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Mini Review

Role of Diagnostic procedures in managing human Bacterial infections: A comprehensive overview

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Abstract

The study of human illnesses brought on by microbes falls under the wide category of infectious diseases. Among all other challenges, infectious diseases have a profound influence on human existence. From local epidemics to global pandemics, infectious diseases have had a huge impact on civilization growth, country destiny, and human history. Only in the late 1800s did scientists discover that infections are caused by microorganisms, leading to the development of the microbe-specific medical diagnostic technique. If identified and treated properly, many infections have mild consequences. Others, however, including pneumonia and meningitis, etc. can be fatal if neglected. With its capacity to pinpoint the precise source of infection and combat varied and widespread outbreaks, diagnostic procedures play a special role in the management of infectious diseases. Diagnosis-aid therapies work better and help the infected patient avoid long-term consequences. The most appropriate course of medication can also be decided through diagnostic testing. Patients who go undiagnosed may unintentionally spread the illness to others. A prompt diagnosis can thus contribute to the control or prevention of outbreaks. In summary, the novelty and contributions of the study lie in its recognition of the pivotal role played by diagnostic procedures in understanding, managing, and controlling infectious diseases. It also acknowledges the historical discovery of microorganisms as the root cause of infections and the development of specific diagnostic techniques, both of which have had a profound impact on the field of medicine and public health.

Introduction

In nature, bacteria are found everywhere, making them omnipresent. In addition to hot springs and glaciers, they are found in water, soil, air, and other places. They also live inside the human body and are usually harmless [1-3]. However, some of these microorganisms can cause illnesses as a result of their reproduction and survival processes. Therefore, diseases brought on by harmful bacteria are more frequently referred to as infectious diseases [4,5]. They can be contagious and spread by contact with an infected person, as well as through the air, water, soil, and contaminated food. The term "zoonotic diseases" refers to contagious illnesses that can occasionally be transmitted through contact with diseased animals, tick bites, or mosquito bites [6]. There are many distinct forms of pathogens, including bacteria, viruses, fungi, and parasites. Of the unicellular microorganisms that cause diseases in people, bacteria are the most common. Most harmful bacteria are able to survive at 37°Celsius, which is the ideal temperature for a human body. Bacteria also produce toxins, exhibit antibiotic resistance, and are capable of building biofilms that make it really difficult to treat them under clinical conditions [7]. Dating back to Antonie van Leeuwenhoek's observation of dental plaque in the early 20th century, many scientists have acknowledged that bacteria in nature exist in surface-adhered aggregations, or biofilms [8]. Bacteria as biofilm can survive in biotic surfaces viz., host tissues, abiotic surfaces viz., water pipes, medical devices, etc. William J.Costerton and Niels Hoiby were among the first ones to recognize the direct correlation of biofilms with recalcitrant infections [9]. Since then, consistent studies have reported the association of biofilm in tissue and medical device-related acute and chronic human infections [10,11]. Numerous bacteria have been linked to chronic infections, including *Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Escherichia coli.* A well-known example of chronic biofilm-

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associated tissue infections is *Pseudomonas aeruginosa* infections of the lungs in cystic fibrosis patients [9]. Another typical instance of biofilm infection is the colonization of the bladder's uroepithelial cells by uropathogenic *E. coli*, which leads to recurrent urinary tract infections. It becomes very challenging to identify and treat these bacterial aggregates since they are not visible in the patient's urine. Additionally, common in the oral cavity, bacterial biofilms can cause periodontitis and dental caries [10]. Additionally, the widespread recognition of bacterial colonization of several medical equipment. A great surface for bacterial adherence and biofilm growth is offered by medical equipment such as catheters, pacemakers, prosthetic heart valves, contact lenses, etc. The first device-related biofilm infection was documented in 1982 in a patient who experienced periods of recalcitrant bloodstream infection connected to a pacemaker that was colonized by *S. aureus* [11]. Due to the high level of antimicrobial resistance in biofilm, it has been shown that there has been a considerable rise in all forms of infections linked to indwelling medical devices since that time. According to the National Institute of Health (NIH), ~ 80% of all microbial infections involve biofilm formation and are the major contributor to nosocomial infections [12]. Biofilm formation is a complicated phenomenon that involves a few basic steps such as adhesion, proliferation and maturation, and dispersion. Bacteria establish biofilms when exposed to certain environmental factors such as nutritional availability, where they switch from a free-floating planktonic to a surface-attached solitary state. Bacteria inheriting biofilm possess extensive antibiotic resistance capability. The increased antibiotic resistance in biofilms is caused by a variety of reasons, such as i) The antibiotics are degraded by the production of antimicrobial modifying enzymes, and the thick biofilm matrix consisting of polysaccharide, eDNA, etc. restricts their penetration to the core areas of biofilm; ii) The presence of hypoxic conditions in the biofilm's deeper layers lowers the outer membrane potentials, which increases the production of membrane efflux pumps and prevents the accumulation of antimicrobials inside cells [13,14] iii) the presence of a slow-growing, metabolically inactive phenotypic group, such as persisters and small colony variants, have higher antibiotic resistance, iv) The biofilm community's members have a wide range of potential for sharing drug-resistant genes [13,14].

