aureus* (*S. aureus*) was isolated (Morikawa *et al.*, 2012; Omitola and Taylor-Robinson, 2020)^[26, 43].



(Kramer *et al.*, 2010).



(Kramer *et al.*, 2010).

2. Erysipelas

Erysipelas is a bacterial disease caused by *Erysipelothrix rhusiopathiae*. It was identified more than 100 years ago and recognized as the etiologic agent of swine erysipelas. Since then, it has been identified as the causative agent in several species of mammals, birds and other animals. Though more common in turkey, the infection has been sporadically reported in several species of poultry including chicken, duck, geese, pheasant and quail (Omitola and Taylor-Robinson, 2020)^[43].

Currently in the European Union (EU) about 85% of commercial layers are kept in cages but Table egg producers are starting to use so called alternative rearing systems such as free range and perchery systems (Madigan and Martinko, 2006)^[22]. These rearing systems increase health problems and stimulate the re-emergence of disease conditions including erysipelas.

For many years erysipelas was not reported in laying hens in Germany. In 1998 a farm with 43,000 free range laying hens developed an increased mortality accompanied with a drop in egg production at 34 weeks of age. The birds showed depression, ruffled feathers, somnolence and diarrhoea. Bacteriological examinations of internal organs resulted in isolation of *Erysipelothrix rhusiopathiae* of serotype 1. In addition, *E. coli* and *Pasteurella multocida* were isolated from ovary and peritoneum. Treatment trials with penicillin were started and the mortality reached 8 % at the end of the production period (Daszak *et al.*, 2007; McArthur, 2019; Omitola and Taylor-Robinson, 2020)^[19, 45, 43].

3. Necrotic Enteritis (NE)

NE is an acute disease caused by *Clostridium perfringens* when it migrates from the large intestine and caeca to the small intestine where it produces toxins (Maccmillan *et al.*, 2018). Toxin type A or C is responsible for damaging the intestinal lining. Dysfunction of the alimentary tract predisposes the animal to infection. Intestinal stasis, intestinal distension, coccidiosis, salmonellosis, crop mycosis and haemorrhagic enteritis (HE) may predispose the birds to infection (Gelberg, 2017). The practice of addition of some feed additives to significantly enhance digestion of nutrients is associated with an increased incidence of NE in poultry flocks in all European countries, and have been found to be among the contributing factors predisposing the intestinal tract to overgrowth by Clostridia organisms. It may also be as a result of the consumption of diets high in energy, protein and fishmeal as well as the consumption of high fibre litter and a wheat based diet. The clinical signs appear suddenly; apparently healthy birds may become acutely depressed and die within hours. Mortality ranges between 2 and 10 %. Affected birds show ruffled feathers, marked depression, inappetance, tendency to huddle, watery droppings and diarrhoea (Madigan and Martinko, 2006; WHO, 2010)^[22].

4. *Ornithobacterium rhinotracheale* (ORT)

Ornithobacterium rhinotracheale (ORT) causes ornithobacteriosis, a contagious disease transmitted horizontally by direct contact, aerosols, or indirectly through drinking water. Vertical transmission is still unclear. ORT is a gram-negative, non-mobile, non-sporulating bacterium [12], belonging to the superfamily V rRNA and family Flavobacteriaceae (Conway *et al.*, 2017; Omitola and Taylor-Robinson, 2020). Initially, ORT bacterium was designated as Pasteurella-like, Kingella-like, Taxon 28 or pleomorphic gram-negative rod before the name *Ornithobacterium rhinotracheale* gen. nov. sp. nov. in the rRNA-superfamily was suggested. The infection occurs worldwide and incriminated as a possible causative agent in respiratory disease (Barbosa *et al.*, 2020). ORT has been isolated from chickens, chukar partridges, ducks, geese, guinea fowl, gulls, ostriches, partridges, pheasants, pigeons, quail, rooks and turkeys. It is an acute, highly contagious disease of chickens and Turkeys. The severity of clinical signs, duration of the disease and mortality are extremely variable and influenced by

