Acta Scientific MICROBIOLOGY (ISSN: 2581-3226)

Volume 4 Issue 8 August 2021

Review Article

Resurgence of Bacterial Diseases, Pathogenesis, Host Immune Responses, Prevention and its Control

Ravi Kant Upadhyay*

Department of Zoology, Deen Dayal Upadhyaya Gorakhpur University, Gorakhpur, UP, India

***Corresponding Author:** Ravi Kant Upadhyay, Department of Zoology, Deen Dayal Upadhyaya Gorakhpur University, Gorakhpur, UP, India.

Received: July 12, 2021

Published: July 28, 2021

Abstract

Present review article describes causes of resurgence, pathogenesis and prevention of serious and potentially life-threatening bacterial diseases i.e. typhoid, cholera, tuberculosis, leptospirosis, Brucellosis, pertussis, shigellosis, leprosy, anthrax, and plague occur in human. This article high lights effect of climatic and weather conditions on vector and food-borne bacterial diseases, its various modes of transmission to humans. This article also explains effect of various toxins on body tissues, cells and organ systems that results in increase in the morbidity in patients. On one side there is a problem in treatment of bacterial diseases and safety of patients and on other side there is rising bacterial resistance to antimicrobials. Development of drug resistant biotypes of bacteria is showing high infectivity, morbidity and potentially devastating consequences of illness with high death rates. These newly resurged bacterial strains are detrimental and making heavy losses to world economy, health, education, tourism, social interaction, religion, labor, markets, transportation, and human freedom. This article emphasizes the various contributing factors which are responsible for emergence and re-emergence of bacterial diseases, and its, diagnostics, treatment and prophylactic measures for community protection.

Keywords: Bacterial Diseases; Drug Resistance; Resurgence; Pathogenesis; Prevention

Introduction

Bacteria are ubiquitous single-celled microorganisms found in nature in diverse forms, different shapes and sizes. They found almost in all environmental conditions i.e. soil, water, air, bodies of organisms, food materials, and wastes. Millions of bacteria normally live on the skin surface, in digestive tract, genitalia and body fluids and on hair surface. There are large numbers of bacteria which do not cause any disease and pass on their life cycle as commensals or non-pathogenic inside its hosts. These usually grow as normal flora in the intestinal tract and other glandular parts of the body. They colonize inside host without causing infection or harm. Contrary to this harmful bacteria invade the organism body and cause bacterial infections are called pathogenic bacteria. Bacterial diseases starts with entry of pathogenic bacteria into the host body, it step wise establish itself and begin to reproduce and replace healthy or commensal bacteria. These harmful bacteria grow in tissues and release various toxins which damage the body tissues and increase the morbidity in patients [1]. Few important pathogenic bacteria which cause serious diseases are *E. coli* and *Salmonella* cause food poisoning, *H. pylori* cause gastric ulcers, *N. gonorrhoeae*

causes gonorrhea, while *N. meningitides* causes meningitis. Bacteria belong to genus *Streptococcus* cause multiple infections and diseases in separate hosts, including pneumonia, meningitis, ear infections and strep throat. *Staphylococcus aureus* causes a variety of infections in the body, including boils, cellulitis, abscesses, wound infections, and toxic shock syndrome *Bacillus anthracis, Brucella sp, Coxiella burnetii, Francisella tularenis, Leptospira, Mycobacterium tuberculosis comlex, Yersinia pestis* cause serious health problems in humans [1] (Table 1). Bacterial infection imposes large and long lasting impact on large impact on public health if they are not cured at time. Bacterial diseases may occur at any site of body. Bacterial infections can be transmitted by a variety of mechanisms. Bacterial infection is transmitted to humans through air, water, food, or living vectors. Bacterial infection or diseases are mainly spread through person to person contact, airborne, sneezed aerosols or droplets, blood transfusion and vehicular. Bacterial diseases or infection is also transmitted by some transmission vectors mainly insects and other animals [2].

Disease	Causative agent	Symptoms	Transmission	Treatment
Typhoid	*Salmonella typhi*	High fever, diarrhea, and vomiting	Contaminated food and drinking water	Antibiotics and fluids, and vaccine
Cholera	*Vibrio cholerae* and its other biotypes	Severe diarrhea, irritation of skin around anus, very watery stool, vomiting and muscular cramps	Contaminated food and water	Antibiotics, fluid transfer, anti-toxins, and vaccines
Tuberculosis	*Mycobacterium tuberculosis*	Heavy cough, sneeze or spit cough, shout, or sing, night sweats and fever.	Person to person through airborne particles	Long course of multiple antibiotics. Partly by vaccine
Leptospirosis	*Leptospira icterohaemorrhagiae*	High fever, headache, bleeding, muscle pain, chills, red eyes and vomiting	Spread through the urine of infected animals	Antibiotics doxycycline or penicillin.
Brucellosis	*B.abortus*, *Brucella suis, B. melitensis*, *B. canis, B. ovis* and B. neotomae, B.melitensis	Joint and muscle pain, fever, weight loss and fatigue. Cough and stomach pain	Use of un-pasteurized dairy products	Antibiotics
Pertusis	*Bordetella pertussis*	Whooping, a runny nose, nasal congestion and sneezing.	Usually spread the disease to another person by coughing or sneezing	Antibiotics and vaccine. Refusal to vaccine
Diptheria	*Corynebacterium diphtheriae*	Toxin, difficulty breathing, heart failure, paralysis, and even death, sore throat, fever, swollen lymph nodes and weakness.	Person to person through respiratory droplets release after from coughing or sneezing	Interruption immunization antibiotics, antitoxins and vaccines
Shigellosis	*Shigella dysenteriae, Shigella flexneri, Shigella sonnei, Shigella boydii*	Intestinal infection, bloody diarrhea, watery diarrhea, abdominal cramping, nausea, and vomiting,	Fecal–oral route, including through direct person-to-person or sexual contact or indirectly through contaminated food, water, or fomites.	Drink plenty of fluids, especially electrolyte solutions, azithromycin, ciprofloxacin, sulfamethoxazole/trimethoprim (Bactrim
Leprosy	*Mycobacterium leprae*	Affects the skin, eyes, nose and peripheral nerves. Light-colored or red skin patches, numbness and weakness in hands and feet.	Spreads from person to person by nasal secretions or droplets	Multidrug therapy

Anthrax	*Bacillus anthracis* spore-forming bacterium.	Skin ulcer with a dark scab to difficulty in breathing.	Working with infected animals or animal products such as wool, hides, or hair. Through inhalation spores that are in the air	Vaccines, Antibiotic treatment cures most infections. Inhaled anthrax is harder to treat and can be fatal
Plague	*Yersinia pestis*	Spread by the bite of rodent flea	Fever, chills, headache, fatigue and muscle aches., swollen lymph nodes	Strong antibiotics
Gonorrhea	*Neisseria gonorrhoeae*	Burning and pain during urination, affects the urethra, rectum or throat. In females, gonorrhea can also infect the cervix	Spreads by sexual contact	Treated with antibiotics.
E. coli infection	*Escherichia coli*	Abdominal cramping, severe watery diarrhea, blood stools, gas, loss of appetite, nausea, vomiting, fatigue, fever	Contaminated food or drink fouled water, bloody diarrhea, dehydration, or even kidney failure.	Anti-diarrheal medications, Intravenous fluid
Tetanus or “lockjaw	*Clostridium tetani* affect both adults and new born	Protracted wounds, local infection painful muscle contractions, extensive tissue destruction	Through broken skin, injuries from contaminated objects, environment mostly soil	A vaccine can easily prevent the infection, which has no cure.
Diarrhea/ Acute diarrhea	*Clostridium difficile*	With a likely infectious cause in an incontinent or diapered patient Enteric pathogen	Through contaminated food or drinking-water	Diarrhea in an adult with a history of recent antibiotic use
Cryptosporidiosis	*Cryptosporidium parvum* via the fecal-oral route from infected hosts, Most sporadic infections occur through person-to-person contact.	Inadequate control in water supply; international travel; increased use of child care facilities.	Diarrheal disease, pathogen lives in the intestine of infected humans or animals, dehydration, nausea, vomiting, fever, weight loss	Not curable, Nitazoxanide control partially
Meningitis	*Streptococcus* pneumoniae, Neisseria meningitidis, Listeria monocytogenes Haemophilus influenzae type b	Inflammation (swelling) of the protective membranes covering the brain and spinal cord, Headache, fever and stiff neck.	By sharing respiratory and throat secretions (saliva or spit).	Uncertain, no vaccine available, broad-spectrum, antibiotic, corticosteroids to ease inflammation

Table 1: Showing bacterial diseases, its causative agents and therapeutics.

There are several factors which contribute development of bacterial infection and diseases. The most important is environment or climatic changes which favor growth, multiplication and transmission of pathogens which also increase the host susceptibility. Fouling or unhygienic environment sets in and favor pathogen multiplication and persistence for longer period. Second rain water, temperature and humidity induce transmission vector population growth mainly breeding that accounts to a major factor in pathogen transfer from one host to another. Presence of pollutants/ contaminants in air, water and in food material in the environment transfers in to food chain, and weakens the body's defenses against bacterial infection. These critically determine beginning of disease following transmission of a bacterial agent. Health status of host is one of the important factors that decide the spectrum of pathogenicity caused by an infectious organism. Another factor is number of susceptible and exposed individuals in a population group.

Pathogenic bacteria invade the host body; weaken the body's protective mechanisms and use large numbers of metabolites for their own growth and multiplication and cause disease. Finally, virulence shows internal changes occurred in physiological pathways inside the organism's body, and its propensity to cause disease. Among internal factors toxins released by bacteria decides invasiveness and level of morbidity caused. Among biological factors pathogen genetic constitution, nutritional status, age, duration of exposure to the organism, and coexisting illnesses also play important role [4]. There are different bacterial species i.e. *Bacillus anthracis, Brucella sp*, *Coxiella burnetii*, *Francisella tularenis, Leptospira*, *Mycobacterium tuberculosis* complex, *Yersinia pestis* major lethal disease. Due to environmental impact as well as high transmission rate they become uncontrolled and unmanageable (Table 1).

Though, bacterial diseases are treatable by different therapeutic and preventive measures which also lower down morbidity and mortality in infected population. But persons which have weaker immunity such as immune compromised, immune deficient and autoimmune were found highly susceptible to types of bacterial infections. Such measures include water treatment, immunization of animals and humans, personal hygiene measures, and safer sex practices. But rising drug resistance in bacterial strains is an important cause of enhancement of infectivity, morbidity and mortality. Hence, rising bacterial resistance to antimicrobials is a very serious rapidly growing problem with potentially devastating consequences [3]. In present time one of the major challenge to pharmaceutical and clinical sciences is rising drug resistance (antibiotics) in various bacterial pathogens [4].

Important bacterial diseases of man

Typhoid

Typhoid is an enteric fever cause caused by *Salmonella typhi* and *paratyphi.* Typhoid is a global health problem every affects large number of people due to poor sanitation, fowling conditions. Typhoid is a systemic infection that is too serious and life-threatening. The typhoid pathogen reaches to the human body through ingestion of contaminated food or water, with human excreta from infected persons. In rainy areas where floods are more frequent and happen almost every year these cause heavy surface water contamination in water bodies. Generally, flood water carries lots of untreated waste that contains typhoid pathogens in large numbers and disease spreads easily through the environment. Children are major targets but disease is also seen in adults. Its major symptoms are typical, continuous fever for 2 - 4 weeks with bradycardia with abdominal pain due to enlargement of lymph nodes and constipation. Typhoid infection spreads from persons mainly infected person work as carriers of the disease. These bacteria also transfer to gall bladder and house inside it. Typhoid fever affects nearly 2 - 3 lakhs of people with more than10, 000 deaths in the state. Typhoid infection usually occurs every year in developing countries mainly in the tropics and results in high mortality (Table 1). *Salmonella typhi* also has acquired antibiotic resistance that is increasing disease incidence and fatalities.