Infectious diseases have distinctive characteristics such as their unpredictable nature and global explosive potential that set them apart from other non-infectious and lifestyle-associated human diseases. They are frequently so mild that they go unnoticed, yet they can be deadly on rare occasions. Infectious diseases are classified into three types: established, re-emerging, and newly emerging infectious diseases. Infections that have been widespread and stable for a long enough length of time that the incidence of mortality and morbidity may be anticipated are classified as established illnesses. Tuberculosis is a prominent example of this sort of disease. Re-emerging illnesses are those formerly controlled diseases that have now resurfaced in a new form, such as methicillin-resistant *S. aureus*, or in a new location, such as polio in portions of Africa. Furthermore, infections that are known to infect humans for the first time, such as the SARS-COVID virus and Nipah virus, are categorized as newly emerging infectious diseases [15,16]. Globally, as many as 25.5% of deaths per year are estimated to be caused by infectious diseases. The realization of the crucial relevance of clean water, basic sanitation, and hygiene for the prevention of a significant number of infectious diseases is just one of the far-reaching implications of scientific advancements in the field of infectious diseases [17]. Additionally, disease-specific preventive and treatment strategies have frequently resulted in the overall management of infections that previously triggered significant death or disability. Even while certain infectious diseases are curable, the best way to manage them is to adopt preventative measures, like becoming immunized, maintaining good hygiene, not sharing straws, needles, or toothbrushes, having safe sex, and avoiding contaminated food, among other things [17]. However, because microbes are capable of evolving, they will continue to fit into new biological niches and infect people in novel or emerging ways. In order to combat these illnesses in the future, we must continually update our diagnostic tools. The goal of this chapter is to discuss the most typical human infections and the diagnostic techniques that are essential to their treatment and recovery.

Common human infections

Infection of the brain

Infections of the brain can be caused by bacteria, fungi, viruses, and occasionally protozoa or parasites. Meningitis is the medical term for the swelling and infection of the meninges, which are the tissue layers that cover the brain and spinal cord. Occasionally, the meningitis-causing agents can spread from the site of infection to the brain, causing inflammation known as encephalitis. The medical condition that arises when the meninges and the brain are both infected is known as meningoencephalitis [18,19]. Table 1 provides a comprehensive summary of the common brain infections in humans.

Table 1: Common brain infections in human.

Infection Name	Causative Bacteria	Symptoms and Complications
Meningitis	Various bacteria, including Streptococcus pneumoniae, *Neisseria meningitidis*, and *Haemophilus influenzae*	Fever, headache, stiff neck, altered mental status, photophobia; severe cases can lead to brain damage, septicemia, and death.
Encephalitis	Various bacteria but usually viral (e.g., herpes simplex virus, West Nile virus)	Fever, headache, altered mental status, seizures, neurological deficits; complications can include brain damage and coma.
Brain Abscess	Various bacteria, including *Staphylococcus aureus*, *Streptococcus species*, and anaerobic bacteria	Headache, fever, focal neurological deficits, seizures, increased intracranial pressure; untreated abscesses can lead to brain damage or death.
Subdural Empyema	Often due to *Staphylococcus aureus or Streptococcus species*	Fever, severe headache, focal neurological deficits, and altered consciousness; can lead to brain compression if not treated promptly.
Epidural Abscess	Usually *Staphylococcus aureus or Streptococcus species*	Back pain, fever, neurological deficits, and spinal cord compression; can lead to paralysis if not treated promptly.

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Meningitis: The three membranes that border the vertebral canal and the skull and enclose the brain and spinal cord are collectively referred to as the meninges. They are dura mater, arachnoid mater, and pia mater. Meningitis is the medical term for meningeal inflammation [20]. Although the symptoms of inflamed meninges have been recorded throughout history in several research works, it wasn't until surgeon John Abercrombie described the illness in 1828 that it was given the name "meningitis". Despite improvements in diagnosis, therapy, and vaccination, there were over 8.7 million meningitis cases reported globally in 2015, leading to 379,000 fatalities [21]. Bacteria, viruses, fungi, and parasites can all cause meningitis. *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae*, and *Listeria monocytogenes* are the four most common bacterial causes of meningitis. Viral meningitis is frequently linked to viruses including coxsackievirus, non-polio enterovirus, echovirus, mumps, herpes virus, arbovirus, etc. *Cryptococcus neoformans*, *Aspergillus*, *Coccidioides immitis*, *Candida*, etc. are examples of common fungus that can cause meningitis. Microbes can enter the cerebrospinal fluid (CSF) directly via infected implanted devices or from infections of nearby tissues like the sinus. They can also enter the CSF by hematogenous seeding, which allows pathogens to breach the blood-brain barrier. Neck stiffness, fever, increased intracranial pressure, and photophobia are all common meningitis symptoms. Additionally, it could cause generalized symptoms including nausea, headaches, dizziness, and disorientation [21,22].

Encephalitis: The name "encephalitis" comes from the Greek word "enkephalos," which means brain, and the suffix "itis," which means inflammation. Therefore, in encephalitis, either microbial infections or autoimmune diseases cause inflammation of the brain's parenchyma. Encephalitis affects 7.9 out of every 1 lakh people worldwide each year, on average. Most often, viral agents such as Rabies virus, Herpes simplex virus, Enterovirus, Arbovirus, and Adenovirus are linked to infectious encephalitis. Less frequently, encephalitis is linked with fungi, bacteria, and parasites. Invasion of the brain parenchyma by pathogens leads the immune system to release pro-inflammatory cytokines, which in turn induces inflammation of the brain. The etiological agents' systemic dissemination can potentially lead to acute encephalitis. Adults frequently have symptoms including disorientation, fever, headaches, seizures, mobility difficulties, stiff necks, irritability, and neurological instability [23-25].

Infections of the oral cavity: There are more than 700 different bacterial species in the human oral cavity. Some of these microorganisms produce dental biofilm, sometimes referred to as dental plaque. Through receptor-mediated non-covalent interactions, salivary glycoproteins create a conditioned layer on the surface of the teeth that starts the adhesion of pioneer bacteria. Other bacteria then join the first colonizers to form a structured biofilm. *Streptococci* are the primary initial colonizers. *Fusobacterium spp.*, *Corynebacterium spp.*, *Actinomyces spp.*, *Porphyromonas spp.*, *Haemophilus spp.*, *Veillonella spp.*, etc. are among the other bacteria that make up the biofilm. The majority of dental biofilms are found in the crevices of the gingival lining and occlusal surface, where the bacteria are safe and undisturbed. They cause periodontal pockets and tooth roots to get infected if left untreated [26]. A comprehensive summary is given in Table 2.

