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Contents

Review Article

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Air Sampling in Wards and Hospitals: What we Know and What we do not

Sayan Bhattacharyya[1], Amit Banik[2], Atul Raj[3]

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Abstract

Bacterial sampling of air for microbes is very important in order to prevent airborne infections. Techniques for this air sampling can be divided into active and passive ones. With time new methods and techniques have been devised. Studying these methods and their relevance is very important and new methods are expected to appear in near future.

Keywords: Air sampling; Sampler; Aerosol.

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Introduction

Microbes are ubiquitous is air, soil and water, especially air via which it can produce many airborne infections; it can come from both endogenous and exogenous sources. Hence microbial sampling of air and containment or purification of the air is important.[1] Post-operative infections comprise about one-third of all the hospital-acquired infections, and a large number of them arise from the contaminated air in the operation theatres.[2]

Need of air sampling

In any closed workplace airborne microbes are important source of infections and hence the bioload of microbes in ambient air needs to be monitored.[1]

Air sampling:

Methods of air sampling for pathogenic microorganisms can be active and passive.[1] In passive method different basal and enriched culture media plates are used as "settle plates". Results can be expressed as CFU/plate/time or in CFU/m2/hour.[3]

In active sampling, by suction a fixed volume of air is drawn in, and colonies are expressed as CFU per cubic metre of air.[1]

Passive method depends on many factors like gravitational field, electrical gradient, thermal gradient and others, which governs the way bioaerosols would settle down; some of them are taken advantage of in passive sampling.[3]

Settle plate method: Here, petri plates containing culture media are placed in the "1/1/1 scheme" , i.e. for 1hour, 1metre above the floor, and at least 1metre away from walls or any obstacle.[4] In this method, agar coated slides can also be used in place of plates.[3] Typically media like Tryptone soya agar can be used for settle plate method, also called sedimentation method, and duration of keeping the plates open for aerosols to settle down is 4 hours.[5]

Advantage of the settle plate method:

According to Charnley, this method reproduces the actual process by which infectious aerosols deposit on biological and non-living surfaces by gravity, and hence are better than active sampling which estimates all suspended bioaerosols.[6]

(a) Media used: Blood agar, MacConkey agar or Tryptone soya agar are the common media used.

(b) Newer media used: Bhattacharyya et al have used successfully milk air for air sampling by settle plate method, and this medium also helped in identification of pathogens by supporting good growth and Staphylococcal pigment production.[7]

Disadvantage and limitations of settle plate method:

The main disadvantage of passive sampling, according to Humphreys, is that this method is not quantitative and selects out only large airborne particles.[8] Hence it is not suitable for operation theatres, but is to some extent useful in these places because it can measure the airborne bacteria nearest to operation site, as reported by Friberg et al.[9]

Active sampling:

Active sampling is better is the sense that it is quantitative, but the results are variable with individual equipments.[10] Literature mentions that the Anderson's sampler is better than Anderson's impactor and other equipments.[10]

Slit sampling:

Centrifugal air sampler: This is a very useful technique where media is in strips at edges of sampler and by centrifugal force particle are impinged on the media. Reuters centrifugal sampler is a very useful equipment where colonies are expressed as CFU per strip per unit time.[11]

Disadvantages of active air sampling: These methods are expensive and noisy, and are also heavy and difficult to sterilize.[12]

Other methods: A 6-stage Anderson's impactor containing media in petri plates has been devised to accurately assess the load of bacteria and fungi in ambient air.[10] However it is not so popular now.

Newer methods: Flow cytometry and Fluorescent in situ Hybridisation have been shown to be useful but lack sensitivity and specificity.[11] Also, microbial metabolites like ATP and DNA can also be studied, but are not vey specific.[12]

Electrostatic precipitation: Electrostatic precipitation using ionisers have been studied since many years for air sampling.[13] However, powerful electric field may damage bacteria, humidity may alter the results , and recovery rates for Pseudomonas fluorescens and M.bovis BCG are low.[13]

Thermal precipitation: In this technique which is also old, air is forced on a heated surface and then onto membrane filter or petri plate with media on to the cooler surface.[14] There it precipitates and colonies are observed the next day.