many environmental factors such as poor management, inadequate ventilation, high stocking density, poor litter conditions, poor hygiene, high ammonia level, concurrent diseases and the secondary infections (WHO, 2010). The disease spreads horizontally by direct and indirect contact. Vertical transmission is suspected since ORT has been isolated at very low incidence from reproductive organs, hatching eggs, infertile eggs and dead embryos. Currently 18 serotypes designated A to R exist (Smith and Fratamico, 2018) ^[44]. Neither the origin nor the serotype of the *Ornithobacterium rhinotracheale* strains effect their pathogenicity. Most of the chicken isolates belong to the serotype A (Patel *et al.*, 2018) ^[5]. Turkey isolates are more heterogeneous and belong to serotype A, B and D. Reports indicate synergism between ORT and Newcastle disease, Turkey rhinotracheitis, Infectious bronchitis, *Bordetella avium*, *Escherichia coli*, and *Chlamydophila psittaci* (Masalha *et al.*, 2010; Barbosa *et al.*, 2020).

5. *Chlamydophila psittaci*

Chlamydia psittaci (Formerly *Chlamydophila psittaci*): *C. psittaci* is a Gram-Negative Bacterium that causes psittacosis in humans. *C. psittaci* is recognised worldwide in most animal species and humans. Infected individuals regardless of clinical history can shed Chlamydia in high concentrations and constitute potential reservoirs of infection for humans and poultry (Beeckman and Vanrompay, 2009). Exposure to birds is the classic risk factor for psittacosis, and greater than 70% of cases have a clear recreational or occupational exposure. Farm personnel and persons working in slaughterhouses are at risk. Infections in turkeys cause severe respiratory disease and latent infections are common. Several outbreaks have been recently reported in turkey farms in Germany, Belgium and Israel where the infection is highly prevalent (Sasseti and Rubin, 2007) ^[32].

6. Avian mycoplasmosis

Mycoplasmas have impacted the poultry industry for years and effective control of infection has been a fundamental stepping-stone to improved performance and productivity. Recently mycoplasmosis appears to be making a comeback. Numerous species of mycoplasmas have been isolated from avian sources (Ferguson-Noe *et al.*, 2019). Two species are recognized as predominantly pathogenic to chickens and turkeys. *Mycoplasma gallisepticum* (MG) affects the respiratory system and is referred as chronic respiratory disease (CRD) in chickens, and infectious sinusitis in turkeys. *Mycoplasma synoviae* (MS) may cause respiratory and joint diseases. Two additional species are known to be pathogenic to turkeys. *Mycoplasma meleagridis* (MM) causes airsacculitis, and *Mycoplasma iowae* (MI) decreases hatchability (El-Ashram *et al.*, 2021). Although these four mycoplasmas are eradicated in primary chicken and turkey breeders, infections with MG, MS and MM still occur in commercial stock and at present seem to be on the increase in some parts of the world (Umar *et al.*, 2107). The disease spreads from flock to flock by vertical transmission via the infected eggs. Infected progeny then transmits the agent horizontally either by direct bird-to-bird contact or by indirect contact through contaminated equipment. The agent also transmits via other species of birds as well as mechanically by other animals and man. On the problems related to re-emergence of *Mycoplasma* infections, mycoplasmas in the past, appeared to have a restricted host range, which should help to limit their lateral spread. This does not seem to be true for MG or MS, both of which have been found in a number of avian hosts (Yadav *et al.*, 2021).