Dental caries: Dental caries are caused by bacteria that ferment carbohydrates to produce organic acids like lactic acid, which demineralizes the dentine and enamel of the teeth. The crucial pH value of 5.5 must be attained for the demineralization of teeth. Excess carbohydrates also aid in the production of extracellular matrix and the reinforcement of the biofilm structure on the surface of the teeth [27].

Pulpitis: The inflammation of the pulp tissue is referred to as pulpitis. The vital pulp is frequently invaded by biofilm bacteria from the saliva and develops a caries lesion that causes pulpitis. In long-term illnesses, the bacteria may enter the inner root canals and expand to the apical tissues, where they can cause necrotic lesions [28].

Gingivitis: The microbiota of a healthy gingival sulcus is mostly dominated by gram-positive *Streptococci.* When anaerobic Gram-positive and Gram-negative bacteria are added to the microflora, the makeup of the microflora changes, causing gingivitis, or inflammation of the gingival lining. Swollen gingival margins, pocket formation, and increased release of protein-rich gingival exudates are all consequences of biofilm growth. The consequences of gingivitis can be reversed by restoring the microbiota after removing the supragingival biofilm and maintaining good dental care [29].

Chronic Periodontitis: Chronic periodontitis causes significant inflammation and destruction to the periodontium, the tissue that supports the teeth. This occurs when subgingival biofilm, which is made of bacteria from the gingival biofilm, forms in the periodontal pockets. The subgingival biofilms are dominated by many Gram-negative bacteria, including *Fusobacterium nucleatum*, *Prevotella spp.* and *Porphyromonas gingivalis*. Deeper tissue biofilm growth causes bone loss and periodontal fiber damage, which ultimately results in tooth loss [30].

Table 2: Common bacterial infections of the human oral cavity.

Bacterial Infection	Causative Bacteria	Clinical Presentation
Dental Caries	*Streptococcus mutans, others*	Tooth decay, cavities, pain, and sensitivity
Gingivitis	Various bacteria	Red, swollen gums, bleeding during brushing/flossing
Periodontitis	*Porphyromonas gingivalis, etc.*	Gum inflammation, pocket formation, tooth loss
Oral Thrush (Candidiasis)	*Candida albicans* (fungi)	White, creamy patches on the tongue and oral mucosa
Acute Necrotizing Ulcerative Gingivitis (ANUG)	*Fusobacterium, Prevotella*	Severe gum pain, ulceration, bad breath, fever
Vincent's Angina (Trench Mouth)	*Fusobacterium, Prevotella*	Painful ulcers, swollen gums, foul odor
Pericoronitis	*Mixed oral bacteria*	Infection around partially erupted wisdom teeth
Ludwig's Angina	*Mixed oral bacteria*	Swelling of the floor of the mouth, difficulty swallowing
Actinomycosis	*Actinomyces israelii*	Chronic infection, abscesses, jaw pain, sinus tracts

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Infection of the respiratory tract

Bacterial infections of the human respiratory tract are a common medical issue that can affect various parts of the respiratory system, including the nose, throat, bronchial tubes, and lungs. These infections are typically caused by pathogenic bacteria and can lead to a range of symptoms and health problems. Table 3 summarizes the common bacterial infections of the human respiratory tract.

Chronic rhinosinusitis: Chronic rhinosinusitis (CRS) is an inflammation of the paranasal sinuses and nose that lasts for 12 weeks or more and is accompanied by symptoms such as nasal obstruction, nasal discharge, hyposmia, face discomfort, headaches, and more. While viruses mostly cause acute rhinosinusitis, chronic problems are linked to the formation of complex polymicrobial biofilms including both bacteria and fungus. Particularly, *S. aureus* contributes 50% of the biofilm in individuals with CRS, followed by *H. influenza* (28%) and *P. aeruginosa* (22%) [31].

Pharyngitis: The inflammation of the pharynx, which can also affect the lingual tonsil and the adenoids, is known as pharyngitis. Hypertrophy of the tonsillar or adenoid tissue can result from recurrent pharyngitis. According to reports, bacterial biofilm contributes to 70% of chronic pharyngitis cases. The wet and warm folds of the tonsils act as a reservoir for the bacteria to survive and cause recurrent infections. Group A Streptococcus (GAS) are the predominant bacteria causing 20% - 30% of pharyngitis followed by *S. aureus, and Haemophilus spp* in both children and adults [32,33].

Ventricular-Associated Pneumonia (VAP): VAP is one of the most frequent hospital-acquired diseases in which pathogenic bacteria colonize the aerodigestive tract and contaminated secretion is aspirated into the lower airway under microbial invasion, resulting in an overwhelming host inflammatory response. Within hours after its insertion, an endotracheal tube (ET) used for mechanical breathing becomes colonized with organisms on its surface, creating biofilms and contributing to VAP. *Staphylococcus* seemed to be the prevalent organism, with the most common being *Staphylococcus epidermidis, Staphylococcus aureus,* and *Staphylococcus saprophyticus. Candida albicans, Pseudomonas aeruginosa*, and *Micrococcus luteus* were also discovered. *E. coli, E. aerogenes,* and *Klebsiella pneumoniae* have been identified within the *Enterobacteriaceae*. [34].

Table 3: Summary of common bacterial infections of the human respiratory tract.