Impingement in liquids: This is also an old method and has also been tried later, and can be devised as air inlet and outlet with a ,liquid culture medium with sieve in between. However this method is also not suitable for P. fluorescens.[15]

Air sampling for fungi: Using different methods of active sampling, Sabouraud's dextrose agar has been used for assessing fungal load in air. DNA isolation and sequencing has also been done from the colonies for accurate identification.[16] Aspergillus spp. are generally found in air inside and outside wards.[16] Passive sampling methods like settle plate method are not recommended for fungal air sampling because fungal spores can remain suspended in air and not settle down indefinitely.[17]

Air sampling for viruses: Newer methods like electrostatic precipitation (ESP)-based bioaerosol sampler , coupled with downstream quantitative polymerase chain reaction (qPCR) analysis, have been found to be very effective in finding Influenza virus in ambient air of hospitals and other places.[18]

Sampling of air for M. tuberculosis: In a study by Mastorides et al, Micropore membrane air sampling , assisted by suction pump, along with PCR analysis has been found to be very effective in detecting M. tuberculosis in air especially near the infected patients' beds.[19]

One health approach:

One health envisages safe human health, animal health and environmental health, and clean and safe air is an essential component of one health.[20]

Future directions: New methods and techniques are awaited that might simplify the air sampling for microorganisms.

Summary and Discussion: Hence the basic methods for studying microbial load in ambient air are:

a. impingement in liquids,
b. impaction on solid surfaces,
c. sedimentation,
d. filtration,
e. centrifugation,
f. electrostatic precipitation, and
g. thermal precipitation.

Conclusion

There are a number of methods for air sampling for microorganisms, and one needs to optimize which method is to be used, which also depends on the setting where it has to be applied. More and more new methods are coming up and this field of research is becoming interesting day by day.

Legends:

CFU: Colony forming units.

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Review Article

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Current Nosocomial Infections-An Update

Madiha Niyaz[1], Aaliya Shah[2], Syed Mudassar[3]

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Abstract

Health care-associated infections are infections that occur while receiving health care, developed in a hospital or other health care facility that first appear 48 hours or more after hospital admission, or within 30 days after having received health care. Multiple studies indicate that during hospital stay patients get exposed to several hospitals associated infections such as pneumonias and catheter associated urinary tract infections .Simple infection control procedures, good sterilization techniques, use of combination antibiotics can prevent or minimize hospital associated infections. Recently Covid 19 pandemic caused a havoc in hospitals and became the most common infection that was spread among health care staff as well as patients leading to many hospitals suspending their surgical procedures and maternity care.

Keywords: Nosocomial infections; Ventilator associated pneumonias; Urinary tract infections; SARS-CoV-2.

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Introduction

Health care-associated infections commonly known as hospital infection or nosocomial infection is a kind of infection which is not present at the time of admission to a hospital or health care facility but occurs duringthe course of stay inthe hospital.[1] They are not linked to the original illness for which the patient has been admitted to the hospital. Health care associated infections are wide spread especially in low and middle income countries affecting vast majority of patients. Main cause of hospital associated infections is antibiotic resistant microbes and ineffective infection prevention set up.[2] Hospitals house large number of patients who are sick with weakened immune systems, poor sanitation and sterilization protocols all contribute to alarming rise in nosocomial infections.In the developed world too such as United States and Europehealth care associated infections from all kinds of microbes contribute to several thousand deaths each year. Health care associated infections result in prolonged hospital stay for patients hence increased burden on hospitals as well as increased mortality rates.[3] There is now an ever increasing demand for an organized and uniform effective infection prevention control programswhich can reduce hospital associated infections.