Bacterial infections and microbial food borne diseases

Food safety is concerned with the hazards associated with poultry meat, eggs and other products that form part of the human diet. Food safety and the quality of food are currently issues of major concern in developed countries. In developing countries, however, efforts to produce sufficient food to meet the requirements of population accompany with bad economic conditions that overshadow food safety. Safe food is a fundamental requirement of all consumers rich or poor. Incidents of food borne disease in humans have increased considerably worldwide in the last few years. Although the sources of infection are mostly unknown, poultry products have repeatedly been implicated. Poultry can harbour different food borne pathogens (El-Ashram *et al.*, 2021). Many reports during recent years have shown that *Salmonella* (especially *S. enteritidis*) and *Campylobacter* sp. Are the most common causes of human food borne bacterial diseases linked to poultry. Recently, verotoxin producing *Escherichia coli* 0157:H7 (VTEC) has surfaced as an additional food borne pathogen causing human illness. Several other microorganisms such as *Clostridium perfringens* and some *Listeria* species can also enter the human food chain via contaminated poultry carcasses. In addition, the development of antibiotic resistance in bacteria, which is common in both animals and humans, is also an emerging public health hazard (Yadav *et al.*, 2021). One such example is certain strains of *Salmonella* Typhimurium. Controlling these food borne organisms requires a better understanding of how microbial pathogens enter and move through the food chain, and the conditions that promote or inhibit growth for each type of organism (Daszak *et al.*, 2007) ^[19]. Some invasive *Salmonella* are the most important source of infection in poultry and appear to be vertically transmitted through contaminated eggs laid by infected carriers. Lateral spread of infection takes place through contaminated feed, water, equipment and the rearing environment. The significant reservoirs for these microorganisms are man, farm animals, pets, pigeons, waterfowl and other wild birds. *Salmonella* has been detected in different species of wild bird near hatcheries and poultry processing units and may contaminate equipment (Contreras *et al.*, 2016). Rodents are recognized as potential reservoirs transmitting infection between houses and contaminating stored feeding stuffs. In addition, insects are a potential source of *Salmonella* infection in chickens (Ursula and Antoine, 2013; Smith and Fratamico, 2018) ^[18, 44].

Table 1: Major emerging bacterial pathogens of the last 50 years

Bacterial species	Diseases	Complications	Transmission	Year
<i>Campylobacter</i> spp.	Diarrhea	Irritable bowel syndrome, temporary paralysis, and arthritis	Eating raw or undercooked poultry and interaction of children with chicken feces, unpasteurized milk.	1973
<i>Clostridium difficile</i>	Toxic megacolon and Pseudo membrane colitis;	Dehydration, Kidney failure and Toxic megacolon	consumption of contaminated raw milk and dairy products, food, or water	1974
<i>Streptococcus bovis</i> group	Endocarditis	Endocarditis, Mycotic aneurysms and embolic complications	An indirect transmission by contaminated surfaces, dust (e.g. animal feed, excreta) and by inhaling or swallowing bioaerosols (e.g. bacteria)	1974
<i>Legionella pneumophila</i>	Lung infection	Severe pneumonia, respiratory failure, shock and acute kidney and multi-organ failure.	Breathe in small droplets of water in the air that contain the bacteria. Less commonly, people can get sick by aspiration of drinking water containing Legionella. This happens when water accidentally goes into the lungs while drinking.	1976
<i>Capnocytophaga canimorsus</i>	Sepsis	Heart attack, kidney failure, gangrene and organs amputation.	Are common in dogs and cats can be spread to people through a bite or after close contact with dogs or cats. Infections are more often linked to dog bites or dog contact	1976
<i>Staphylococcus aureus</i> Toxin	Toxic shock syndrome	Nausea, vomiting, retching, stomach cramping, and diarrhea. In more severe cases, dehydration, headache, muscle cramping, and changes in blood pressure and pulse rate may occur	Can be transmitted by food workers.	1981
<i>Escherichia coli</i> O157:H7	Hemorrhagic colitis, Hemolytic uremic syndrome	Renal failure, anemia, and dehydration especially for children (Hemolytic Uremic Syndrome) and spontaneous bleeding, organ failure, and mental changes.	Can be transmitted by the consumption of contaminated foods, such as raw or undercooked ground meat products and raw milk.	1982
<i>Borrelia burgdoferi</i>	Lyme disease	Chronic joint inflammation (Lyme arthritis), particularly of the knee. Neurological symptoms, such as facial palsy and neuropathy. Cognitive defects, such as impaired memory.	Spread through the bite of infected ticks. The blacklegged tick (or deer tick, Ixodes scapularis) spreads the disease	1982
<i>Chlamydia pneumoniae</i>	Lung infection	Chronic infection and might contribute to chronic conditions, such as asthma, arthritis, and atherosclerosis	By coughing or sneezing, which creates small respiratory droplets that contain the bacteria, which get attached to surfaces.	1983
<i>Helicobacter pylori</i>	Gastric ulcers	Damage the stomach and small intestine protective lining	Commonly transmitted person-to-person by saliva. The bacteria can also be spread by fecal contamination of food or water.	1983
<i>Rhodococcus equi</i>	Pneumonia in immunosuppressed	Retroperitoneal abscess, peritonitis, meningitis, pericarditis, osteomyelitis, endophthalmitis, lymphadenitis, lymphangitis, septic arthritis, periprosthetic joint infection, osteitis, bloody diarrhea, subcutaneous abscess, brain abscess, thyroid abscess,	Exposure to farm soil, animals or manure has frequently been reported to cause human cases of disease by inhalation, ingestion or direct inoculation	1986