Bacterial Infection	Causative Bacteria	Clinical Features
Streptococcal Pharyngitis (Strep Throat)	*Streptococcus pyogenes*	Sore throat, fever, swollen tonsils
Pneumonia	Various bacteria (e.g., *Streptococcus pneumoniae, Haemophilus influenzae)*	Cough, fever, chest pain, difficulty breathing
Tuberculosis (TB)	*Mycobacterium tuberculosis*	Persistent cough, weight loss, night sweats, fatigue
Bronchitis	Usually viral (can be bacterial)	Cough with mucus, chest discomfort
Sinusitis	Usually viral (can be bacterial)	Facial pain, congestion, thick nasal discharge
Whooping Cough (Pertussis)	*Bordetella pertussis*	Severe coughing fits, "whoop" sound, vomiting
Legionnaires' Disease	*Legionella pneumophila*	High fever, cough, muscle aches, pneumonia
Diphtheria	*Corynebacterium diphtheriae*	Sore throat, thick gray membrane in the throat
Mycoplasma Pneumonia	*Mycoplasma pneumoniae*	Mild pneumonia symptoms, persistent cough

Cystic Fibrosis: Cystic fibrosis (CF) is a genetic disorder characterized by poor mucociliary clearance and reduced periciliary fluid volume caused by a mutation in the gene encoding cystic fibrosis transmembrane conductance regulator (CFTR). CFTR is a cAMP-regulated chloride channel found on the apical surface of epithelial cells. CFTR dysfunction impairs chloride transport in epithelial cells and inhibits sodium ion channels (ENaC) and basolateral potassium channels. Because CFTR is expressed in multiple organ systems, including the respiratory, reproductive, and gastrointestinal tracts, its failure leads to critical clinical disorders involving these organs. However, most doctors retain the name CF for individuals who are developing an incurable lung condition. 90% of CF fatalities are caused by pulmonary ailments. In CF patients with compromised defense mechanisms, inflammatory defensive responses dominated by polymorphonuclear lymphocytes (PMN) are activated. Inhaled microbe phagocytosis is triggered by PMN releasing highly reactive oxygen species (ROS) that damage surrounding tissue. Bacteria and other particles that become entangled in the viscous surface fluids of the airway increase the contact duration between bacteria and airway cells, producing inflammation [35,36].

Tuberculosis (TB): In 1882 Robert Koch originally discovered *Mycobacterium tuberculosis* as a possible pathogen that causes tuberculosis in humans. Tuberculosis is an airborne infection that predominantly affects the pulmonary system but can infect any part of the body. Most of the time, *M. tuberculosis* produces latent infections and hence remains asymptomatic. Active tuberculosis is infectious and causes symptoms such as fever, lack of appetite, weariness, hemoptysis (bloody cough), and weight loss. In this form, the pathogen is easily identified using culture and molecular methods. TB is still one of the leading causes of illness and mortality in underdeveloped nations [37].

Infections of the digestive tract

Bacterial infections of the human digestive tract refer to a range of illnesses caused by pathogenic bacteria that invade and disrupt the normal functioning of the gastrointestinal system. These infections can result from the ingestion of contaminated food or water, poor hygiene practices, or the overgrowth of harmful bacteria normally present in the gut. Here is a summary of bacterial infections of the human digestive tract:

Bowel disease and colorectal cancer: The mucosal layer serves as a barrier to shield the luminal microorganisms from the colon epithelium in a healthy gut. In pathological

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circumstances, the integrity of the barrier is impaired, which allows bacteria to invade the deeper layers of the colon epithelia and cause inflammatory bowel disorders, or IBD. IBD includes symptoms including diarrhea, exhaustion, and weight loss are most frequently associated with Crohn's disease and ulcerative colitis. According to the study report, IBD may be caused by *Bacteroides fragilis* and *Enterobacteriaceae* adhering to the epithelium in biofilms. The ability to eradicate the infection is diminished as a result of the disruption of microflora balance. *Fusobacterium spp., Shigella spp.,* and *E. coli* predominate in ulcerative colitis and keep the infection going, whereas *Enterobacteriaceae, Pseudomonas spp.,* and *Bacteroidetes* predominate in Crohn's disease. Additionally, 10-30% of patients with IBD are more likely to develop subsequent colorectal cancer (CRC) [38]. Table 4 summarizes the common infections of the human digestive tract.

Skin and wound infections

In humans, *Staphylococcus spp., Propionibacterium spp.,* and *Corynebacterium spp*. predominate the skin flora. Cuts, burns, surgeries, etc. damage the dermal tissues, rupturing the innate barrier and opening the door for microbial invasion, leading to wounds and various skin infections such as otitis externa, necrotic fasciitis, impetigo, necrotic fasciitis, and acne vulgaris. From chronic wounds of dermal tissues, bacteria that produce biofilms, including *S. aureus, P. aeruginosa, E. coli, S. epidermidis, E. faecalis,* and *K. pneumoniae,* are found. *S. aureus* alone is responsible for 88% - 98% of the wound infections among them, followed by *P. aeruginosa*. *S. aureus and P. aeruginosa* co-infections in chronic wounds are extensively documented. Studies show that co-infection with *P. aeruginosa* and *S. aureus* increases antibiotic resistance and is advantageous to both microbes. *P. aeruginosa* is found in the deeper layers of the wound, whereas *S. aureus* lives on the wound's surface [38].

Table 4: Common bacterial infections of the human digestive tract.

Bacterial Infection	Causative Agent	Clinical Features
Salmonellosis	*Salmonella spp.*	- Causes diarrhea, abdominal cramps, fever -Usually transmitted through contaminated food
Campylobacteriosis	*Campylobacter jejuni*	- Leading cause of bacterial gastroenteritis - Symptoms include diarrhea, fever, abdominal pain
E. coli Infection	*Escherichia coli*	- Some strains produce Shiga toxins (e.g., EHEC) - Causes diarrhea, bloody stools, kidney damage
Cholera	*Vibrio cholera*	- Severe watery diarrhea, can be life-threatening - Transmitted through contaminated water
Shigellosis	*Shigella spp.*	- Causes bloody diarrhea, abdominal cramps - Highly contagious, person-to-person transmission
Clostridium difficile Infection	*Clostridium difficile*	- Common in healthcare settings, antibiotics are a risk factor - Causes diarrhea, colitis, can be severe
Helicobacter pylori Infection	*Helicobacter pylori*	- Associated with peptic ulcers and gastritis - Chronic infection, may not always cause symptoms
Typhoid Fever	*Salmonella typhi*	- Causes high fever, abdominal pain, and constipation