The commonest healthcare-associated infections include hospital associated and ventilator associated pneumonia, Urinary tract infections and hospital associated gastroenteritis.In 2019 novel Corona virus pandemic emerged as a global health challenge and took a centre stage of hospital acquired infections. International hospitals and health care systems suffered huge losses and struggled to cope. The poor and middle developed countries the impact was greater and surgical procedures, cancer and maternity care suffered a setback leading to rise in mortality cases.[4]

Types of Health Care Associated Infections

Hospital associated and ventilator associated pneumonia

Hospital-acquired and ventilator associated infections remain a major health concern and have been associated with a higher mortality than any other nosocomial infection. An onset of pneumonia at least 48 hours after hospital admission is referred to as hospital-acquired pneumonia. Hospitalacquired and ventilator associated infections are attributed to lengthy hospital stay and greater hospital expenditures as compared with patients without hospital-acquired and ventilator associated infections.[5] The incidence of hospital acquired pneumonia is highest in intensive care unit where it is a major cause of morbidity and mortality. Evidence suggests that 25% of patients admitted in ICU who receive mechanical ventilation develop pneumonia which is reasonably greater than in non ICU patients.[6] Because of its severity, and the fact that the mechanically ventilated population is much more likely to have significant underlying disease and receive more intensive therapy, many physicians have referred to hospital associated pneumonia occurring in mechanically ventilated patients as ventilator-associated pneumonia

A number of patient-related factors have been identified. These factorsgenerally reflect preexisting conditions which impair host defenses and includeage over 70 years; the severity of the underlying illness; malnutrition; coma orother causes of impaired consciousness; prolonged hospitalization; and certainco morbid conditions, including diabetes mellitus and chronic obstructivelung diseases.[7] The presence of these factors can substantially increase therisk for hospital acquired pneumonia.For example, advanced age is associated with a two- to threefoldincreased risk of hospital acquired pneumonia probably because the elderly are more likely to haveco morbid conditions or weakened immune systems, reside in long-term carefacilities, and have an increased risk of aspiration.Chronic obstructivepulmonary disease (COPD) increases the risk for hospital acquired pneumonia up to fourfold, probablybecause of impairments of mucociliary clearance.[8]

The common pathogens causing these infections include gram negative bacilli (e.g. Pseudomonas aeruginosa, E coli, Klebsiellapneumonia Enterobacter spp, Acinetobacter spp) and gram-positive cocci (e.g., Staphylococcus aureus, which includes methicillin-resistant S. aureus, Streptococcus spp). Differences in host factors and in the hospital microbial flora of the hospital affect the patterns of the causative pathogens.[9] Hospital associated pneumonias occur if microbial organism reaches lower airways and attacks the host lungs. The patients who are at extreme risk include those with weakened immune systems, elderly as wells as some times patients are affected with a highly virulent strain.[10] To determine optimal anti microbial therapy it is essential to determine the causative microbes. Determining the exact cause of infections can improve patient outcomes[11] although in medical setting it is often confusing as several organisms are isolated hampering the optimal anti microbial therapy.[12]

Hospital associated infections are derived from either an endogenous or exogenous source.[13] Endogenous infections are the most common cause of infections and can occur with hospital acquired pathogens that attack the host.[14] Exogenous infection with nosocomial pathogens acquired from the hospital environment is less common and generally occurs late in the ICU admission.[14] Precise data concerning the etiology of Hospital acquired and ventilator associated pneumonia are limited and the main reason for that is the lack of proper microbial diagnosis. Effective microbiological studies and identification of the causative pneumonia causing pathogen and development of effective therapy can reduce hospital associated pneumonias.