Rising antibiotic resistance against broad spectrum antibiotics organisms is a major threat imposed by microbes more especially in bacteria. There are bacterial strains which have gained resistance to more than one drug or showing multiple drug resistance that creates major obstacle in treatment of typhoid. *Salmonella enterica* serovar Typhi, has emerged as a separate genetic clades, a haplotype H58 S, associated with the MDR phenotype. H58 *S* Typhi express multiple antibiotic resistance determinants and persisting within the human population since much longer time. This is the main cause of devastating threat posed by *Salmonella enterica* serovar Typhi MDR phenotype H58 *S* [5]. Genetic *variants* of *Salmonella typhi* shows m*utation* in PARK2 that is a single-nucleotide polymorphism of PARK2_e01(−2599). It displays a weak association but high susceptibility to *typhoid fever* and paratyphoid *fever*. More often, these environmentally adapted human genetic variants infectivity, uncontrolled physical illness and mortality. The main reason behind induction in infection, is binding its antigens to toll-like receptor (TLR) 4, TLR5, interleukin (IL-) 4, natural resistance associated macrophage protein 1 (NRAMP1), VAC14, PARK2/PACRG, cystic fibrosis transmembrane conductance regulator (CFTR), and major-histocompatibility-complex (MHC) class II and class III. These polymorphisms in genetic variants could be related to multiple mechanisms in eliminating both intracellular and extracellular *Salmonella* typhoidal species [6]. Further, rising disease burden could be lower down by prompt treatment with antibiotics. For better control prophylactic, health hygiene, sanitation and vaccination could become major ways to break the typhoid transmission cycle in the long term (Table 1).

Cholera

Cholera is a dreadful fast invading acute diarrheal disease. This is caused by *Vibrio cholerae* (*V*. *cholerae*), a gram-negative bacte-

rium found mostly in brackish water. Cholera severely contagious acute bacterial infection and its epidemics suddenly evoke and spread very fast and cause abruption and create an acute public health problem. In beginning infection remains mild or symptomatic, but within 3 - 4 hours time it multiplies very fast in intestine. It heavily colonizes and multiplies inside the intestine and start secreting toxins. It inflammates gut lining and start rupturing brush boarder cells, causes very severe pain, vomiting and diarrhea. In lack of any treatment infection become uncontrolled and reached to peak and causes large numbers of deaths. A new sero group of *V. cholerae* O139 phages has been identified, phage type 1 was the predominant type. Molecular studies reported substantial changes in the CTX phage genome of O139 strains (Table 1).

Cholera epidemic is largely supported by climate and change its rhythms according to environment variables, as low precipitation and high temperatures in warmer months bacterial replication occurs faster than other months [7]. Weather conditions mainly increase in ambient temperature, humidity and rainfall increase the cholera incidences [8,9]. Climate changes are also responsible for its outbreaks as water-borne and food-borne infectious diseases [10-12] particularly in undeveloped/developing countries [13-15]. Cholera spreads by using contaminated water, vegetables and foods [16]. Cholera infection evokes due to seasonal changes, travels, natural catastrophes, warfare, poverty, and poor health and hygiene conditions [17]. Cholera starts just after high rainfall and floods [18-20]. Flood water affect nutrient concentrations, salinity and pH of water resources and induces bacterial survival [21]. RTX toxin belongs to a four-component type I secretion system (TISS) encoded by *rtxB*, *rtxD*, *rtxE*, and *tolC is secreted by Vibrio cholerae*. It shows single alanine substitutional mutation that may lower down the interaction between cholera toxin A1 and stimulatory G protein. At 484 kDa, the *V. cholerae* RTX toxin is the second largest single-polypeptide toxin known and causes cell rounding and depolymerization of the actin cytoskeleton in a broad range of cell types [22] (Table 1).

Tuberculosis

Tuberculosis (TB) is a highly contagious disease caused by *Mycobacterium tuberculosis. This pathogen* largely attacks lungs, brain and spinal cord. Disease progresses slowly and sometimes remain asymptomatic and cause high morbidity and deaths in young and adults both. According to an estimate about 3 million individuals die every year due to tuberculosis. It accounts for 18.5% of all deaths in the 15 and 59 age groups. About 1.79 billion people, roughly one-third of the world's population, have been with the causative agent *M. tuberculosis* or they are at high risk of developing the disease. This organism is spread easily, and pulmonary infection usually results from inhalation of small droplets of respiratory secretions containing a few bacilli. Disease spread due to talks, laughs, sneezing, or singing by infected patient tiny water droplets release that contain the germs. If someone breathe in this infected area or surrounding he or she will get exposure of germs it. The main symptoms of disease are coughs, sneezes, lung infection, skin coloration, night sweats chill fever, loss of appetite and weakness. Today, tuberculosis is curable by taking regular treatment of antibiotics. Tuberculosis is a worldwide public health problem, particularly in the Third World countries. Tuberculosis is India's biggest public health problem. According to an estimate 5 lakh deaths occur due this highly contagious. Due to huge population structure chances of tuberculosis bacterium exposure from person to person is increased. For instant control of spread of disease, social distance or isolation infected patient from healthy people is highly essential. The disease more likely develops in one room space living of family members, overcrowding of community places, poor nutrition, and low socio-economic condition in slums. This is the main reason that vast majority of cases are reported in rural and semi-urban areas mainly in slum-dwelling young population. In eastern U.P. both simple tuberculosis and drug resistant tuberculosis patients have been reported in higher number. Here, infection rate is quite higher than other urban and rural areas, it is due to heavy population pressure and person to person contact [23] (Table 1).

Disease found in different forms. In Latent TB, germs multiply almost at constant rate, weaken the immune system and make person sick. These active TB cases are related to drug-resistant *M. tuberculosis* and are treatable by drug regimens. Different drug -resistant TB types are reported in different patients. Few strains of bacterium are resistant to at least one first-line anti-TB drug and spread in same manner as drug-susceptible TB spreads. In multidrug-resistant TB (MDR TB) the there are bacterium of TB who have acquired resistant to more than one anti-TB drug and at least isoniazid (INH) and rifampin (RIF). In few cases those who used rifampicin antibiotic for treatment, they develop to resistance to rifampicin (RR). Drug resistance strain could be identified using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs.

It includes any resistance to rifampicin, in the form of mono-resistance. Contrary to this bacterium has also developed resistance to many antibiotic drugs at the same time; it is called poly-resistance, MDR or XDR. MDR- TB. Drug resistance in microbes develops due use of mild spectrum antibiotics/drugs used to treat TB or by mismanagement of dose and time duration [24]. This spreads due to misuse or mismanagement in those people who do not complete a full course of TB treatment, or pass through a wrong prescribe treatment, or drugs are not available. A single or mono resistance in bacterium shows resistance to one first-line anti-TB drug only while poly resistance or multi-drug resistance develops after using of more than one first-line anti-TB drug, other than both isoniazid and rifampicin.

Extensive drug resistance (XDR) is reported in patients which have used any fluoroquinolone drug, and at least one of three second-line drugs i.e. capreomycin, kanamycin and amikacin through injection. It also happens due to generation of new variations and mutations in disease causing genes and acquisition of new drug resistant genes after fluoroquinolone drugs [25]. More often new mutations occurs due extra high dosage levels, time duration and age. Structural changes in genes are reported as amino acids changes or its replacement are observed due to change in respective codon positions in candidate genes. These also indicate drug sensitivity and potency. *Mycobacterium tuberculosis* genomic mapping has revealed important reasons of drug resistance with the help of a program BWA with the algorithm "mem" in its H37Rv strain [26]. Control of multidrug-resistant TB (MDR TB) is the biggest challenge as it become resistant to more than one anti-TB drug and impose more severe multiple pathological changes in patients and results in high mortality [27] (Table 1).

Body immunity controls tuberculosis

In response to *M. tuberculosis* invasion patient body generates cell-mediated immune response [28]. This is maintained by T cells mainly CD4+ T cells. CD4+ T cells get activated after invasion of bacteria within 2 - 6 weeks; it induces the infiltration of large numbers of activated macrophages. These cells wall off the organism inside a granulomatous lesion called a tubercle and large number of activated macrophages is collected and results in the concentrated release of lytic enzymes. These enzymes destroy nearby healthy cells and do tissue necrosis and form circular regions or lesion with a caseous (cheese like) consistency. In addition, the inhaled bacilli are ingested by alveolar macrophages. These are able to survive and multiply intra-cellularly by inhibiting formation of phagolysosomes. Lesions formed inside lungs also rupture and/or are spread through the blood and lymphatic vessels to the pleural cavity, bone, urogenital system, meninges, peritoneum, or skin. When the infected macrophages lyse, large numbers of bacilli have been come out. These activated macrophages suppress proliferation of the phagocytosed bacilli. Further, IFN-y in the immune response to mycobacterium kill infected cells. Similarly, cytokines produced by CD4+ T cells (TH1 subset) play an important role in the response by activating macrophages. More specifically, extrapulmonary tuberculosis is vaccine preventable rather than sporadic use of antibiotics [29]. Drugs which are prescribed for treatment of tuberculosis drugs are provided in combination i.e. isoniazid, rifampin, streptomycin, pyrazinamide, and ethambutol. The combination therapy of isoniazid and rifampin found more effective.

BCG vaccine provides 80% efficacy in vaccinated individuals against tuberculosis; but in some cases it gave negative results. But multidrug-resistant strains of *Mycobacterium species* have created the problem and vaccine was not found much successful [30]. Multidrug resistant and other forms of tuberculosis are vaccine preventable and successful rate is very high and no chance of resistance left behind [31]. Hence, more advance vaccine must be developed to fight this dreadful slow going dreadful infection fetal to human being [32].

Leptospirosis

Leptospirosis is a zoonotic disease that shows moderate morbidity and mortality. It is caused by *Leptospira icterohaemorrhagiae* a bacterium belongs to genus Leptospira. It is reported in many tropical countries and recognized as cane field fever or cani- cola fever, field-fever, mud fever, seven day fever or swineherd disease. Rats transmit Leptospirosis pathogens in human habitations. *Leptospira icterohaemorrhagiae* usually found in soil contaminated with urine of infected animals. When someone reaches in the vicinity of cattle urine, rat urine or to foetal fluids from cattle he or she may get infection unknowingly. Normally pathogen easily targets sewage and agricultural workers, butchers, meat inspectors, and workers those who comes in contact with contaminated waters [33]. Veterinarians generally remain at risk as they every day come in contact with livestock during treatment. Person to person transmission has not been reported. *Leptospira* enters the body through

injured skin or through mucous membranes. It also enter in the human body by drinking water contaminated or taking a bath in it. The organisms multiply in the blood and tissues of the body and severely affect body, kidney and liver. Pathogen shows a long incubation period from 10 - 20 days. New molecular biology tools mainly complete genome sequences of *Leptospira* and revealed so many facts and insights into the biology and pathogenesis of this pathogen [34]. A *ligB* mutant was constructed by replacing a portion of the *ligB* coding sequence, by spectinomycin resistance (Spc^r) gene through allelic exchange in *L. interrogans* [35] (Table 1).