Invasive infections

Infective Endocarditis (IE): Infective endocarditis (IE) denotes bacterial colonization and infection of the endocardium of the heart, typically affecting heart valves and other implanted devices such as pacemakers, prosthetic valves, and vascular grafts [39]. Intractable congestive heart failure, myocardial abscesses, and significant valvular inefficiency are among the consequences of IE. *Staphylococcus, Streptococci,* and *Enterococci spp.* are accountable for 80% of IE cases [40]. *Staphylococcus spp.* causes severe invasive pathogenesis in prosthetic valves and leads to an overall higher mortality in IE patients [41]. Both bacterial and host components make up the biofilm on the endothelium surface or on implanted devices. As the biofilm develops, damage to the endothelium surface attracts platelets and fibrin, which causes a clot to form at the site of injury. The bacteria in the biofilm use specialized adhesions to adhere to the thrombus; for example, the glucans in *S. mutans* help the bacteria adhere to damaged valves and create microcolonies, which eventually grow into mature biofilm. Blood leaks from closed valves when biofilm is present, while blood flow is reduced in opened valves when biofilm is present. Additionally, mature biofilm fragments that have been discharged into the circulation and are disseminated might generate emboli in other organs including the brain. [42].

Osteomyelitis: Osteomyelitis is a medical term for bone infection. Its origin may be hematogenous or contiguous. It is more prevalent in babies and children than in adults and is caused by the hematogenous spread of germs in 20% of cases [43]. *S. aureus, H. influenzae, S. agalactiae, E. coli,* and *S. pyogenes* are the most frequently isolated bacteria in newborns and young children. *S. aureus,* however, predominates in adults [44].

Table 5 summarises the common invasive infections in humans.

Urogenital infections

Vaginosis: The vaginal microbiota, which is made up of many bacteria, is a dynamic, balanced ecology found in the human vagina. *Lactobacillus spp.* make up the majority of the microbiota, with *Lactobacillus crispatus, Lactobacillus iners, and Lactobacillus jensenii* being the most common. They serve as an essential first line of defense against infections [45]. Bacterial Vaginosis (BV) can be brought on by the colonization of pathogenic bacteria in the vaginal microbiota, which can be brought on by sexual activity, douching, or hormonal imbalance. 60% of vulvovaginal infections caused by BV are responsible for serious health issues such as vulvovaginal bleeding, preterm delivery, endometritis, pelvic illness, and a number of STDs [46]. Clinical signs of BV include an elevated vaginal pH, homogenous, foul-smelling vaginal discharge with clue cells (exfoliated epithelial cells with bacteria attached to their surface), and increased production of amines such as trimethylamine, cadaverine, and putrescines that give the vaginal discharge a fishy smell when 10% KOH is added [47].

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Table 5: Common invasive bacterial infections.

	Bacterial Infection in the Heart	Bacterial Infection in Blood	Bacterial Infection in Bones
Causative Bacteria	*- Streptococcus species (e.g., Streptococcus pyogenes) - Staphylococcus aureus - Enterococcus species - Mycobacterium tuberculosis*	*- Escherichia coli - Streptococcus species - Staphylococcus aureus - Neisseria meningitidis - Salmonella species*	*- Staphylococcus aureus - Streptococcus species - Escherichia coli - Pseudomonas aeruginosa - Mycobacterium tuberculosis*
Common Infections	- Infective endocarditis - Myocarditis	- Bacteremia - Septicemia	- Osteomyelitis - Septic arthritis
Transmission	- Usually enters through the bloodstream from another infected site - Dental procedures - Intravenous drug use - Skin infections	- Contaminated medical equipment - Catheter-associated infections - Skin infections - Endocarditis	- Contiguous spread from nearby soft tissue infections - Hematogenous spread from other infected sites
Clinical Symptoms	- Fever, Heart murmur, Fatigue, Chest pain, Shortness of breath, Joint pain	- Fever, Chills, Rapid breathing, Hypotension, Organ dysfunction	- Localized bone pain, Swelling, Fever, Limited joint mobility
Complications	- Heart valve damage, Heart failure, Embolism, Abscess formation	- Sepsis, Organ failure, Endocarditis, Stroke	- Bone deformities, Joint destruction, Spread to nearby tissues, Chronic infection

The main cause of recurring BV infections is their propensity to form biofilm in addition to the dramatic change in microbiota. A major component of the polymicrobial biofilm that causes 60% - 95% of BV infections is *Gardnerella vaginalis.* It attaches to the epithelial cells and is a facultative anaerobic, Gram-negative to Gram-variable, pleomorphic rod that can withstand a high oxidation-reduction potential in the vaginal environment. Another facultative anaerobic that co-exists with *G. vaginalis* is *Atobium vaginae* [48]. *Atobium vaginae* is linked to 86% of *G. vaginalis* biofilms, which make up about 40% of the total mass of biofilms. *Prevotella bivia* and *Mobiluncus mulieris* have also been found in BV biofilms together with *Atobium vaginae* [49].

Urinary tract infections: One of the most typical community- and hospital-acquired infections is a urinary tract infection (UTI). The urinary bladder's urothelial cells are coated in glycosaminoglycan mucin, which inhibits bacterial adherence. If germs get beyond this first line of defense, a healthy person's immune system gets rid of them. If the immune system fails to clear the uropathogens, UTI may develop. By creating adhesions, such as FimH, toxins, and siderophores [50], uropathogens penetrate and colonize the urinary tract. Average UTI symptoms, which can be either serious or mild, affect 35% of healthy women. *Escherichia coli* (UPEC) is frequently responsible for uncomplicated infections. On the other hand, complicated UTIs are associated with functional, metabolic, or anatomical abnormalities that impair innate immunity. A significant nosocomial infection that accounts for 80% of instances of urinary tract infections (UTI) is catheter-associated urinary tract infection (CAUTI) [51]. The surface properties of the catheter are changed by the presence of uropathogens and a conditioning film made up of magnesium and calcium ions, which in turn promotes the growth of biofilm. *Escherichia coli, Citrobacter freundii, Enterococcus faecium, Klebsiella pneumonia,* and *Pseudomonas aeruginosa* are the pathogens most often identified from CAUTI; they also have a significant potential to build biofilm in catheters. Along with the previously listed species, *Staphylococcus aureus, Staphylococcus epidermidis, Proteus vulgaris, Morganella morganii, Proteus mirabilis, Enterobacter aerogenes,* and *Candida albicans* have been identified from catheters [52,53]. Table 6 summarises the clinical features of common urogenital infections in humans.