Urinary tract infection

A urinary tract infection (UTI) is an infection involving any part of the urinary system, including urethra, bladder, ureters, and kidney. UTIsare the most common type of healthcare-associated infections reported in hospitals.UTIs are huge burden on hospital resources as well as on patients extending their hospital stay and increasing the costs manifold. According to one study account for 40% of total hospital acquired infections.[2] Centre for disease control and prevention (CDC) reports that among the UTIs occurring in the hospital more than 75% are due to urinary catheter and every time about 15-25% of hospitalized patients receive urinary catheters during their hospital stay. In addition to catheters increasing age, diabetes, obstructions, stone also predispose a patient to UTIs.[15] In one study conducted in Norway they reported the urinary tract infection to be the commonest nosocomial infection followed by respiratory tract infections.[16]

UTIs are the main cause of morbidity and mortality in hospital admitted patients in general, and in post-operative surgical patients in particular.

Treatment is mostly complicated due to resistant bacteria not treated well with latest antibiotics.[17] Nowadays efforts need to be taken to prevent complicated UTIs to reduce their occurrence worldwide.Numerous studies have published data regarding hospital acquired urinary tract infections.[18] Most of the Nosocomial UTIs originate at the moist place and the causative bacteria are more complicated than those causing simple UTIs

It is imperative that every hospital or health care facility should have proper procedure and protocols in place to minimize hospital associated UTIs. Since UTIs are the commonest nosocomial infections occurring mostly due to use of urinary catheters, discontinuation of catheters in patients as soon as it's possible would be of help in reducing these resistant UTIs. Patients with resistant bacterial infection need their urine samples to be sent to microbiology laboratory to identify causative bacteria andeffective combination of antibiotics be administered to treat the infection. Impregnation of catheters with antibiotics can also reduce infections.

Gastroenteritis

Gastroenteritis refers to inflammation of intestinal tract. It includes a combination of symptoms such as diarrhea, abdominal pain and vomiting although all need not be present to make a diagnosis. Nosocomial or hospital acquired gastroenteritis has become a cause of attention in past decade due to its increasing prevalence. However unlike other hospital acquired infections there is no proper method to detect exact cases of hospital acquired gastroenteritis. Therefore our understanding of accurate incidence and its effect on hospitals is limited.In one study conducted in three hospital systems in England from 2002-2003 a total of 2,154 patients (2.21 cases/1,000-hospital-days) and 1,360 healthcare staff (0.47 cases/1,000-hospital-days) were affected in 227 unit outbreaks and in about 63% causative agent was noro virus.[19] Gastroenteritis outbreak often leads to ward closure and disruption of hospital activity with attacks on both patients as well as staff.[20] Gastroenteritis out breaks most commonly effect elderly and children. Several studies have demonstrated that stringent infection control measures and contact tracing can rapidly cease the norovirus outbreak and prevent a second wave of infection. Children with unexplained vomiting and those with contact history of gastroenteritis should be properly, isolated, and investigated for possible infective causes, including norovirus-induced gastroenteritis.[21]

Nosocomial COVID-19 infection- a challenging situation.

COVID-19 emerged as a huge challenge in 2019. Originated in the Wuhan province of China it soon spread globally causing the WHO to declare it as a pandemic in March 2020.There has been a huge pressure on medical health care professionals who have been on forefront fighting this Covid 19 battle. COVID-19 caused huge mortality rates worldwide. Also reluctance of the public to visit hospitals for diagnosis or treatment due to COVID-19 fear also contributed to excess mortality.The causative virus novel corona virus SARS-CoV-2 causes flu like symptoms and pneumonia like complications. While most people have only flu like symptoms such as fever, fatigue, cough some people go on to develop extreme complications like acute respiratory distress syndrome and death. Despite serious efforts in hospitals, hospital acquired Covid 19 infection has been a huge problem. It has put patients with other medical problems at serious risk. Transmission of COVID-19 infection among admitted patients resulted in increase in mortality cases. COVID-19 burdened the hospitals causing huge losses. Reduction in hospital beds and operating rooms has led to considerable delays in surgical and semi elective surgical procedures.[22] The SARS-Cov2 virusis highly contagious. It mainly transmits through person to person contact and has the potential to be viable on surfaces for up to three days. Prior to the current COVID-19 pandemic, nosocomial infections mostly hospital acquired pneumonia and urinary tract infectionalready caused significant burden on hospitals and health care systems. Hospitals are currently engulfed in Covid 19 storm and have become an important source of viral transmission with even health care facilities in the developed world struggling to prevent nosocomial COVID-19. A case series study conducted in China estimated that 44% of 179 COVID-19 infections were nosocomial in nature.[23] The catastrophic effect of hospital or nosocomial acquired COVID-19 came from a study conducted very recently in South Africa where investigators demonstrated how a single unsuspected case of COVID-19 led to spread of infection among five hospital wards with infection confirmed in 39 patients with half of them dead and eighty staff members.[24] Margo et al., carried out a study in General district hospital North west of England and concluded that out of 239 cases testing positive for COVID-19 16.2% were hospital acquired infections and such patients endured longer hospital stays.[25] Wang et al described a case study of 138 patients with COVID-19 out of which