Brucellosis

Brucellosis is a zoonotic disease caused by various strains of Brucella. Disease normally occurs in animals and is occasionally transmitted to humans by direct or indirect contact with infected animals. Disease persists as endemic wherever cattle, pigs, goats and sheep found in large numbers. Disease is also known as undulant fever, Malta fever or Mediterranean fever. The important hot spots of Brucellosis are Mediterranean zones, Europe, Central Asia, Mexico and South America. In India animal Brucellosis has been reported many states, but no statistical data is available about intensity and area of infection in various parts of the country. It is very difficult to collect data of Brucellosis affected and unaffected population. Because, in rural areas large numbers of cases remains undiagnosed due to no apparent sign or symptom of disease. Even it is true that physicians are not familiar with the disease. The disease persists for several days, months or occasionally, even years. *Brucella* are highly homogeneous, the genus is classified currently into six species: *Brucella abortus*, *Brucella suis, Brucella melitensis*, *Brucella canis, Brucella ovis* and *Brucella neotomae.* A new variant of *Brucella melitensis was isolated from humans* [36]. New *Brucella* strains have been emerged due to drug exposure, social and agricultural changes [37-39] (Table 1).

Pertussis

Pertussis is highly contagious severe respiratory infection characterized by a very rough coughing and sneezing. It is caused by *Bordetella pertussis*, an approximately infect 16 million cases and 195,000 deaths worldwide [40]. Pertussis spreads as an infected patient sneeze and large numbers of tiny wet drops are released in air, if some passes through it or inhale the air of this region may receive infection. Pertussis bacterium mostly targets infants and young children pregnant women, hospital maids, caretakers and household members [41]. The bacterium of infection targets lungs and respiratory system. Disease spread by infected people with whooping cough as droplets released during runny nose until 3 weeks after their cough starts initiate infection in healthy persons [42]. This disease is antibiotic preventable if right medicine is used for 5 - 7 days. In year 2014 pertussis epidemic was evoked in California and Alameda County with reported 11,203 cases with 3 deaths in infants less than 5 weeks of age (Table 1).

Diphtheria

Diphtheria is a dreadful disease caused by *Corynebacterium diphtheriae.* It was first identified by Klebs in 1883. Later on Loeffler established the cause of diphtheria occurrence in guinea pigs and rabbits. This is a gram-positive, rod like bacterium that releases toxins which cause tissue damage in human respiratory tract. The disease is transmitted from one individual to another by release of airborne respiratory droplets from patient's nasal openings. Disease starts with mild symptoms of sneezing and respiratory inflammation. It progresses as soon as its bacterium colonizes the nasopharyngeal tract and entered inside superficial layers of the respiratory mucosa [43]. The toxins released by bacteria invade kidney and nerve cells and affect nerve conduction in throat region that causes difficulty in swallowing. More specifically, diphtheria toxins flow in bloodstream and damage heart muscles and cause inflammation (myocarditis). Patient also feel problem in breathing, and myocarditis that leads to congestive heart failure and sudden death.

Corynebacterium diphtheria releases potent exotoxin cause destruction of the underlying tissue, resulting in the formation of a tough fibrinous membrane ("pseudomembrane") composed of fibrin, white blood cells, and dead respiratory epithelial cells. The tox gene carried by phage regulates synthesis of exotoxin. Exotoxin contains two disulfidelinked chains, a binding chain and toxin chain. The binding chain interacts with ganglioside receptors on susceptible cells, facilitating internalization of the exotoxin. Toxicity results from the inhibitory effect of the toxin chain on protein synthesis. Diphtheria exotoxins are highly active, it is single molecule can kill a cell. Removal of the binding chain prevents the exotoxin from entering the cell, thus rendering the exotoxin nontoxic (Table 1). Diphtheria disease is preventable by making toxoid

against toxins, these are also used for immunity enhancement and immunization.

Prevention

For making toxoid diphtheria are treated toxins with formaldehyde. The reaction with formaldehyde cross-links the toxin, resulting in an irreversible loss in its toxicity while enhancing its antigenicity. The toxoid is administered together with tetanus toxoid and inactivated. First of all Emil von Behring produced antiserum toxin that was found able to prevent death in infected animals. He prepared a toxoid by treating the toxin with iodine trichloride. These toxoids induce the synthesis of protective antibodies and neutralize the exotoxin toxicity [44].

Because antitoxin levels decline slowly over time, booster doses are recommended at 10-year intervals to maintain antitoxin levels within the protective range. Interestingly, antibodies specific for epitopes on the binding chain of the diphtheria exotoxin are critical for toxin neutralization because these antibodies block internalization of the active toxin chain (Table 1).

Diphtheria is a common illness in young children; it is partially treated with antibiotics in mild cases. But for providing a protection cover to young age children vaccination is highly important. A combined DPT vaccine has been prepared against Diphtheria, whooping cough and Tetanus. It's small doses are administered to children beginning at 6 - 8 weeks of age. The latest version of this vaccine is also prepared as DTaP vaccine for children and the Tdap vaccine for adolescents and adults. These are used for children of age 7 with one immunization dose and first booster shot that is provided after attaining an around age 11 or 12. The next booster shot is recommended 10 years later, and booster dose at 10-year intervals [45] (Table 1).

Shigellosis

Shigellosis or bacillary dysentery is caused *Shigella* a facultative anaerobic Gram-negative rod shaped bacterium [46]. *Shigella* spp. causes bloody diarrhea and infection in intestine. Worldwide > 160 million cases of Shigellosis and 700,000 deaths are reported approximately almost each year. Shigella is transmitted from person-to-person by close personal contact or exposure to feces of an infected person during sexual contact. This disease also spreads by eating foods or liquids contaminated by an infected person, or swallowing untreated recreational water (such as lakes or water park play fountains). The main symptoms of Shigellosis appear after 2 days; these are diarrhea (sometimes bloody), abdominal cramps, nausea, severe bleeding from rectum, fever and inflammatory bowel disease. Patients, who have weakened immune systems especially young children, and older adults, require hospitalization because of severity of disease. Few patients show blood stream infections, seizures, kidney failure or arthritis. Healthy patients do not require any medical treatment, but weak and more severely ill patients need intravenous rehydration and antibiotics. The main target of disease is children younger than five years. Four different *Shigella* species, *S. dysenteriae*, *S. flexneri*, *S. boydii*, *S. sonnei* cause shigellosis in humans. *S. flexneri* has six serotypes and two variants (X, Y) including subserotypes [47-49] (Table 1).

Antibiotic therapy is generally used for elimination of *Shigella* from the stool. But this parasite has acquired multidrug resistance against first, second and third line of antibiotics. As for the treatment of shigellosis ciprofloxacin is provided in combination to three second-line antibiotics; pivmecillinam, azithromycin and ceftriaxone. In India, fluoroquinolones resistance has been detected in two isolates of *S. flexneri* collected from Kerala hospital. It has limited the treatment options [50-53]. These showed mutations in *gyrA* and *parC* genes. Shigellosis usually evokes due to seasonal changes and geographical distribution and climatic conditions [55].

Leprosy

Leprosy is an infectious disease caused *Mycobacterium leprae*. Leprosy is prevalent since ancient times and exists almost on every continent. *M. leprae* is a slow growing bacterium that affects skin, disfigure it, eyes and the thin tissue lining the inside nasal regions. Bacterium disturbs nerves of arms and legs and outside brain and spinal cord, mainly peripheral nerves. Leprosy patient shows disfiguring of skin sores, lumps, or bumps which persist for several weeks or months. There are three forms of leprosy tuberculoid a less severe form of leprosy, in which only few patches of flat, skin become pale-colored. It is also known as paucibacillary leprosy. It is less contagious than other forms. Leptomonas form of leprosy is more severe form that is characterized by numbness, muscle weakness and skin bumps and rashes. It is multibacillary form of leprosy severely affect nose, kidney and male reproductive organs [56]. Multibacillary generates blood coagulation abnormalities in leprosy patients and is highly contagious [57]. Third category of leprosy patients shows symptoms of both the tuberculoid and lepromatous forms (Table 1).

Diaminodiphenylsulfone (dapsone) is used as a first-line drug worldwide for the treatment of leprosy. But thalidomide is prescribed to treat skin nodules but it suppresses immune system and imposes birth defects. For treatment of multibacillary leprosy a drug combination i.e. rifampicin, ofloxacin, minocycline, clofazimine and dapsone is provided. These regimens are well tolerated and effective in killing the bacilli. Patients facing erythema nodosum lepromatosum (ENL) are provided steroids in highly bacillated group (Table 1).

M. leprae has acquired multidrug resistance and it is increasing severity to the leprosy patients as drug regimens are almost failed against it [58]. *In M. leprae* three (2.89%) mutations in two genes, folP and rpoB, have been reported. *M laprae* strains possess folP and gyr genes have developed resistance against dapsone and rifampin [59]. All these happened due to nucleotide substitutions that has increased the susceptibility to dapsone. More specifically point mutations were observed at codon 53 or 55 of the *M. leprae folP1* gene that is responsible for dapsone resistance [59]. Mutations are also detected in the particular region of folP, rpoB, and gyrB gene in *M. leprae* [60].

Anthrax

Anthrax is a rare, potentially fatal disease that is mostly infect livestock and occasionally to humans [61]. It is caused by a Gram-positive rod-shaped bacterium *Bacillus anthracis* an. It is obligate bacterial pathogen belongs to genus *Bacillus*. *B. anthracis* is 3 to 5 µm in length and 1 to 1.2 µm width. Its genome possesses 5,227,293 bp in a single circular DNA. It possess two extrachromosomal DNA plasmids, pXO1 and pXO2, which are responsible for pathogenicity. *Bacillus anthracis* is also used in biological warfare in World War I and II, the bacterium produce: cutaneous, gastrointestinal, and inhalation anthrax in man [62]. Infection spreads due to inhalation of bacterial spores, contaminated food, soil or water, or skin wounds. Anthrax is also caused due to exposure of spore-contaminated soil [63]. Anthrax affected person feels headache, muscular pain, fever, severe chest pain, problem in breathing, fatigue and profuse sweating. In severe infection itchy blisters or bumps are formed over skin, nausea, vomiting, abdominal pain and bloody diarrhea. Anthrax bacterium causes skin ulcer (sore) with a black center and swollen lymph nodes in last stage or bloom disease. For treatment few commonly used antibiotics i.e. ciprofloxacin (Cipro®) and doxycycline (Doryx®) are used. Anthrax is vaccine and anti-toxin (BioThrax®) treatable; these successfully neutralize anthrax toxins in the body.

Anthrax endospore are used as popular biological weapons. These contain protective layer inside which bacterium persists in inactive state for many years and suddenly evokes under suitable environmental conditions. This protein capsule cover made up of poly-D-gamma-glutamic acid) invade the immune response. It feeds on the heme of blood protein haemoglobin using two secretory siderophore proteins, IsdX1 and IsdX2 [64,65] (Table 1).

Plague

Plague is a dreadful disease that is caused by the bacterium, *Yersinia pestis* (formerly *Pasteurella pestis.* This is a gram-negative, non-motile, rod-shaped, facultative anaerobic occobacillus bacterium, without spores. Plague is transmitted by bite of Oriental rat flea (*Xenopsylla cheopis*) and infects both humans and other mammals. Plague, found in three forms i.e. pneumonic, septicemic and bubonic. The highly virulent agent of plague was used as biological weapon in many wars mentioned archives of human history [66]. Plague was persisting in middle age and during war millions of people died due to use of biological weapon. In modern age plague bacterium was also used during war after deliberate release of pathogen bomb shells [68]. The major common sign of bubonic plague is rapid development of a swollen and painful lymph gland called a bubo. But many cases no sign of particularly septicemic and pneumonic plague noted. Before treatment accurate diagnosis or laboratory testing of disease is highly important [67] (Table 1).