Standard diagnosis techniques used to identify infectious diseases

Infections are suspected by doctors based on a patient's symptoms, and the findings of a physical examination. Doctors first determine if the patient is infected or suffering from another condition. Once identified with infection, the next step is to identify the precise bacterium that is causing the clinical conditions [54]. An infection may be brought on by a variety of different microbes. It is necessary to use a specific treatment strategy for each bacterium, which may involve growing the microbe, microscopy, and the identification of host immune factors in response to the infection. Experienced microbiologists, pathologists, and immunologists are needed for all of these findings.

Collection of samples

The patient's bodily parts where the suspected infection could be present might be used to collect samples. The following sample types are regularly taken from patients:

- Blood
- Pus
- Sputum Swabs for the nose and throat
- Bronchial fluid
- Urine
- Stool
- Fluids from the genitalia, such as mucus or pus
- Tissues
- Cerebrospinal fluid

Stool, mucus, and sputum are a few examples of samples that include bacteria that often do not cause disease. Differentiating between bacteria that are pathogenic and commensal bacteria is therefore necessary. Blood, spinal fluid, cerebrospinal fluid, and specimens of urine are typically devoid of germs; hence, the presence of any bacterium in these samples indicates infection [54,55].

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Table 6: Infections of the human urogenital tract.

Infections	Causative Agent(s)	Clinical Characteristics
Urinary Tract Infection (UTI)	*Escherichia coli (E. coli), Klebsiella, Proteus, Staphylococcus saprophyticus, Enterococcus*	Common symptoms include frequent urination, painful urination, cloudy or bloody urine, and lower abdominal pain. UTIs can affect the bladder (cystitis) or kidneys (pyelonephritis).
Gonorrhea	*Neisseria gonorrhoeae*	Symptoms may include painful urination, abnormal discharge (yellow or green), pelvic inflammatory disease (PID) in women, and can lead to infertility if left untreated.
Chlamydia	*Chlamydia trachomatis*	Often asymptomatic, but can cause urethritis, cervicitis, or PID. If left untreated, it can lead to infertility and ectopic pregnancy in women.
Syphilis	*Treponema pallidum*	Progresses through primary (chancre sores), secondary (rash, fever), and tertiary (organ damage) stages if untreated.
Bacterial Vaginosis (BV)	*Gardnerella vaginalis*	Common symptoms include abnormal vaginal discharge (gray, white, fishy odor), itching, and discomfort.
Pelvic Inflammatory Disease (PID)	Various bacteria (e.g., *Chlamydia, Gonorrhea*)	Infection of the female reproductive organs leads to pelvic pain, fever, and long-term complications like infertility and ectopic pregnancy.
Prostatitis	Various bacteria (e.g., *Escherichia coli*)	Inflammation of the prostate gland leads to pain and urinary symptoms.
Urethritis	Various bacteria (e.g., *Neisseria gonorrhoeae, Chlamydia trachomatis*)	Inflammation of the urethra causes painful urination and discharge.
Vaginal Infections	Various bacteria (e.g., *Gardnerella vaginalis*)	Besides BV, other vaginal infections can be caused by bacterial imbalances, leading to symptoms like itching, burning, and abnormal discharge.

Laboratory tests

Isolation of the pathogen in culture: The majority of the microorganisms that are cultivated in microbiology labs for isolation are bacteria. A comprehensive understanding of the commensal microbiome at the sample location and the possible pathogenic strains that might cause infectious disease in that region is necessary for an accurate interpretation of the culture findings. For example, whereas the presence of *E. coli* may indicate commensal flora or a pathogenic contaminant, the presence of *M. tuberculosis* certainly indicates an infection. A variety of methods are used to recover certain pathogens, including the use of customized culture media with the right nutrients, inhibitors, salts, differential colors, etc., as well as ideal growth conditions with the right temperature, air pressure, and surrounding pH. The choice of selective, non-selective, or differential culture medium depends on the clinical history and specimen source. Whether it is a routine or anaerobic culture, or the pathogen is slow-growing like *Mycobacterium spp.*, the culture must be retained for a longer length of time to isolate the pathogen [56,57].

Detection of the immune response: Our immune system has developed to prevent and regulate illnesses within our bodies. In the laboratory, this method is also used to diagnose an underlying infection. The cellular immune response produces antigen-specific T cells, and adaptive immunity responds to antigens by producing particular antibodies. Various serology labs use immunofluorescence, ELISA, Western blot, agglutination assays, and other techniques to detect and assess a patient's antibodies produced against a certain kind of antigen, which aids in the identification of the illness [58].

Microscopic identification: Microscopy is an integral part of the diagnosis protocol. Most of the samples including sputum, blood, wound exudate, cerebrospinal fluid, tissues, etc. are stained with specific dyes that stain the microbes and the diseased cells, causing them to stand out from the background.

Fungi and protozoa can be identified based on the differences in their cell wall construction, pigment secretion, reproduction, and alterations to their cellular structures, such as the existence of kinetoplasts in flagellate protozoa, and size [59,60].

Certain viruses can produce pathological alterations in the affected cells, such as the development of multinucleated massive cells and the deposition of proteins that are colored with eosin or hematoxylin inside the cell. Based on the presence of cytopathic symptoms and acidic or basic cellular components, a specific diagnosis can be made. It is also feasible to recognize a number of viruses, such as members of the Herpes virus family, that cause the same pathological changes [61].