<i>Ehrlichia chaffeensis</i>	Human ehrlichiosis	Headache, myalgia, thrombocytopenia and leukopenia, and elevations in hepatic transaminases	Most people get ehrlichiosis from the bite of an infected tick.	1987
Non-diphtheria <i>Corynebacterium</i> spp.	Endocarditis in immunosuppressed, patients with underlying valve disease or prosthetic valve; other invasive infections	<ul style="list-style-type: none"> Paralysis, polyneuropathy, myocarditis and Kidney failure. 	Spread from person to person through respiratory droplets, like from coughing or sneezing.	1990's
Spotted fever group <i>Rickettsia</i> spp.	Spotted fever rickettsiosis	Hearing loss, myocarditis and cerebral infarction	Zoonotic and are usually transmitted to humans by arthropods (tick, mite, flea, louse, or chigger).	1990's
<i>Anaplasma phagocytophilum</i>	Human granulocytic anaplasmosis	<ul style="list-style-type: none"> Haemorrhage, respiratory failure, Kidney failure and Septic shock. 	Phagocytophilum is primarily spread to people by the bite of an infected tick.	1990
<i>Tropheryma whipplei</i>	Whipple's disease	Whipple disease, fatigue, weight loss, joint pain whipple disease is a progressive and potentially fatal disease.	<i>Tropheryma whipplei</i> is known to be viable in human fecal and saliva samples, suggesting that the bacterium might be transmitted through both fecal-oral and oro-oral routes. Depending on the living conditions of the subjects, either method of transmission may be prevalent.	1991
<i>Vibrio cholerae</i> O139	Diarrhea	Paralysis and leukopenia	Transmission occurs through the ingestion of contaminated water or food. Sudden large outbreaks are usually caused by a contaminated water supply.	1992
<i>Bartonella henselae</i>	Cat-scratch disease, bacillary angiomatosis	Cat scratch disease and bacillary angiomatosis, a multisystem disorder seen primarily in patients with the acquired immunodeficiency syndrome.	Usually spread through contaminated water.	1992
<i>Aerococcus</i> spp.	UTI, endocarditis	Sepsis with a urinary tract focus and infective endocarditis	Are opportunistic pathogens that are mainly pathogenic in vulnerable patients. They are not known to be transmitted from human-to-human.	1992
<i>Wolbachia</i> spp.	Associated with onchocerciasis and lymphatic filariasis	lymphatic filariasis	Transmission between hosts is primarily vertical, taking place exclusively through the female germ line, although horizontal transmission has also been documented.	1995
<i>Simkania negevensis</i>	Lung infection	Complicated lung infection	Amoebae and arthropods vectors.	1997
<i>Actinobaculum schaalii</i>	UTI	Causes UTI Mainly in elderly patients with underlying urological predispositions. It also cause Skin infections.	Can be transmitted via transfusion of infected blood, and via other unhygienic living conditions.	1997
<i>Parachlamydia acanthamoebae</i>	Lung infection	Complicated human lung infections	May be zoonotically transmitted but infection through contaminated water, uncooked meat, milk or sexual contact might also be the mode of transmission to humans.	1997
<i>Waddlia</i>	Miscarriages	Human placental complications	So far, the epidemiology of W.	2007