Plague is mostly evokes in semi-arid upland forests and grasslands where many wild rodent species i.e. rock squirrels, wood rats, ground squirrels, prairie dogs, chipmunks, mice, voles, and rabbits inhabit. Cats found more susceptible to plague, because they eat upon infected rodents. Wild carnivores easily get infection after eating other infected animals. It also occurs after large floods and after earthquakes because most of the rodent species dye and rat fleas use their bodies as habitat and plague spores easily come in air at infection site. There are two categories of plague i.e. bubonic plague or septicemic plague. Plague also spreads due to inhalation of aerosols or bacteria containing droplets from infected persons mainly pneumonic plague patient.

For control of plague control of rat flea is most essential. DEET is most usable repellent that repel rodent fleas more efficiently. To

kill rat flea in clothing and other washable belongings permethrin is used. Pets should bath by using flea killing soaps or liquids and by applying repellent cream also flea control products. Do not allow dogs or cats exposure, do not take them in lap and ban their entry inside roam in endemic areas, not to sleep them on your bed.

Plague is antibiotic treatable which inhibit the formation of cell wall, cell membrane, the nucleic acid synthetic pathway, and the ribosome [69]. For better protection an earlier diagnosis and therapeutic and medical care found more appropriate for control of plague, and provide better chances of full recovery. More specifically, pneumonic plague patients mainly in endemic area should need health care immediately. For control of plague **i**mmunization with live, attenuated (non-pigmented) strains or subunit vaccines with F1 (Caf1) antigen is found effective against bubonic and pneumonic [70]. It generates strong plague-protective immunity and humoral immune responses against plague.

Mixed bacterial infections

Different bacteria also cause mixed infection in man which cause suspicion in diagnosis (Table 2). There are series of mixed infections caused by bacteria or by other microbes. Few of them are respiratory infection, chronic bronchitis, UTIs infections, pharyngitis, pelvic inflammatory diseases, tonsilitis, gonorrhea, ashtma, pneumonia, and food poisoning (Table 2). Few bacteria also cause skin and hair infection in man i.e. bacterial folliculitis, trichomycosis or Axillaris or trichobacteriosis, sepsis, wound infections, cellulitis, acne and cutaneous infections (Table 3).

Disease	Causative agent	Symptoms	Transmission	Treatment
Acute sinusitis	Bacterial infection or fungus infection	Cavities around the nasal passages become inflamed. swell, blocked, triggered by a cold or allergies, replace normal nasal flora	Through sneezing, used towels, bad sheets and gloves	Pain medication, nasal decongestants and nasal saline rinses. Chronic sinusitis may require antibiotics.
Urinary tract infection	Most UTIs are caused by bacteria, but some are caused by fungi and in rare cases by viruses.	Common in women bladder or urethra, but more serious infections involve the kidney.	Urination at contaminated place	Treatment is with antibiotics
Respiratory infection	Streptococcus pyogenes, *Streptococcal pharyngitis*	Inflammation and accumulation of fluids and white blood cells in the alveoli	Secrete erythrogenic toxin, scarlet fever	**β**-lactams remain effective; oral amoxicillin and Intramuscular penicillin G are those most commonly prescribed.
Chronic bronchitis	Bacterial infection noxious irritants. caused by smoking cigarettes,	Chronic obstructive pulmonary disease, inflammation of the bronchi.	Alpha-1 antitrypsin deficiency can play a role in causing chronic bronchitis.	Broad spectrum antibiotics and expectorants, inhalers
Infectious diarrhea	Advanced colonization of the gut by hemolytic enteropathogenic E. coli Salmonella spp, Campylobacter jejuni, and enterohaemorraghic Escherichia coli	Increased intestinal secretion of fluid and electrolytes, predominantly in the small intestine	Undercooked meat or seafood, unpasteurized milk, or soft cheese	Fluid and electrolyte replacement. Oral rehydration therapy (ORT), antimicrobial agents Ciprofloxacin
Pelvic inflammatory diseases	Lower abdomen and includes the fallopian tubes, ovaries, cervix, and the uterus	Infection of the female reproductive organs.	Painful sex, painful urination, irregular breeding, through unclean clothes, use of common toilets	Two different types of antibiotics, sexually transmitted bacteria
Otitis	Bacterial infection inflammation or infection located in the middle ear	Ear pain, fever, adenoid swelling, drainage of fluid from the ear or hearing loss. irritability	By airborne spread of the causative infectious agents in droplets	Ibuprofen or acetaminophen

Pharyngitis	Pharynx, which is in the back of the throat. It's most often referred to simply as "sore throat by	Overuse of voice, a burn from hot food, very dry mouth or sleeping with the mouth open. spread when droplets of infected fluids, such as saliva, nasal discharge, or mucus, come in contact with another person's nasal or oral mucosa or conjunctivae	Inflammation of the mucous membranes that line the back of the throat, or pharynx. Difficulty in swallowing	Antibiotics, analgesics, or topical anesthetics, Amoxicillin (Amoxil) Penicillin V (Veetids), Acetaminophen, Ibuprofen
Tonsilitis	*Streptococcus* pyogenes (group A *streptococcus*), the bacterium that causes strep throat.	Swollen tonsils, sore throat, and difficulty in swallowing and tender lymph nodes on the sides of the neck.	Avoid eating contaminated foods, ice creams, chilled water and practice good hygiene	Broad spectrum antibiotics
Gonorrhea	*N. gonorrhoeae*	Sexually transmitted bacterium	Painful urination and abnormal discharge from the penis or vagina. Men may experience testicular pain	Antibiotic treatment, azithromycin by mouth, antibiotic-resistant strains of gonorrhea is a growing challenge, and doxycycline
Asthma	A chronic disease of the airways with links to the immune system	Inflammation of airways and lungs, bronchial tubes, difficulty breathing, chest pain, cough and wheezing	Allergens trigger, pet dander from animals like cats and dogs, airborne allergens, such as pollen, dust mites, mold spores, pet dander or particles of cockroach waste	Inhalers, corticosteroids and other anti-inflammatory medications , breathing exercises
Pneumonia	*Legionella pneumophila* S. pneumoniae, H. influenzae *Mycoplasma pneumoniae*	Cough with phlegm or pus, fever, chills and difficulty breathing.	Sneezing and air droplet inhalation	Some forms of pneumonia can be treated by antibiotics and prevented by vaccines
Clostridial food poisoning	Spore-forming pathogenic bacterium of the genus *Clostridium*	Watery diarrhea and abdominal cramps, acute gastroenteritis	Improperly cooked and stored foods.	Treatments are an antitoxin injection and breathing assistance.
Botulism	*Clostridium botulinum*	Antibiotic-associated diarrhea, Facial weakness and paralysis	Enterotoxin cause food poisoning, spread through contaminated food or infect a wound.	Treatments are an antitoxin injection and breathing assistance.
Staphylococcal food poisoning	*Staphylococcus aureus* (Staph) bacteria.	Eating foods or food products contaminated with toxins	Toxins produced by the bacterium Gastrointestinal illness	Soda and fruit juices, sugar and electrolytes
Food borne infection or intoxication	Mixed bacteria, viruses, parasites or toxins.	Ingesting food having toxins formed by bacteria	Cramping, nausea, vomiting or diarrhea.	Adequate hydration
Salmonellosis	Salmonella sp.	Diarrhea, fever, and stomach cramps	Eating foods contaminated by feces, raw meat, poultry and seafood, raw eggs, fruits and vegetables	Severe infections may require medical care, including IV fluids and sometimes antibiotics.

Camphylobacteriosis	*Campylobacter* commonly *C. jejuni.* Campylobacter fetus and Campylobacter coli	Abdominal cramping, fever, dizziness, nausea, headaches, dry mouth, tiredness, and oliguria	Contaminated food and water	Erythromycin, ciprofloxacin, and azithromycin
Helicobacteriosis	Helicobacteriosis	Infect lining of upper gastrointestinal tract	pets and farm animals	Broad spectrum antibiotics

Table 2: Mixed bacterial infections caused in man.

Disease	Causative agent	Symptoms	Transmission	Treatment
Bacterial folliculitis folliculitis decalvans, tufted hair	*Staphylococcus aureus*	Clusters of small red bumps or white-headed pimples that develop around hair follicles, Sycosis barbae	Infection transfer through cut or other wound.	Antibacterial ointment and using a body wash with chlorhexidine
Trichomycosis or Axillaris or trichobacteriosis	Bacterial infection	Infection affect pubic or under arm hair, irritation and discomfort.	Non-transmissible	clindamycin or erythromycin lotion
Furuncle or boil	*Staphylococcus aureus*	Hair follicle becomes infected, inflamed, furuncle looks like a red, raised bump on skin.	Non-transmissible	Broad spectrum antibiotics
Sepsis	Bacteremia or blood infection	Severe organ dysfunction such as sepsis	Non-transmissible	Broad spectrum antibiotics
Wound infections	*P. aeruginosa*	Formation of biofilm in or bound,	Exposure of wound to microbes	Polymyxin B, gentamycin, fluoroquinolones, topical antibiofilm agents
Necrotizing fasciititis	*S. pyogenes, Klebsiella, Clostridium*	Infection of fascia, tissue death, septic shock and death	Entry of bacteria through cut mark	Intravenous antibiotic fluid therapy or dose
Staphylococcal scalded skin syndrome	*S aureus.*	Erythema and sever peeling of skin	Infection of skin and mucous membranes	Intravenous antibiotic fluid therapy or dose
Cutaneous anthrax	*Bacillus anthracis*	Spots at site of infection, septicemia and become fatal	Endospores enter through cut or abrasion	Penicillin, erythromycin, tetracycline
Acne	Propionate bacterium ace	White and black heads, pseudocysts, pustules	Entry through clogged pores	Erythromycin, clindamycin
Cellulitis	*S. pyogenes*	Localized inflammation of dermis and hypodermis, skin become red, warm and painful to the touch	Entry through cut or abrasion	Oral intravenous antibiotics
Erysipelas	*S. pyogenes*	Inflammed, swollen patch of skin, on face	Entry through cut or abrasion	Oral intravenous antibiotics
Erythema nodosum	*S. pyogenes*	Small red nodules on skin	Mixed streptococcal infection	Anti-inflammatory drugs
Impetigo	*S. aureus, S. pyogenes*	Vesicles, pustules, bullae around nose and mouth	Spread through contact	Topical or oral antibiotics

Table 3: Hair and skin infection caused by bacteria in man.