Gram staining may be used to distinguish between different types of bacteria based on their morphology and cell wall makeup. Gram-positive bacteria leave a purple stain, whereas Gram-negative bacteria leave a pink stain. For the purpose of identifying *Mycobacteria*-associated TB, acid-fast staining is very helpful. *Leptospira* and *Treponema* are a couple of bacteria that are difficult to identify with routine stains and may be detected using silver impregnation staining techniques [62].

Nucleic acid detection: There are distinct sections in each microorganism's genome that are unique to that microbe. Deoxyribonucleic acid (DNA) makes up the majority of the genetic material in diverse microbes. However, certain microorganisms, particularly viruses, have evolved to have ribonucleic acid (RNA) as their genetic material. Microbes that are difficult to detect using standard procedures such as culturing are exposed to molecular approaches that target distinct areas of their genetic material that are particular to that microbe. For this kind of test, polymerase chain reaction (PCR) is a potent method. Short DNA sequences are amplified into millions of replicas in a brief period of time. In the case of RNA viruses, the conversion of RNA to DNA is a prerequisite that involves reverse transcriptase enzymes. A single particular

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bacterium is the focus of each genetic test. To put it another way, a genetic test for the HIV virus only finds that virus and nothing else [63,64].

Insitu hybridization: In order to identify infections, this method also uses nucleic acid. A targeted nucleic acid sequence that creates a visual byproduct is found using a tagged homologous RNA or DNA sequence that is present in the intracytoplasmic or intranuclear area of infected cells or tissues. This technique makes it possible to identify microorganisms that are closely related [65-67]. Table 7 comprehensively summarises the diagnostic techniques used to identify different bacterial infections in the human body.

Lastly, the fields of diagnostics and fundamental research work together to manage the problems posed by infectious illnesses. The identification of new infections has been aided by conventional technology and a keen understanding of microbiology, pathology, and immunology. Today, it is even feasible to determine the genus of the pathogen and the precise virulence factors that cause antibiotic resistance with the use of diagnostic technologies. Additionally, this aids in choosing the proper antimicrobials to treat the condition that was previously unknown.

Conclusion

Infectious diseases have been a part of human history since the beginning of civilization. Their impact goes beyond just physical health; it also affects the economy, social structures, and political systems. Although infection occurrence is common in humans, they can be difficult to diagnose and treat. Being able to recognize the symptoms of infectious diseases and seeking proper diagnosis from a healthcare provider is crucial in order to prevent further health complications. By understanding the impact of pandemics on our past, we can better prepare for the future and mitigate the effects of future outbreaks. The lessons learned from historical pandemics, such as the importance of public health measures, the development of new medical technologies, and the need for international cooperation, are still relevant today. Governments around the world should invest in public health infrastructure and implement measures such as quarantine, isolation, social distancing, and other necessary measures required to control the spread of infectious diseases. The development of new medical technologies, such as vaccines and therapeutics, is also crucial to controlling the spread of infectious diseases in the future. By learning from the past, we can better prepare for the future and ensure that the impact of future pandemics is minimized.

Table 7: Differential diagnostic techniques for identification of bacterial infections.

Technique	Sample Type	Infection Background
Diagnosis of the brain infections		
1. Cerebrospinal Fluid (CSF) Analysis	CSF obtained via lumbar puncture	Common for detecting meningitis, encephalitis, or brain abscess. Elevated white blood cells, protein levels, and bacteria can be indicative of infection.
2. Blood Culture	Blood sample	Useful for detecting systemic bacterial infections that may have spread to the brain, such as septicemia or endocarditis.
3. Imaging (CT/MRI)	Radiographic images of the brain	Reveals structural abnormalities, abscesses, and inflammation in the brain, aiding in the diagnosis of brain infections.
4. Gram Stain and Culture	Brain tissue or biopsy samples	Directly examines brain tissue for bacterial presence. Used in cases of suspected brain abscess or localized infection.
5. Polymerase Chain Reaction (PCR)	CSF or tissue samples	Detects bacterial DNA or RNA in the sample, allowing for specific identification of the infecting bacteria.
6. Antibody Tests	Blood serum	Measures antibodies produced by the immune system in response to specific bacterial infections, such as neurosyphilis.
7. Next-Generation Sequencing (NGS)	CSF or tissue samples	Utilizes advanced genetic techniques to identify the DNA or RNA of various pathogens, including bacteria, in the brain.
8. Radiolabeled Scans	Injected radiotracers	Used to locate sites of infection in the brain, particularly helpful for diagnosing brain abscesses.
9. Biopsy	Brain tissue biopsy	Directly samples brain tissue to identify the type of bacteria causing the infection. Often done in severe or localized cases.
Diagnosis of oral cavity infections		
1. Clinical Examination	Clinical observation	Visual inspection of oral tissues for signs of infection
2. Microbial Culture	Saliva, dental plaque, pus	Identifies specific bacterial species through culturing
3. Gram Staining	Swabs from infected sites	Differentiates bacteria based on cell wall properties
4. Polymerase Chain Reaction (PCR)	Saliva, swabs, tissue biopsies	Amplifies bacterial DNA for identification
5. Serological Tests	Blood, serum	Detects antibodies against specific oral bacteria
6. Salivary Diagnostics	Saliva	Analyzes saliva composition for bacterial markers
7. Imaging Techniques	X-rays, CT scans, MRI	Reveals bone and tissue changes due to oral infections
8. Biopsy	Tissue biopsy	Provides a sample of infected tissue for analysis
9. Antibiotic Sensitivity Testing	Bacterial cultures	Determines which antibiotics are effective against bacteria
Diagnosis of respiratory tract infections		
1.Sputum Culture	Sputum	Used to identify the presence of bacteria in the respiratory tract. It is commonly used for diagnosing chronic bronchitis, pneumonia, and tuberculosis.