12.3% cases had hospital acquired COVID-19 and had been admitted to hospital for other reasons.[26] Zhou et al., conducted a meta analysis and review study in China and found that in the early outbreak proportion of nosocomial infection in patients with COVID-19 was upto44%.[27] Wake et al., conducted a study at NHS trust in South London and concluded that out of 662 patients admitted with COVID-19,45 patients had acquired COVID-19 in hospital. These patients had no evidence of respiratory or influenza-like illness on admission and developed symptoms, with positive SARS-CoV-2 PCR test results, more than 7 days after admission and 40 of these patients had shared a ward with a confirmed COVID-19 case prior to testing positive.[28] Nosocomial COVID-19 infections have high mortality rates. In a study conducted by Rickman et al in one of the biggest teaching hospitals of London 15% cases of COVID-19 admitted patients between 2 March and 12 April 2020 were definitely or probably hospital-acquired, through different transmission routes and the fatality percentage was 36%.[29] Several studies conducted in hospitals around the world as well as many independent health care professionals strongly suggest the use of simple surgical masks to reduce hospital transmission among patients as well as health care workers. The use of masks has proven to be very effective in hospitals where total physical distancing is not possible.Astudy conducted by Seidelmanet al on 21000 health care workers found that hospital acquired COVID-19 infections were drastically reduced after strictly implementing universal masking policy.[30] Use of masks and other protective gear can go a long way in protecting both patients and hospital staff from nosocomial or hospital acquired COVID-19 infection.

Conclusion

Hospital associated infections or nosocomial infections are a reality in health care set up worldwide. Several infections such as pneumonias, urinary tract infections, gastroenteritis effects many admitted patients globally and cause increased hospital stay as a result excessive burden on hospitals , increased costs for patients as well as high mortality . There is an imperative need to improve infection control measures , develop good sterilization techniques especially in developing countries to reduce the nosocomial infections and thus avoid preventable deaths.In 2019 SARS-CoV-2 came as a huge challenge to medical fraternity. Declared as a global pandemic by WHO it spread quickly through out the world killing millions of people.Hospitals became a huge source of COVID-19 spread with infections spreading rapidly among both patients as well as hospital staff.It affected the functioning of even the best hospitals worsening the surgical and maternity care with even forcing closure of healthcare facilities at some places. Recent studies have demonstrated that good hygiene protocols, distancing measures and masking are effective in preventing COVID-19. Use of surgical masks and other protective gear by both patients and staff can lessen this contagious infection in hospitals.

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Review Article

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Fungi-An Overview

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Abstract

Fungi are eukaryotic, non-photosynthetic organisms. Most of the fungal organisms are saprophytic or commensals but some are parasitic as well, causing a myriad of diseases in animals and humans. Some of the fungal organisms are of zoonotic significance and hence can be transmitted from animals to humans. Fungal infections are chronic in nature and only few antifungals are available till date. Risk of fungal infection increases if the indivisual is immunocompromised, suffering from metabolic diseases, old aged and is undergoing prolonged antibiotic therapy. Antifungals are drugs aimed to treat fungal infections. These target the fungal cell, cell membrane, metabolism, nucleic acid, growth and divisions. But as fungi are eukaryotic organisms, antifungals aimed to kill the fungal organism can also potentially harm the host cell.