Factors that contribute in the emergence or reemergence of bacterial infectious

There are so many factors which are responsible for emergence or re-emergence bacterial infectious diseases. First factor is presence of transmission vector and presence of pathogen in human cultural environment. However, to control a bacterial disease, tracing of mode of transmission, and identifying reservoirs of infection is highly important. A second factor is appropriate diagnosis for prevention and control of disease as early as possible. Besides this, human, environmental, ecological and genetic factors are responsible for emergence and re-emergence of bacterial diseases [71]. These factors play critical role in perpetuating emergence of new bacterial strains mainly drug resistant killer strains [72]. Additionally, inappropriate drug regimens, or wrong prescription of drugs is responsible for changes bacterial genetics sudden appearance of new drug resistant biotypes bacterial pathogens. These biotypes are more efficiently transmitted between hosts and vectors and recalculate in human population. These new biotypes remain uncontrollable and evoke epidemics which later on become more serious, frequent, complex, and harder to prevent control. These new bacterial strains emerged are showing high infectivity, mortality, and morbidity due to demographic, ecological, anthropogenic, bacterial pathogen and host related factors. Therefore, for quick control of bacterial diseases/infection tracing, testing and treatment is highly important. There is a immense need to study contributing factors which play active role in emergence and re-emergence of novel pathogens is highly essential at global or at level of country.

Drug resistance

Antibiotics are used for treatment of bacterial infection; these significantly inhibit bacterial growth and control them. Antibiotics show inhibitory effects against bacterial growth, by inhibiting their multiplication or kill them out rightly. Antibiotics can either impede bacteria from multiplying or kill them outright. But due to constant use and exposure some bacteria develop resistance to certain classes of antibiotics by making genetically changes for detoxification of drugs in long term. Thus, bacteria very easily acquire resistance to first line antibiotic drugs by one of a growing variety of mechanisms. Due to drug exposure bacterial cells start identifying the drug structure and start secreting enzymatic scissors to cut these drug structures and do its simplification or neutralization.

Mechanisms of development of antibiotic resistance

Drug resistance develops in many serial steps. In first step microbes expose with drug formulae and its concentration, second resistant strain is developed against particular antibiotic. These strains of bacteria show selective action, they even survive in the presence of antibiotics. For antibiotic resistance microbe genome get changes in genes or it acquires some new genes that synthesize enzyme which cleave of functional groups or changes into a less active group of antimicrobial drugs. It leads to evade the action of antibiotics. It happens in hospitals where few antibiotics are more commonly used and so many patients body has a modified slightly modified pathogen [73]. After changing a host, as soon as disease pathogen is transmitted to next host acquire resistance after making structural changes in or around the target molecule that inhibit the drugs' ability to bind to it. Resistant strains results in reduction in permeability of the cell membrane to the drug. It inhibit the pumping of drug out of the cell after back to inside, it hampers the drug action and inactivate the antibiotic after it has been taken up by the cell.

When someone first time use antibiotic they show more cidal activity against microbes, but this get reducing as soon as start secretion of catalytic and hydrolyzing enzymes the amount of the target molecule increase, and drug become "less susceptible" to a drug. Therefore, a higher drug level starts adversely affecting body physiology but not microbes. Resistance in microbes is developed as the patient take the antibiotic dose, it normally expose all of the microbes of body and not just the organism causing infection. Because, antibiotics attack invading microbes, kill them efficiently when used first time. They provide quick relief become an essential to combat the disease pathogen, but in return it gives rise resistance. Further over use and wrong prescription of antibiotics generates resistance in microbes. For examples use of antibacterial agents for treatment of viral infections, cause susceptible in patient to the antibiotic used. This is a wrong prescription; similarly use of steroids is also dangerous for the health of patient in post recovery period. Another example of misuse is the consumption of broad-spectrum antibiotics is to take low doses for longer time; they never kill or inhibit the growth of a wide variety of organisms. Simultaneously, it makes the target molecule functionless as in true sense a narrower spectrum drug to a non-functional drug.

Transfer of antimicrobial-resistance genes

Bacterial cells contain circular extra chromosomal DNA molecules i.e. plasmids. These autonomously replicate and transfer to bacterial genes to other species. It carries resistance genes to other companion of the same species or transfers to across species of conjugating bacteria and assist in development of resistance. These resistance genes are transferred by various genetic exchange mechanisms. Initially, antibiotic resistance develops due to acquiring mutations to existing genes; however, most bacteria acquire genes by genetic exchange rather than experience the mutation themselves. *Escherichia coli* and *Salmonella* species can transfer extra-chromosomal genetic material through conjugation. Many plasmids carry genes for resistance to multiple antibiotics; thus, one conjugation event can simultaneously transfer resistance to several antibiotics. Another method of gene transfer in some species of bacteria is bacterial transformation. Next method of mechanism of genetic exchange in bacteria is transduction. It occurs due to invasion of bacteria cells by viruses. Virus attach to the bacterial surface mainly plasma membrane and dislodge it due to catalytic action of virus spike proteins or surface proteins. Invading virus releases its short genome either DNA or RNA, inside the bacterium and prepares its own genome and start regulating the cell's metabolism, directing synthesis of its genetic material and production of the components of the viral particle. In second step, the host bacterial DNA is degraded, different proteins participate to make new virions are assembled; its genetic material is encapsulated in a protein coat. Lastly a piece of the host bacterial DNA is packaged in a viral particle known as "transducing particle". Now, this new viral gains the ability to invade the bacterium and shows the ability to attach to a recipient bacterium. It transfer its genetic material in to a new bacterium where transducing particle may be a bacterial gene for drug resistance to an antibiotic. Transposons are DNA sequences which are capable of inserting themselves randomly into genomes. Many bacterial strains possess transposons which carry antibiotic resistance genes.

Emerging and re-emerging infectious diseases

Emerging infectious diseases are diseases are seen first time in humans and never seen before. Exceptionally, there are some diseases whose outbreak occurred many times in human history but in recently they have been evokes as distinct diseases due to an infectious agent (Lyme disease and gastric ulcers are examples). Re-emerging infectious diseases are those which were sometimes major health problems globally or in a particular country. All of a sudden they disappeared dramatically, but again with the time evoked again and become health problems for a significant proportion of the population. These reemerging diseases are plague, anthrax, tuberculosis and malaria [74]. Many specialists placed infectious diseases with re-emerging diseases in a subcategory of emerging diseases [75].

Bacterial infection starts with the attachment of bacterial cells to host cell surface. After entered inside host cell, they start dividing, proliferation and invade the host tissue. Severity of pathogenesis is increased due to toxin induced damage to host cells. So many bacteria defy host defenses by using surface structures or molecules that enhance their ability to attach to host cells. However, pili or long hairlike projections are used for making attachment to the membrane of the intestinal or genitourinary tract by a number of gram-negative bacteria. Few adhesion molecules are secreted by *Bordetella pertussis*, which assist it to associate with ciliated epithelial cells of the upper respiratory tract. Few proteases *are secreted by bacteria i.e. Neisseria gonorrhoeae*, *Haemophilus influenzae,* and *Neisseria meningitidism* specially cleave the secretory IgA at the hinge region. This is the main reason that Fab and Fc fragments derived from antibodies do not show their ability to agglutinate microorganisms. Some bacteria evade the IgA response of the host by changing these surface antigens. Some bacteria change their surface structures mainly polysaccharide capsule that serve to inhibit phagocytosis.

Host immune responses to bacterial infection

Body of animals generate antibody in response to bacterial antigens to combat the infection. Initially innate immune barriers check the entry of bacterium inside the body. For taking entry into host body bacterial pathogens follow number of natural routes e.g. the respiratory tract, the gastrointestinal tract, and the genitourinary tract, skin wounds and injury or through normally inaccessible routes opened up by breaks in mucous membranes. The major players of innate immunity are sebum in skin, low pH, catalytic enzymes, mucus membranes, cilia, ions, and buffers. Body responds in many ways as bacterium starts intracellular growth; hence, in response to it delayed-type hypersensitivity reactions are mediated. There are several mechanisms which are seen in various types of bacteria. Few import events are attachment of bacterium to host, where it is inhibited by the secretion of proteases

that cleave secretory IgA dimers and cell secreted IgA antibodies (*Neisseria meningitidis, N. gonorrhoeae, Haemophilus influenzae*). In *N. gonorrhoeae* antigenic variations due to certain shifts have been identified in attachment structures i.e. pili. For instant control of bacterial infection phagocytic cells proliferate and its increased number makes phagocytosis at larger scale.

Few bacterium avoid immune defense and entered inside phagocytic cells and inhibits phagocytosis by making Ab- and production of surface structures like polysaccharide capsule, M protein, fibrin coat. These also secret elastase that inactivates C3a and C5a complements in Pseudomonas. Thus, antibodies bind to accessible antigens on the surface of a bacterium. These in association with the C3b component of complement, behave as an opsonin and increases phagocytosis and massively eliminate bacterial cells. Thus, antibody mediated complement activation of phagocytosis directly lyses the microbial cells and induce the localized production of immune effector molecules. It also evokes an amplified and more effective inflammatory response. The complement split products C3a, C4a and C5a act as anaphylatoxins, that induce local mast-cell degranulation. It causes vasodilation and the extravasation of lymphocytes and neutrophils from the blood into tissue space. Similarly, a complement localized inflammatory response mediated lysis is maintained by induction of apoptosis in macrophages by *Shigella flexneri*. Further, insertion of membrane-attack complex is prevented by long side chain LPS and invasion of host tissues Ab-mediated agglutination in few gram-negative bacteria.

Immune responses can contribute to bacterial pathogenesis

In response to toxins secreted by bacterial pathogen both cell mediated and humeral immune responses are generated. Some bacteria defy cell mediated defense and house inside the infected cells that results in chronic antigenic activation of CD4+ T cells. Besides this, few bacteria massively invade T helper cells by secreting endotoxins, that results in overproduction of cytokines and activate T helper cells. These endotoxins also activate macrophages, that results in release of high levels of IL-1 and TNF-α, that causes septic shock, food poisoning and toxic-shock syndrome. Endotoxins, contain lipopolysaccharides (LPS), secreted from bacterial cell walls. These generate cell-mediated immune response, specifically, delayed type hypersensitivity.

Besides this, staphylococcal food poisoning and toxic-shock syndrome, occurs due to production of exotoxins which function as super-antigens. These also activate T cells and leads to destruction of tissue by a cell-mediated response and induce delayed-type hypersensitivity reaction. In response to bacterial toxins CD4+ T cells secrete cytokines and IFN-α, which activate macrophages to kill bacterial pathogens by ingestion or phagocytosis more effectively. Subsequently, cytokines secreted from activated CD4+ T cells show extensive accumulation and activation of macrophages. It forms localized granulomas that contain high levels of lysosomal enzymes and do extensive tissue necrosis. It is one of the important reasons behind bacterial septic shock, food poisoning, and toxic-shock syndrome. Infection by extracellular bacteria induces production of humoral antibodies, which are ordinarily secreted by plasma cells in regional lymph nodes and the submucosa of the respiratory and gastrointestinal tracts. The humoral immune response is the main protective response against extracellular bacteria.

Besides this, innate immunity also plays some role against intracellular bacteria which activate NK cells. Bacterial cells are entrapped by mucosal lining and beating of cilia check its attachment to host cells and defy bacterial invasion of host cells. Few enzymes and secretory IgA antibodies also block bacterial attachment to mucosal epithelial cells and are the main host defense against bacterial attachment.