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2. Blood Culture	Blood	Helpful for identifying bacteria that have entered the bloodstream due to severe respiratory infections, such as sepsis or bacteremia.
3. Nasopharyngeal Swab	Nasopharyngeal swab	Primarily used to diagnose respiratory infections like streptococcal pharyngitis, whooping cough (pertussis), and diphtheria.
4. Throat Swab	Throat swab	Typically employed to diagnose streptococcal pharyngitis (strep throat) caused by *Streptococcus pyogenes.*
5. Bronchoscopy with BAL	Bronchoalveolar lavage (BAL) fluid	Useful for detecting bacterial infections deep in the lungs, including pneumonia and tuberculosis.
6. Chest X-ray	X-ray of the chest	Provides visual evidence of lung abnormalities associated with bacterial pneumonia and other respiratory infections.
7. Polymerase Chain Reaction (PCR)	Respiratory secretions, nasopharyngeal swabs	A highly sensitive method for detecting bacterial DNA and RNA. Used for various respiratory infections, including *Mycobacterium tuberculosis* (TB).
8. Serological Tests	Blood	Measures the presence of specific antibodies against bacteria, helpful in diagnosing atypical bacterial infections like *Mycoplasma pneumoniae* or *Legionella pneumophila.*
9. Urine Antigen Tests	Urine	Mainly used to diagnose *Streptococcus pneumoniae* and *Legionella pneumophila* infections, such as Legionnaires' disease.
10. Rapid Antigen Tests	Nasopharyngeal swabs	Provides quick results for certain bacterial infections like *Streptococcus pyogenes* (strep throat) and *Neisseria meningitidis* (meningococcal infection).
Diagnosis of digestive tract infections		
1. Stool Culture	Stool (feces)	Common for detecting enteric pathogens like *E. coli, Salmonella, Shigella, and Campylobacter.*
2. Polymerase Chain Reaction (PCR)	Stool, rectal swab	Used to detect specific bacterial DNA, including pathogens like *Clostridium difficile and Helicobacter pylori.*
3. Blood Culture	Blood	For detecting bacteremia or septicemia caused by bacteria that may have spread from the digestive tract.
4. Upper Endoscopy	Biopsy of the stomach lining	Useful for detecting *Helicobacter pylori* infection and related gastritis or peptic ulcers.
5. Colonoscopy	Biopsy of the colon lining	Can identify infections like *Clostridium difficile* colitis and inflammatory bowel disease.
6. Breath Test	Exhaled breath	Specifically used for detecting *Helicobacter pylor*i infection by measuring urease activity in the stomach.
7. Serological Tests	Blood	Detects antibodies against specific bacterial pathogens, useful for chronic infections like *H. pylori.*
8. Imaging Studies	X-rays, CT scans, MRI	To identify complications or structural issues related to infections, such as abscesses or fistulas.
9. Fecal Immunochemical Test (FIT)	Stool	Primarily used for colorectal cancer screening but can indirectly suggest the presence of infection.
10. ELISA Assays	Stool, blood	Useful for detecting toxins or antigens produced by certain bacterial infections, like *C. difficile.*
Diagnosis of the invasive infections		
Heart Infections		
1. Blood Culture	Blood	Endocarditis, infective carditis
2. Echocardiography	Imaging	Valvular infection, abscesses, vegetation
3. Cardiac Catheterization	Blood samples	Myocarditis, endocarditis
4. Serological Tests	Blood	Detect antibodies against causative bacteria
5. Polymerase Chain Reaction (PCR)	Blood	Detect bacterial DNA or RNA
Bone Infections		
1. Aspiration and Biopsy	Bone tissue	Osteomyelitis, septic arthritis
2. Imaging (X-ray, MRI, CT)	Imaging	Bone abscesses, deformities
3. Blood Culture	Blood	Systemic spread of bone infection
4. White Blood Cell Count	Blood	Elevated WBC count may indicate infection
Bloodstream Infections		
1. Blood Culture	Blood	Bacteremia, sepsis, endocarditis
2. Complete Blood Count (CBC)	Blood	Leukocytosis (increased WBC) and signs of infection
3. C-reactive Protein (CRP)	Blood	Elevated CRP levels indicate inflammation
4.Procalcitonin (PCT)	Blood	Elevated PCT levels may indicate a bacterial infection
5. Gram Stain and Culture	Blood	Identify the causative bacteria
Diagnosis of Urogenital infections		
1. Urinalysis	Urine	Common for urinary tract infections (UTIs) such as cystitis and pyelonephritis.
2. Urine Culture	Urine	Used to identify the specific bacteria causing UTIs and assess antibiotic susceptibility.
3. Gram Stain	Urethral or vaginal discharge	Helps identify Gram-positive or Gram-negative bacteria in cases of urethritis or vaginitis.

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4. PCR (Polymerase Chain Reaction)	Urine, swabs, or fluid samples	Detects bacterial DNA, useful for various urogenital infections, including chlamydia and gonorrhea.
5. Blood Culture	Blood	Severe urogenital infections that may lead to bacteremia, such as pyelonephritis or sepsis.
6. Imaging (e.g., Ultrasound, CT scan)	Imaging of urogenital organs	Used to detect structural abnormalities or complications of infections like abscesses or kidney stones.
7. Serology	Blood or serum	Detects antibodies produced in response to certain bacterial infections like syphilis or *Mycoplasma genitalium*.
8. Nucleic Acid Amplification Tests (NAATs)	Urine, swabs, or fluid samples	Sensitive for detecting sexually transmitted infections (STIs) like chlamydia and gonorrhea.
9. Vaginal Wet Mount	Vaginal discharge	Identifies *Trichomonas vaginalis*, a protozoan causing vaginitis.
10. Pap Smear	Cervical cells	Screens for the presence of human papillomavirus (HPV) which can lead to cervical cancer.
11. Culture of Endocervical Swabs	Swab from cervix	Used for diagnosing infections like *Chlamydia trachomatis* and *Neisseria gonorrhoeae*.

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