Keywords: Antifungals; Fungal diseases, Fungal nutrition and culture media, Zoonosis.

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Introduction

Fungi are eukaryotic, non-photosynthetic, slow growing, strictly aerobic chemoorganotrophic, unicellular (yeast) or multicellular (moulds) organisms under the kingdom Fungi in Whittaker's Classification system. Fungal organisms are mostly saprophytes or commensals while some are parasitic as well. They are often acid tolerant and can grow at an acidic p H as well, although the optimum p H for growth is 6 and temperature is 20-30 degree. The cell wall of fungi is made up of chitin. Yeasts are oval, unicellular organisms. Candida albicans and Coccidia immitis are some of the examples of yeast. Moulds are generally filamentous with branching filaments or hyphae like Aspergillus. Some fungi exist in a dimorphic form as well i.e they can exist both as yeast and mould like Histoplasma, Blastomyces, and Cryptococcus etc. Yeast form is seen in infected indivisual or in enriched media at around 37 degree C whereas mould form is seen in environment or when grown at 25 degree C. Fungal toxins are neither exotoxin nor endotoxin in nature rather these are the metabolic byproduct of the fungi responsible for causing mycotoxicosis. One common example is aflatoxicosis. Some fungi form Pseudohyphae in the animal tissue like Candida albicans. Pseudohyphae are yeast like budding structures unseparated from the mother cell. Some of the characters shared by fungi with the animals are mode of nutrition, storing nutrients in the form of glycogen rather than starch. Some of the characteristics shared with plants are, sessile nature, presence of cell wall, chitin, glucans, xylans and mannans in their cell wall, presence of vacuoles etc, but fungi are considered more animal like than plants.

Classification of fungi

Fungal classification is governed by ICBN, Indian Council of Botanical Nomenclature. They are classified on the basis of morphology, spore characteristics, mode of nutrition etc. Fungi can be classified based on the reproductive characteristics into five phyla called Chytridomycota, Zygomycota,

Ascomycota, Basidiomycota, and Deuteromycota. Chytridomycetes are the primitive fungi with some members having cellulose in their cell wall along with chitin. Zygomycota are also called conjugated fungi. It includes the bread mould, Rhizopus and Mucor. These have coenocytic hyphae. Ascomycota are the sac fungi. Ascospores are the sexual spores in a sac like structure (ascus is the Greek word for sac). Morels, truffles, yeasts, Candida, Claviceps, Penicillium, and Aspergillus are some of the important fungi under the Phylum Ascomycota. Basidiomycota are the club fungi that include the edible mushrooms, toadstools, rusts and smut etc. Deuteromycota are the imperfect fungi. Sexual mode of reproduction is absent in these fungi. When sexual stage is discovered in any fungi imperfecti, they are transferred to Ascomycetes. The asexual state is called anamorph and the sexual state is called telomorph. Telomorph of Cryptococcus neoformans is Filobasidiella neoformans. Phylum Ascomycota together with Basidiomycota forms the Dikarya.

Fungal Nutrition and Culture Media

Most of the fungi grow on media rich in carbohydrate such as Potato Dextrose Agar, Malt extract Agar, Cornmeal Agar. Preferred carbohydrates used by the fungus are xylose, glucose, sucrose but they can also use insoluble carbohydrates like cellulose, hemicellulose and lignin from wooden barks for their carbohydrate requirement. They do so by secreting depolymerising enzymes. As the fungi have to defend their territory from which they obtain food, they do so by synthesizing antibiotics and other toxic metabolites. Fungi also require minerals like iron as haeme, sulfur from cysteine, nitrogen and phosphorus etc. Sabraud Dextrose Agar (SDA) is one of the most common Medias used in mycology. It was used formulated by Sabraud in the year 1892 for culturing dermatophytes. Brain Heart infusion agar is mostly used for culturing dimorphic fungi. Other Medias like BiGGY Agar is used mainly for identification of Candida spp. Birdseed Agar is a selective and differential media for isolation of Cryptococcus neoformans. Cryptococcus neoformans can utilize the caffeic acid as a substrate due to the presence of an enzyme, Phenoloxidase producing melanin. Cornmeal Agar is mostly used for inducing sporulation in Candida spp. Chloramphenicol and cyclohexamide are used in media for their antibacterial and antifungal actions respectively.