Neutralization of bacterial toxins

Most of the bacterial strains secrete toxins, either endotoxin or exotoxin. These show cytotoxicity and cause pathogenesis in various manner. For example, diphtheria pathogen secretes exotoxins, which exerts a toxic effect on the cell by blocking protein synthesis. However, toxic effects of bacterial toxins is neutralized by neutralization antibodies of anti-toxin generated in animals. There are several mechanisms which are used to combat the toxin induced toxicity. These neutralized antibody mainly bacterial toxin binds to the toxin and neutralize them. Later on these antibody-toxin complexes are cleared by phagocytic cells. Antitoxin antibodies generated against microbial exotoxins binds to Fab portion of antibodies and interact with host target cells. Neutralizing antibodies neutralize the toxic effects of bacterial toxins for examples IgG neutralizes toxins in tissues while IgA neutralizes toxins at mucosal surfaces within the body. However, neutralizing antibodies eliminates the infectious particle before beginning of any infection takes place [76]. These are also known as sterilizing antibodies which inhibit the infectivity by binding to the pathogen and block the molecules needed for cell entry. It become possible as antibodies statically

interfere with the pathogens or toxins attaching to host cell receptors. These generate humoral response against intracellular bacteria and microbial toxin. It is noted that neutralizing antibody neutralizes diphtheria antitoxin and eliminate its biological effects [77]. But these neutralizing antibodies were not found effective against extracellular bacteria and could not prevent bacteria from replicating. Because in external medium many factors work together and binding specifically to surface structures (antigen) on an infectious particle, remain low. Therefore, in such cases antibodies, show opsonisation and kill bacteria in association to complement activation, to kill the bacteria [78]. More specifically, antibody-mediated mechanisms strongly defy the infection caused by extracellular bacteria. Further, complement activation on bacterial surfaces operates complement-mediated lysis of bacteria. Complement C3b bind to bacteria, and serve as opsonins to increase phagocytosis, at the same time C3a, C4a, and C5a, are generated by antibody initiated complement activation. These might induce local mast cell degranulation, releasing substances that mediate vasodilatation and extravasations of lymphocytes and neutrophils. Few other complement split products and chemotactic factors are secreted from neutrophils and macrophages which accelerate phagocytosis and eliminate bacterial pathogens.

Diagnosis of bacterial pathogens

Maintenance of bacterial cultures

For identification of bacteria its laboratory culture is maintained on various specific and non specific, selected and non selected media from blood, sputum, and urine, body tissues and soil samples. Normally bacteria are plated on solid nutrient-rich media or inoculated into broth in glass Petri dishes. Normally solid media is used for growing cocci and suspension culture is maintained for bacilli. In agar-agar solid media, bacteria can grow and produce colonies composed of thousands of cells. Bacterial colonies have been identified on the basis of bright shining star shaped structures. Different bacterial colonies have its separate characteristic appearances which help in their identification. Normally in microbiology laboratory for identification of strains bacterial cultures are maintained on agar plates in controlled aseptic conditions to encourage the growth of microorganisms. There are bacteria which grow on most common medium but few are fastidious and need specific medium for their growth. Factors which are controlled i.e. temperature for incubation, and the amount of oxygen available and pH of the medium. There are anaerobes which grow in absence of oxygen and aerobes they need oxygen that is given by incubators. Normally bacterial growth is measured by counting bacterial cells in 1 mm cube of culture media, and by counting colonies directly from solid agar petri plates just after 12 hrs of inoculation of starter culture. In broth bacterial growth can be determined by reading level of turbidity. For identification bacterial colonies are studied under microscope after Gram staining. Particular bacterial strain is also identified by testing its ability to produce enzymes and metabolize sugars as detected by simple tests, and by its ability to utilize various substrates for growth. For determination of antibiotic susceptibility to various antibiotics bacterial strains are grown separately in absence and presence of broad spectrum antibiotics and no resistance, susceptibility and cidal activities can be studied. Few bacterial pathogens they need natural media or host cells for their growth. However, Chlamydia and rickettsia are grown on artificial media and in presence of host cells. Few other bacteria like *Mycobacterium leprae* and *Treponema pallidum* only grow in living animals.

Genetic material testing

These are also identified by using DNA or RNA tests. Sequencing of DNA and RNA provides more authentic information about microorganisms' gene mutations and shifting of bases or codons both in control and test resistant microorganism exposed with drug. Quantitative tests which could determine MIC and MBC values can also be used to monitor how well treatment is working. Antibiotic susceptibility tests are also conducted to determine the effectiveness of broad spectrum antibiotics against particular bacteria. By knowing the radiation zone diameter no resistance, mild resistance or susceptible and resistant dose levels of selected antibiotics, can be calculated in bacterial cultures.

Coagulase test

Coagulase is an enzyme that converts fibrinogen to fibrin. It causes cell clumping in plasma. The coagulase test differentiates coagulase-positive *Staphylococcus aureus* from coagulase-negative staphylococci (Table 4).

Catalase test

Catalase test is used to differentiate catalase-positive staphylococci and micrococci from catalase-negative streptococci. Catalase is an enzyme that degrades hydrogen peroxide into hydrogen and oxygen. Therefore, bacterial sample are treated with hydrogen peroxide. In positive cases oxygen bubbles are generated (Table 4).

What blood tests are done in bacterial infections?

Various blood cell based parameters are measured to test the bacterial infection. In blood tests full blood cell count is done in

Test	Principle	Procedure	Common use	Precision level
Citrate utilization test is a part of the MViC test (Indole, Methyl Red, Vogues-Proskauer, and Citrate Test)	Medium produce an enzyme, citrate-permease, capable of converting citrate to pyruvate. Pyruvate can then enter the organism's metabolic cycle for the production of energy.	Differentiate among the Gram-Negative bacilli in the family Enterobacteriaceae. When the bacteria metabolize citrate, the ammonium salts are broken down to ammonia, which increases alkalinity. The shift in pH turns the bromothymol blue indicator in the medium from green to blue above pH 7.6.	Growth is indicative of utilization of citrate, an intermediate metabolite in the Krebs cycle.	0.1 gm
Gelatin liquification test	During reaction, gelatinases degrade gelatin to polypeptides. Then, the polypeptides are further converted into amino acids	This test is used to determine the ability of an organism to produce extracellular proteolytic enzymes (gelatinases) that liquefy gelatin	This test is helpful in identifying and differentiating species of Serratia, Proteus, Bacillus, Clostridium, Pseudomonas and Flavobacterium	0.1 gm
Decarboxylase (Lysine, ornithine, arginine	arginine decarboxylase, ornithine decarboxylase, and lysine decarboxylase, members of Enterobacteriaceae from other gram negative rods.	Decarboxylases are a group of enzymes which acts by hydrolyzing an amino acid to form an amine	The decarboxylation of the amino acid yields in an alkaline pH and a change in color of pH indicators bromocresol and cresol red from orange to purple is observed.	0.1 gm Positive result, Alkaline (purple) color change compared with the control tube
Beta-galactosidase Test	Bacterial organism possesses beta-galactosidase, the enzyme will split the beta-galactoside bond, creating a yellow color change in the suspension.	An ONPG disk is added to 0.5ml of the suspension. If the organism possesses beta-galactosidase, the enzyme will split the beta-galactoside bond, creating a yellow color change in the suspension.	the organism is taken from a medium containing a high concentration of lactose and is inoculated into the ONPG Broth	0.1 gm
Carbohydrate fermentation test	Tests for the presence of acid or gas produced from carbohydrate fermentation	Utilization of carbohydrate	Carbohydrate substrate results in acidification of the medium, used phenol red as indicator 0f pH, it detects the production of acid from fermentation Tubes are inverted for gas production	0.1 gm of carbohydrate, of a positive carbohydrate fermentation reaction.
Coagulase test (CONS).	Coagulase is an enzyme-like protein and causes plasma to clot by converting fibrinogen to fibrin. Staphylococcus aureus produces two forms of coagulase: bound and free.	Mix dense liquid suspension of bacteria with plasma, incubate and observe, look for clumping of the organisms within 10 seconds.	Differentiate Staphylococcus aureus (positive) which produce the enzyme coagulase, from S. epidermis and S. saprophyticus (negative) which do not produce coagulase. i.e. Coagulase Negative Staphylococcus	0.1 gm

Catalase	Enzyme decomposition of hydrogen peroxide	By adding a drop of H2O2 to thick culture and look for o2 bubbles	Bacillus (+) Clostridium (-) Micrococcus, Streptococcus	0.01

Table 4: Few enzymatic assays used for detection of bacterial pathogens.

biological samples collected from an infected person. WBCs are counted in case of neutrophilia and red cells in case of anemia. C-reactive protein (CRP) test is also done to know the level of inflammation in case of serious bacterial infections. Procalcitonin is a marker of bacterial infection induced sepsis. Serology tests are also performed to find out immune response to a particular organism. Rapid Plasma Reagin (RPR) test is used to detect syphilis in suspected cases. Blood culture is done to test the high fever > 38°C.

Serology

There are so many tests which are based on antigen–antibody interactions. These are used to determine the presence of a bacterial infection such as syphilis and brucellosis. These tests also have some limitations as most cases need for several weeks to pass in order for the body to develop an immune response to the infection. Commercial kits are available in the market; these are used to identify a variety of organisms i.e. *in* body fluid specimens and in swabs, skin roughs, feces and urine samples. For rapid diagnosis antigen-antibody tests can easily identify level bacterial antigens in blood samples. These tests are immunodouble double diffusion, rocket electrophoresis, and precipitin tests. ELISA is most efficient method used to detect level of antigens in blood samples.

Enzyme-linked immunosorbent assay (ELISA):

ELISA test is a rapid test based on antigen-antibody interaction. It is performed to detect bacterial antigen level upto 0.0001 gm/mL quantity. By knowing the level of antigen disease status could be identified. Type of antibody also confirms causative agent of disease. ELISA is rarely used for the detection of plague, tuberculosis, syphilis, anthrax, typhoid pathogens in various samples collected from patients It is also used to identify *Borrelia burgdorferi* in Lyme disease, *Treponema pallidum* in syphilis (Table 5). Besides ELISA their there are so many antibody-antigen interaction based clinical tests are available which provide high accuracy and precision in bacterial infection diagnosis (Table 5).

Name of method	Principle	Procedure	Common use	Precision level (µg)
Precipitation reaction in fluids	interaction of antibodies developed against bacterial antigens,	Two soluble reactants that come together to make one insoluble product, the precipitate, formation of lattices (cross-links) when antigen and antibody exist in optimal proportions.	To find bacterial antigens in biological samples	20-200
Precipitation reactions in gel				
Mancini radial immunodiffusion	Quantitative estimation of antigen	To detect the concentration of antigen by measuring the diameter of the precipitin ring formed by the interaction of the antigen and the antibody at optimal concentration	The diameter of the precipitin ring is proportional to the concentration of antigen. With increasing concentration of antigen, precipitin rings with larger diameter are formed	10-20