<i>chondrophila</i>			chondrophila remains largely unexplored and zoonotic, waterborne or interhuman transmission has been considered.	
<i>Alloscardovia omnicoles</i>	UTI	Prematurity and the possibility of developing infectious chorioamnionitis, which can be lethal for the mother and newborn.	Sexually transmitted infections	2007
<i>Neoehrlichia mikurensis</i>	Neoehrlichiosis : Systemic inflammatory response; Vascular and thromboembolic events	Erysipelas-like rash, and thromboembolic complications and complications associated with Neoehrlichia infection.	he transmission cycle of tick-borne pathogens is mostly unknown. <i>Candidatus Neoehrlichia mikurensis</i> (CNM) and <i>Anaplasma phagocytophilum</i> are both tick-borne pathogens, and rodents are discussed to serve as main reservoir hosts for CNM.	2010

(Daszak *et al.*, 2007; Greub, 2009; Lamoth *et al.*, 2015; Vouga and Greub, 2015; McArthur, 2019; Bergwerff and Debast, 2021).

Koch's Postulates established to determine the principles of microbial disease causation

Koch's postulates are sets of four criteria intended to establish a causative relationship between a microbe and its relation to a disease. Robert Koch and Friedrich Loeffler in 1884 formulated these postulates, based on earlier concepts described by Jakob Henle and refined and published by Koch in 1890. This postulates were applied by Koch to understand and describe the etiology of cholera and tuberculosis, caused by *Vibrio cholera* and *Mycobacterium tuberculosis* (CDC, 2019; Uves, 2021)^[14].

At the time they were developed, these postulates were invaluable and remain largely valid for a relatively few defined circumstances in which bacteria can be precisely tied to the cause of a particular clinical syndrome. In today's changing world of advanced disease diagnosis, different forms of viral agents (which are obligate intracellular parasites) associated with cancers along with many non-cultivable bacteria which can only be demonstrated by molecular probes, Koch postulates seems inapplicable, and however, the postulates have been controversially generalized to other diseases (Berman, 2019)^[13]. More modern concepts in microbial pathogenesis cannot be examined using Koch's postulates, including viruses and asymptomatic carriers (Cohen, 2017)^[23].

Koch's postulates, which require the presence of that particular agent in all cases of the disease in question, its absence in all those without the disease, and the isolation of the agent in pure cultures, were initially very important to identify infectious aetiologies. However, it had limitations (Van-Zyl, 2021)^[16]. There are many countless organisms that do not satisfy this conditions, hence they cannot be cultured. Moreover, the association between infectious agent and disease isn't always controlled by a single agent, but factors such as the environment, the study population as well as their level of herd immunity along with other factors plays a role in disease causation. Many different infections could be present without causing disease or may not be the only cause the disease in question (Daszak *et al.*, 2007; Berman, 2019; Uves, 2021)^[19, 14, 13].

Emerging Infections Priority Issues

The Center for disease control (CDC) 2019 antibiotic resistance threats report which is intended to, Serve as a reference for information on antibiotic resistance, provide the latest antibiotic resistance burden estimates for human health as well as highlight emerging areas of concern and additional action needed (CDC, 2019). These Emerging Infections Priority Issues are;

- a. Infections that cause chronic diseases
- b. Opportunistic infections
- c. Antimicrobial resistance
- d. Vaccines
- e. Food and water safety
- f. Vectors and animal health
- g. Blood safety
- h. Maternal and child health
- i. Health of travellers and refugees

Factors contributing to the emergence of infectious diseases

1. **Agent:** this is one of the most important factor that contributes to the emergence of newer variants of infectious diseases. This include; the Evolution of pathogenic infectious agents, Mutations, multiple and extremely drug resistance and vectors resistance to pesticides.
2. **Environment:** the environment contains both the infectious agent as well as the population at risk. Different Environmental factors plays a role in disease causation, these are; urbanization and deforestation, food

processing technologies and food handling, climate and changing ecosystems, changes in agricultural practices, uncontrolled Urbanization, migration and emigration, unsafe water, poor sanitation, overcrowding and indoor air pollution among many others (Sasseti and Rubin, 2007; CDC, 2019; Van-Zyl, 2021) ^[32, 16].