Disease caused by fungi

Diseases caused by fungi are called Mycosis. It can be categorized as superficial mycoses, subcutaneous mycoses and systemic mycoses. Fungi cause damage by tissue invasion (mycotic); toxin production (Mycotoxic) and induction of hypersensitivity.

Some of the factors that predispose to fungal diseases include immunosuppression, immunological defects, prolonged antibiotic therapy, metabolic and neoplastic diseases, immaturity, aging and malnutrition, exposure to heavy challenge of fungal spores, traumatized tissue, persistent moisture on skin surface etc.

Dermatophytes are fungi that grow on superficial layer of skin (skin, hair, claws) utilizing keratin. Dermatophytic infections are commonly referred to as ringworms. Dermatophytes affecting animals mostly belong to genera Microsporum and Trichophyton. Dermatophytes can be geophilic saprophytic, zoophilic or anthropophilic. Microsporum canis causes ringworm in cats, but it can also affect dogs and humans, hence it is considered to be of zoonotic significance. Ringworm in dogs is most commonly caused by Microsporum canis, but Microsporum gypseum and Trichophyton mentagrophytes can also be associated with canine dermatophytosis. Microsporum canis and Microsporum gypseum infections are usually acquired from soil. Trichophyton verrucosum causes ringworm in cattle whereas ringworm in horses is mostly caused by Trichophyton equinum and Trichophyton mentagrophytes. In pigs, Microsporum nanum is most commonly associated with dermatophytosis. Trichophyton mentagrophytes is usually found in rodents and some companion animals. It is also considered to be zoonotic.

Aspergillosis in animals is mostly caused by Aspergillus fumigatus (most common), Aspergillus flavus, Aspergillus niger, Aspergillus nidulans, Aspergillus terreus etc. A. flavus is most commonly associated with aflatoxicosis. In birds, Aspergillus mostly causes respiratory diseases like brooders pneumonia (mostly in the newly hatched chicks), air sac infections, and bronchopulmonary infections. Dissemination of infections to the brain is also seen, manifested by torticollis and disturbance in equilibrium. Yellow nodules are often seen in the respiratory organs or in the body cavities. In ruminants, it causes mycotic abortion, mycotic

pneumonia. In horses it causes gutturomycosis manifested by epistaxis and dysphagia, nasal granulomas, intestinal aspergillosis in foals. It causes otitis externa, chronic rhinitis in dogs

Candida albicans are commensals in the intestinal and genital tract (mucocutaneous areas) and are mostly responsible for localized mucocutaneous diseases. In birds, it causes 'Thrush' of mouth, oesophagus or crop (crop mycosis, sour crop). Candidiasis is often called as moniliasis. In cattle, it causes mastitis. Cryptococcus neoformans are yeasts found normally in the environment, in soil and pigeon droppings. Infection is acquired mainly due to inhalation of the spores or due to contamination of wound.[1] In dogs, it can cause nasal granulomas; central nervous system involvement and eye involvement causing blindness are also seen.[2] In cattle, it causes mastitis. In immunocompromised humans, it causes Cryptococcal meningitis and lung infections.