Ouchterlony double immunodiffusion	Antigen-antibody diffusion and interaction is used to identify antibodies to various pathogenic organisms	Detection or measurement of antibodies and antigens by their precipitation which involves diffusion through a substance such as agar or gel agarose.	Used for detection, identification and quantification of antibodies and antigens	20–200
Immunoelectrophoresis	Separation and identification of proteins based on differences in electrical charge and reactivity with antibodies.	The separating medium is usually an agarose gel. The gel has alternating wells and slots cut into it.	The antibodies diffuse laterally to meet diffusing antigens, and lattice formation and precipitation occur permitting determination of the nature of the antigens.	20–200
Rocket electrophoresis	Negatively charged antigen samples are electrophoresed in an agarose gel containing antibody which is specific to that antigen	The area of precipitin has the shape of a rocket and its height is proportional to the concentration of antigen in the corresponding well.	Immunoglobulin and serum protein isolation	2
Direct				
Pas Passive agglutination	Passive hemagglutination of erythrocytes sensitized with antigen is an extremely simple method for the detection of antibody	Pallidum passive particle agglutination assay (TP-PA), which uses the same antigen mix, but attached to red gelatin beads instead of erythrocytes.	Used to detect infectious bursal disease (IBD) virus antigen	0.006–0.06
Agglutination inhibition	Hemagglutination occurs when measles viruses and red blood cells are mixed	Agglutination inhibition or hemagglutination inhibition refers to the inhibition of these reactions by soluble antigen which reacts with the combining sites of the antibodies and thereby prevents their binding to and agglutination of the particles.	Used to detect or quantify antibodies to influenza A viruses, antibodies can also clump together cells or particles	0.006–0.06
Radioimmunoassay	When radioisotopes instead of enzymes are used as labels to be conjugated with antigens or antibodies, the technique of detection of the antigen-antibody complex is called radioimmunoassay (RIA).	Basic principle of radioimmunoassay is competitive binding, where a radioactive antigen ("tracer") competes with a non-radioactive antigen for a fixed number of antibody or receptor binding sites. ...	Radioimmunoassay (RIA) is an in vitro assay that measures the presence of an antigen with very high sensitivity.	0.0006–0.006
Enzyme-linked immunosorbant assay (ELISA)	Antigen and antibody interaction specific and non specific binding of an antigen to antibody	ELISA testing and allows for identifying specific protein antibodies and antigens, with only small amounts of a test by using primary and secondary antibodies and horse-radish peroxidase enzyme	Used for diagnosis of HIV infection, pregnancy tests, and blood typing, used to detect and quantify substances, including antibodies, antigens, proteins, glycoproteins, and hormones.	0.0001–0.01

Flow cytometry	Utilizes laser –based technology to count sort, and profile	By utilizing highly specific antibodies labeled with fluorescent conjugates	Disease pathogens	0.001-0.01
The VIDAS ECO test is an enzyme-linked fluorescent immunoassay (ELFA)	A fluorescent substrate (4-methyl-umbelliferyl phosphate) is introduced in the SPR. Enzyme remaining on the SPR wall will then catalyze the conversion of the substrate to the fluorescent product, 4-methyl-umbelliferone	For E. coli O157 antigens present in the sample bind to the anti-E. coli O157 antibodies coating the interior of the SPR. A final wash step removes the unbound conjugate.	VIDAS E. coli O157 assay	0.0001–0.01

Table 5: Few important clinical diagnostic tests for detection of bacterial pathogens.

Polymerase chain reaction

Polymerase chain reaction (PCR) is used to amplify a small amount of DNA with the help of a probe in machine in presence of enzymes at particular temperature. In consecutive cycles certain known genes can be amplified in a specimens without the necessity for culture. Sequences of many disease genes i.e. *E. coli* or cholera, *Helicobacter pylori*, gonorrhea and chlamydia and *Mycoplasma pneumoniae* have been amplified. Within hours PCR technique is used to produce many copies of a gene from a microorganisms in the laboratory, it assists in its identification. PCR is used to isolate and amplify lengths of bacterial DNA from skin, blood or other tissue samples. PCR is proved useful for slow-growing bacteria such as anaerobic bacteria and mycobacteria (tuberculosis and atypical mycobacteria) no standard cultured method is being available to test them.

Stains and microscopy

The morphological and cellular identification of bacterial cells are stained with Gram stain that is prepared from series of stains or dyes on a sample. It has both developer and washer that limits the stain. Bacteria if take stain and seen used light microscope are known as Gram-positive while no stain as Gram-negative. A Gram stain is only used for original samples, but it is also used in laboratory cultures of bacteria. On the basis of shape of bacteria like round in shape are cocci, rod-shaped are Bacilli and some bacteria also found in clusters. Immunofluorescent-labeled antisera is also used to identify hemolytic streptococcus, plague, and syphilis bacterium. Dark field microscopy is to identify spirochetes agents of syphilis and yaws. These could be visualized under fluorescent microscopy, with or without special dyes. For identification of *Mycobacteria* UV light source is used in microscopy.

Public health measures to prevent infectious diseases

For maintaining good health and keep people healthy various infection control strategies must be applied for instant control and stop the spread of infectious diseases. These public health measures are widely concerned with elimination of pathogen from its reservoir or from its transmission vector or route. Few important measures are hand washing to remove of pathogen come from contact, bearing of mask to avoid droplet and airborne infection, decontamination of individuals and disinfection of equipment and the environment, quarantine and prophylaxis of infected persons. Other public health measures are control of the vectors of infection, ensuring a safe water supply, effectively managing sewage treatment and disposal, and initiating food safety, animal control, and vaccination programs.

Safe water

To avoid gastrointestinal pathogens public water must be guarded against contamination from sewage drinking water. All water supply stations must use purification methods include settling, filtration, and chlorination to treat the supply water with chlorine.

Sewage treatment and disposal

Sewage water carries the pathogens of many waterborne diseases, including giardiasis and hepatitis A. Therefore, to ensure public safety sewage must be treated to eliminate pathogens. Waste can be treated by collection, sedimentation of sewage waters, sepa-

rating solid matter (sludge) from the liquid (effluent) portion of sewage. The effluent is chlorinated to kill pathogens before it is released to rivers or lakes. The left over sludge is burned or dumped. Decomposition of municipality waste and effluent can decompose 90 percent of the organic wastes and eliminate pathogens. It could be sued as manure for plants. This is the best way to prevent the disease. In tertiary treatment chemicals are also used to eliminate the pathogens.

Food safety programs

Food safety is highly important for public health. More often, unsafe food creates a vicious cycle of disease and malnutrition. Unsafe food easily affects large numbers of infants, young children, elderly and they become sick after its use. Hence, food must be free from microbes, nutritious and of good quality. WHO has issued directive for prevention, detect and respond to public health threats associated with unsafe food at global level. Milk must be pasteurized for de-contamination. Food packing material must be eco-friendly. Regulations must be applied on food preparation, handling, storage and distribution. Standards must be maintained for canning and preserving foods are maintained through periodic quality control checks.

Animal control programs

For better control of any bacterial disease its reservoir host, carrier and primary host must be killed or controlled. Animals are carriers of many diseases that also affect humans. Mostly plague, anthrax, brucellosis, and shigellosis could be controlled by this method. Many diseases, including bubonic plague, are spread by rodents; if rats are controlled disease could be finished. Similarly, insects also transmit large numbers of bacterial pathogens, if breeding sites of insects are destroyed the spread of insect-borne diseases can be controlled. Many imported animals must quarantined for specific diseases to prevent the introduction of those diseases into the country.

Vaccination programs

For control of bacterial diseases so many vaccines have been produced either against toxins and bacterial surface antigens. For better safety cover infants and children up to age of 12 years have been vaccinated according to one W.H.O. released chart. Besides this, in many countries vaccination has been made essential for school going children, teachers, house maids, and parents. In wider interest of public health vaccination must be supported by all religions sects, communities, ethnic groups and travelers to feel safer against sudden evoking bacterial infections. Purpose of immunization is to care the health of individual as well as public health. If any portion of a population remains unvaccinated disease will not finish and pathogen may persist for longer period of time. Unfortunately, it will appear all of a sudden and will prove more fatal for human race. Hence, it is essential to eliminate the pathogen completely, because once the infected host recovers or dies, there will not be enough new, susceptible hosts for the pathogen to infect. Testing, tracing and treatment is the main key to eliminate disease pathogen from the population. Further, study of contribution factors, advancement of diagnostic and treatment facilities must be updated for better clinical care to end any epidemics. However, both naturally infected and vaccinated people will come under the cover of herd immunity and thus epidemics may end.

Public health organizations

It is great fact that no international or national scheme launched for eradication of any bacterial disease become successful. There was noted a greater role of non-governmental organizations as they assist in national policy formation in the areas of health care. These play assist in making social dialogue, connectivity and preparatory role to convince people for vaccination, medication, camping, and collection of surveillance data from remote field areas. They interplay between government and health organization and integrate services mainly medical, social and psychological. They could play in form of good mediator and working force for care and nursing, transportation of vaccines, vaccination, and can provide education and information and aware the people about health maintenance. Non-governmental organizations have important role in monitoring and reporting of real time field data on social structure, disease incidence, health status and incidence of particular diseases to state and federal agencies.

Conclusion

Few important pathogenic bacteria cause serious diseases in humans and impose high morbidity and mortality. These are very harmful to other animals also. Bacterial infections largely impact public health cause great economic and social losses. Few bacteria cause food poisoning, gastric ulcers, gonorrhea, meningitis, typhoid, plague and tuberculosis and anthrax are gaining drug

resistance. Today multidrug resistant TB is a biggest challenge. *Staphylococcus aureus* causes a variety of infections in the body, including boils, cellulitis, abscesses, wound infections, and toxic shock syndrome impose large and long lasting impact on public health if they are not cured at time. Bacterial diseases may occur at any site of body and transmitted very easily by a variety of mechanisms. Most of the bacterial infections are transmitted through air, water, food, or living vectors and animals. Most of the bacterial infections are spread through contact and food and water contamination. Hence, appropriate diagnosis, treatment and prophylaxis must ensure to remove of the fear from human society. There must be long term plan to combat bacterial infections with strict guidelines to follow, personal protection, hospital care, health, hygiene and environmental cleanliness and vitality must be maintained.

Acknowledgements

Authors are thankful to H.O.D., Department of Zoology for research facilities.

Disclosure of Conflict of Interest

Bibliography

1. Doron S and Gorbach SL. "Bacterial Infections: Overview". *International Encyclopedia of Public Health* (2008): 273-282.
2. Bannister BA., *et al*. "Structure and classification of pathogens". 2nd edition. Blackwell Science Ltd; Oxford, UK (1996): 23-34.
3. Benenson AS. "Control of Communicable Diseases Manual". 16th edition. American Public Health Association; Washington, DC (1995).
4. Evans AS and Brachman PS. "Bacterial Infections of Humans: Epidemiology and Control". 3rd edition. Plenum Publishing Corporation; New York (1998).
5. Dyson ZA., *et al*. "Antibiotic Resistance and Typhoid". *Clinical Infectious Diseases* 68.2 (2019): S165-S170.
6. Ma PY., *et al*. "Human Genetic Variation Influences Enteric Fever Progression". *Cells* 10 (2021): 345.
7. Asadgol Z., *et al*. "The effect of climate change on cholera disease: The road ahead using artificial neural network". *PLoS ONE* 14.11 (2019): e0224813.
8. Olago D., *et al*. "Climatic, socio-economic, and health factors affecting human vulnerability to cholera in the Lake Victoria basin, East Africa. AMBIO": *A Journal of the Human Environment* 36.4 (2007): 350-358.
9. Luque Fernández MÁ., *et al*. "Influence of temperature and rainfall on the evolution of cholera epidemics in Lusaka, Zambia, 2003–2006: analysis of a time series". *Transactions of the Royal Society of Tropical Medicine and Hygiene* 103.2 (2009): 137-143.
10. Semenza JC., *et al*. "Mapping climate change vulnerabilities to infectious diseases in Europe". *Environmental Health Perspectives* 120.3 (2011): 385-392.
11. Greer A., *et al*. "Climate change and infectious diseases in North America: the road ahead". *Canadian Medical Association Journal* 178.6 (2008): 715-722.
12. Mills JN., *et al*. "Potential influence of climate change on vector-borne and zoonotic diseases: a review and proposed research plan". *Environmental Health Perspectives* 118.11 (2010): 1507-1514.
13. Tonnang HE., *et al*. "Predicting and mapping malaria under climate change scenarios: the potential redistribution of malaria vectors in Africa". *Malaria Journal* 9.1 (2010): 111.
14. González C., *et al*. "Climate change and risk of leishmaniasis in North America: predictions from ecological niche models of vector and reservoir species". *PLoS Neglected Tropical Diseases* 4.1 (2010): e585.
15. De Magny GC., *et al*. "Cholera outbreak in Senegal in 2005: was climate a factor?" *PLoS One* 7.8 (2012): e44577.
16. Emch M., *et al*. "Seasonality of cholera from 1974 to 2005: a review of global patterns". *International Journal of Health Geographics* 7.1 (2008): 31.
17. Morens DM and Fauci AS. "Emerging Infectious Diseases: Threats to Human Health and Global Stability". *PLOS Pathogens* 9.7 (2013): e1003467.
18. Hashizume M., *et al*. "The effect of rainfall on the incidence of cholera in Bangladesh". *Epidemiology* 19.1 (2008): 103-110.