3. **Biological agents:** these are attractive instruments of terror, which can be used in Bio-warfare. Agent such as bacteria and viruses such as *B. anthracis*, *C. botulinum toxin*, *F. tularensis*, *Y. pestis*, Variola virus, and viral haemorrhagic fever viruses. These agents are easy to produce, and when released into the environment, it is capable of producing mass casualties in short time, they are difficult to detect and can cause widespread panic and global economic meltdown (Sasseti and Rubin, 2007; CDC, 2019; Fernández *et al.*, 2020) ^[32, 38].
4. **Climate changes:** climate change comes with different environmental hazards. The ozone layer depletion by human activities contributes to climate change and these effects can be seen in the melting of glaciers as a result of higher earth temperatures which may eventually results to flooding and may create new breeding habitats for mosquito vectors and increases in mosquito-borne infections, decreases salinity which can increase toxic bacteria, increases vegetation which increases rodents as well as increase in runoff into drinking reservoirs.

Prevention and control of Emerging Infectious Diseases

1. The quality of treatment as well as accurate disease diagnosis and prompt identification and reporting rests on Microbiology laboratories, as most of the emerging infectious agents respond to several drugs and choice lies with optimal selection based on Antibiograms, as resistance is not a menace with emerging newer and uncommon isolates.
2. Infrastructure, Training and community sensitisation
3. Ensure prompt implementation of prevention strategies and enhance communication of public health information about emerging diseases.
4. Enhance communication: locally, regionally, nationally, globally
5. Increase global collaboration and share technical expertise and resources
6. Provide training and infrastructure support globally
7. Ensure political support
8. Ensure judicious use of antibiotics
9. Vaccines for all
10. Public enlightenment about their responsible drug compliance, Emergence of new agents and Infection sources and the importance of dose completion therapy.
11. Vector control and Malaria prophylaxis
12. The modern generation of Microbiologists should be familiar with other novel and rapid means of disease diagnosis and microbes identification.
13. Surveillance and Response
14. Applied Research
15. Web public enlighten via social media networks and other platforms on the importance of safe practices for a healthier environment.
16. Need for global help to Developing countries: Commitment to technology transfer and global collaboration is essential if we are to have the agility required to keep pace with emerging infectious diseases. Pathogen surveillance and discovery can promote global interaction via collaborations on matters that know no national or political boundaries but simply reflect our common goals (WHO, 2010; CDC, 2019; Fernández *et al.*, 2020; Van-Zyl, 2021) ^[38, 16].

Conclusions and Future Prospects

Many bacterial emerging and re-emerging diseases can be considered opportunistic infections. Increasing demands for protein necessitate increased levels of farming. Food can provide a vehicle for spread of pathogens from animals to humans. Contact with animals during farming, hunting, or by animal bites can increase transmission of diseases. Changing patterns of farming, life style, and transportation influence the dynamics of pathogen ecology. Pathogens are subjected to changes by many intrinsic and extrinsic factors. Mutation, recombination, selection, and deliberate manipulation can result in new traits acquired by pathogens and result in potential epidemic consequences. Re-emergence of diseases through opportunistic host switching is likely to continue as a major source of human infectious disease. Strategies to improve public health have focused on improved surveillance in regions of perceived high likelihood of disease (re-emergence). To recognize and combat emerging/ re-emerging infections there is the need to identify pathogens, their vertebrate hosts, and their methods of transmission. Identification should include knowledge of spatiotemporal disease patterns and their changes over time. These features can be used to identify dynamic processes involved in pathogen transmission, which can be used to account for observed disease patterns and ultimately forecast spread and establishment into new areas.

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