19. Ruiz-Moreno D., *et al*. "Cholera seasonality in Madras (1901–1940): dual role for rainfall in endemic and epidemic regions". *EcoHealth* 4.1 (2007): 52-62.

20. Hashizume M., *et al*. "Cholera in Bangladesh:" Climatic Components of Seasonal Variation". *Epidemiology* (2010): 706-710.

21. Lipp EK., *et al*. "Effects of global climate on infectious disease: the cholera model". *Clinical Microbiology Reviews* 15.4 (2002): 757-770.

22. Boardman BK and Satchell KJ. "*Vibrio cholerae* strains with mutations in an atypical type I secretion system accumulate RTX toxin intracellularly". *Journal of Bacteriology* 186.23 (2004): 8137-8143.

23. Nicole Fogel. "Tuberculosis: A disease without boundaries". *Tuberculosis* 95.5 (2015): 527-531.

24. Keshavjee S and Farmer P. "Tuberculosis, drug, resistance, and the history of modern medicine". *The New England Journal of Medicine* 367.10 (2012): 931-936.

25. Prasanna A and Niranjan V. "Classification of Mycobacterium tuberculosis DR, MDR, XDR Isolates and Identification of Signature Mutation Pattern of Drug Resistance". *Bioinformation* 15.4 (2019): 261-268.

26. Solari L., *et al*. "Mutations in Mycobacterium tuberculosis Isolates with Discordant Results for Drug-Susceptibility Testing in Peru". *International Journal of Microbiology* (2020): 8253546.

27. Nahid Payam., *et al*. "Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis". *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America* 63.7 (2016): e147-e195.

28. Bekale Raymonde B., *et al*. "*Mycobacterium Tuberculosis* and Interactions with the Host Immune System: Opportunities for Nanoparticle Based Immunotherapeutics and Vaccines". *Pharmaceutical Research* 36.1 (2018): 8.

29. Berry MPR., *et al*. "Systems approaches to studying the immune response in tuberculosis". *Current Opinion in Immunology* 25.5 (2013): 579-587.

30. Andersen J and Woodworth S. "Tuberculosis vaccine – rethinking the current paradigm". *Trends in Immunology* 35.8 (2014): 387-395.

31. Hawn Thomas R., *et al*. "Tuberculosis vaccines and prevention of infection". *Microbiology and Molecular Biology Reviews: MMBR* 78.4 (2014): 650-671.

32. Sable SB., *et al*. "Tuberculosis Vaccine Development: Progress in Clinical Evaluation". *Clinical Microbiology Reviews* 33.1 (2019): e00100-001119.

33. Wynwood Sarah Jane., *et al*. "Leptospirosis from water sources". *Pathogens and Global Health* 108.7 (2014): 334-338.

34. Ko AI., *et al*. "Leptospira: the dawn of the molecular genetics era for an emerging zoonotic pathogen". *Nature Reviews Microbiology* 7.10 (2009): 736-747.

35. Julio Croda Claudio., *et al*. "Targeted Mutagenesis in Pathogenic Leptospira Species: Disruption of the LigB Gene Does Not Affect Virulence in Animal Models of Leptospirosis". *Infection and Immunity* 76.12 (2008): 5826-5833.

36. Lucero NE., *et al*. "A new variant of *Brucella melitensis*". *Clinical Microbiology and Infection* 12.6 (2006): 593-596.

37. Verger JM., *et al*. "Classification of Brucella strains isolated from mammals using DNA-DNA hybridisation and ribotyping". *Research in Microbiology* 151 (2000): 797-799.

38. Cloeckaert A., *et al*. "Classification of Brucella spp. isolated from marine mammals by DNA polymorphism at the omp2 locus". *Microbes and Infection* 3 (2001): 729.

39. Godfroid J., *et al*. "From the discovery of the Malta fever's agent to the discovery of a marine mammal reservoir, brucellosis has continuously been a re-emerging zoonosis". *Veterinary Research* 36 (2005): 313-326.

40. Borska K and Simkovicova M. "Studies on the circulation of *Bordetella pertussis* and *Bordetella parapertussis* in populations of children". *Journal of Hygiene, Epidemiology, Microbiology, and Immunology* 16 (1972): 159-172.

41. Leber AL. "Pertussis: relevant species and diagnostic update". *Clinics in Laboratory Medicine* 34 (2014): 237-255.

42. Kilgore Paul E., *et al*. "Pertussis: Microbiology, Disease, Treatment, and Prevention". *Clinical Microbiology Reviews* 29.3 (2016): 449-86.

43. "Diseases of the Respiratory System". *Veterinary Medicine* (2017): 845.

44. Wenzel Esther Veronika., *et al*. "Human antibodies neutralizing diphtheria toxin in vitro and in vivo". *Scientific Reports* 1001 (2020): 571.

45. Shafiee Fatemeh., *et al*. "Targeted Diphtheria Toxin-Based Therapy: A Review Article". *Frontiers in Microbiology* 10 (2019): 2340.

46. Qiu S., *et al*. "Multidrug-resistant atypical variants of *Shigella flexneri* in China". *Emerging Infectious Diseases* 19.7 (2013): 1147-1150.

47. Sack DA., *et al*. "Antimicrobial resistance in shigellosis, cholera and campylobacteriosis". (2013).

48. Van Der Ploeg CA., *et al*. "Laboratory protocol: Serotyping of *Shigella* spp". WHO Global Foodborne Infections Network (2010).

49. Zhang W., *et al*. "Wide dissemination of multidrug resistant Shigella isolates in China". *Journal of Antimicrobial Chemotherapy* 66 (2011): 2527-2535.

50. Mandal J., *et al*. "The recent trends in shigellosis: A JIPMER perspective". *Journal of Clinical and Diagnostic Research* 6 (2012): 1474-1477.

51. Pazhani GP., *et al*. "Molecular characterization of multidrug-resistant Shigella species isolated from epidemic and endemic cases of shigellosis in India". *Journal of Medical Microbiology* l57 (2008): 856-863.

52. Srinivasa H., *et al*. "Magnitude of drug resistant shigellosis: A report from Bangalore". *Indian Journal of Medical Microbiology* 27 (2009): 358-360.

53. Taneja N. "Changing epidemiology of shigellosis and emergence of ciprofloxacin-resistant Shigellae in India". *Journal of Clinical Microbiology* 45 (2007): 678-679.

54. Divya MP., *et al*. "Mutations in gyrA and parC genes of *Shigella flexneri* 2a determining the fluoroquinolone resistance". *Indian Journal of Medical Research* 141.6 (2015): 836-838.

55. Lee Hu Suk., *et al*. "Seasonal and geographical distribution of bacillary dysentery (shigellosis) and associated climate risk factors in Kon Tam Province in Vietnam from 1999 to 2013". *Infectious Diseases of Poverty* 6.1 (2017): 113.

56. Silva Débora Santos da., *et al*. "Blood coagulation abnormalities in multibacillary leprosy patients". *PLoS Neglected Tropical Diseases* 12.3 (2018): e0006214.

57. Gaschignard Jean., *et al*. "Pauci- and Multibacillary Leprosy: Two Distinct, Genetically Neglected Diseases". *PLoS Neglected Tropical Diseases* 10.5 (2016): e0004345.

58. Da Silva Rocha Adalgiza., *et al*. "Drug and multidrug resistance among *Mycobacterium leprae* isolates from Brazilian relapsed leprosy patients". *Journal of Clinical Microbiology* 50.6 (2012): 1912-1917.

59. Noboru Nakata., *et al*. "Mutation Analysis of the Mycobacterium leprae folP1 Gene and Dapsone Resistance". *Antimicrobial Agents and Chemotherapy* 55.2 (2011): 762-766.

60. Se-Kon Kim., *et al*. "Detection of gene mutations related with drug resistance in Mycobacterium leprae from leprosy patients using Touch-Down (TD) PCR". *FEMS Immunology and Medical Microbiology* 36.1-2 (2003): 27-32.

61. Severin Paul N and Phillip A Jacobson. "Types of Disasters". *Nursing Management of Pediatric Disaster* (2020): 85-197.

62. Klietmann WF and KL Ruoff. "Bioterrorism: implications for the clinical microbiologist". *Clinical Microbiology Reviews* 14.2 (2001): 364-381.

63. Finke Ernst-Jürgen., *et al*. "Review: The risk of contracting anthrax from spore-contaminated soil - A military medical perspective". *European Journal of Microbiology and Immunology* 10.2 (2020): 29-63.

64. Makino S., *et al*. "Effect of the lower molecular capsule released from the cell surface of Bacillus anthracis on the pathogenesis of anthrax". *The Journal of Infectious Diseases* 186 (2002): 227-233.

65. Spencer RC. "Bacillus anthracis". *Journal of Clinical Pathology* 56.3 (2003): 182-187.

66. Inglesby TV., *et al*. "Plague as a biological weapon: medical and public health management". *The Journal of the American Medical Association* 283 (2000): 2281-2290.

67. Anderson RM and May RM. "Infectious diseases of humans: Dynamics and control". New York: Oxford University Press (1992).

68. Ansari Issmaeel., *et al*. "Deliberate release: Plague - A review". *Journal of Biosafety and Biosecurity* (2020): 10-22.

69. Sebbane Florent and Nadine Lemaître. "Antibiotic Therapy of Plague: A Review". *Biomolecules* 11.5 (2021): 724.

70. Quenee LE., *et al*. "Yersinia pestis caf1 variants and the limits of plague vaccine protection". *Infection and Immunity* 76.5 (2008): 2025-2036.

71. Cohen ML. "Epidemiology of drug resistance: Implications for a post-antimicrobial era". *Science* 257 (1992): 1050-1055.

72. Gudipati Smitha., *et al*. "Can the One Health Approach Save Us from the Emergence and Reemergence of Infectious Pathogens in the Era of Climate Change: Implications for Antimicrobial Resistance?". *Antibiotics* 9 (2020): 599.

73. Davies J and Webb V. "Antibiotic resistance in bacteria". In: Krause RM, editor. Emerging infections": Biomedical Research Reports. San Diego, CA: Academic Press (1998).

74. Morse S. "Factors in the emergence of infectious diseases". *Emerging Infectious Diseases* 1.1 (1995).

75. Fauci AS. "New and reemerging diseases: the importance of biomedical research". *Emerging Infectious Diseases* 4.3 (1998): 374-378.

76. Treffers Henry P. "Neutralizing antibody". Access Science. McGraw-Hill (2014).

77. Janeway's immunobiology (8th edition.). Garland Science (2012): 388.

78. Diphtheria antitoxin contains polyclonal antibodies against the diphtheria toxin 26.

Volume 4 Issue 8 August 2021