Histoplasmosis is usually caused by the inhaling the spores of Histoplasma capsulatum found in soil contaminated with the droppings of birds and bats.[3] It is manifested by lesions in the lungs and intestine of humans and companion animals. In equines, Histoplasma farciminosum causes Epizootic Lymphangitis. Coccidioidomycosis also known as Valley fever is caused by the fungus Coccidioides immitis. Humans and dogs mostly acquire the infection from soil. It is not contagious and hence cannot spread from one infected animal to another. It is considered as a major biohazard for the laboratory personnel. Sporothrix schenckii causes sporotrichosis in horses, companion animals and humans manifested mostly as skin or cutaneous lesions. It is mostly found in soil, plants, hay etc. It is contagious and also has significant zoonotic risk. Blastomyces dermatitidis causes North American Blastomycosis in dogs and humans.

Mycetoma is a chronic, progressive destructive morbid inflammatory disease affecting foot or other body parts. It occurs due to entry of the fungal organism through the penetrating wounds characterized by drainage of the 'grains' of fungal colonies from the wound.4It is caused by the fungus Cuvularia geniculata, Madurella mycetomatis, Pseudallescheria boydii etc.

Rhinosporidiosis caused by Rhinosporidium seeberi in humans, horses, cattle and dogs is a granulomatous disease affecting the mucous membrane of respiratory tract, conjunctiva and rectum.

An insight into Antifungal Therapy

Antifungal drugs are the drugs aimed to treat fungal infections by targeting various structural and functional components of the fungal organism essential for its survival like the cell wall, cell membrane, nucleic acid synthesis, growth and division etc. Antifungals that aim the fungal cell walls are called cell wall synthesis inhibitors. These act by inhibiting the b-(1, 3)-glucan synthase thus preventing the formation of b-(1, 3)-glucan in the cell wall leading to osmotic instability and death of the fungus. Hence, these are also known as the penicillin of antifungal drugs. Echinocandins like Caspofungin, Micafungin, and Anidulafungin etc comes under this category. Caspofungin is the first commercially available drug under this group obtained from a fungus, Glarea lozoyensis, used to treat Candidiasis and Aspergillosis. As cell wall is not a component of animal cells, these antifungals are more selective in action and less harmful to the host. Fugal cell membrane has ergosterol as prominent sterol rather than cholesterol. Antifungals target the fungal cell membrane in two ways. They can directly bind to ergosterol causing pore formation and leakage of ions resulting into internal acidification and death of fungus like the Polyene antibiotics. Amphotericin B, Nystatin, Natamycin are the Polyene antibiotics. AMB is the drug of choice for systemic mycoses caused by dimorphic fungi in immunocompromised animals. The other category of drugs acts by interfering with the ergosterol biosynthesis. Allylamines and Azoles are the drugs under this category. Allylamines act by inhibiting squalene epoxidase, preventing the conversion of squalene to ergosterol. Squalene alters the membrane permeability and results into fungal death. Allylamines like Terbinafine and Naftifine are mostly used to treat Dermatophytic infections. Azoles act by inhibition of 14alpha-demethylase which is a cyt 450 dependent enzyme and thus inhibit ergosterol synthesis, leading to disruption of fungal membrane and membrane bound enzymes, whereas cholesterol synthesis in mammals is not affected because it doesn't require 14alpha-demethylase. It also leads to inhibition of mitochondrial cytochrome oxidase leading to accumulation of peroxides that cause auto digestion of the fungus. Ketoconazole, Miconazole, Enilconazole, Clotrimazole, Fluconazol, Itraconazole, Voriconazole are some of the azoles available for use. It can be used to treat systemic mycotic infections. Some of the side effects of using Ketoconazole in man are gynecomastia, embryo

toxicity and teratogenicity. The third category of drugs is the nucleic acid synthesis inhibitors like Flucytosine. It is analogue of cytosine, so it enters the fungal cells via cytosine specific permease which is not found in mammalian cell. Flucytosine converts into active metabolite, 5-fluorouracil after entering the fungal cell. 5-fluorouracil acts as anti-metabolite by competing with uracil, ultimately interfering with the RNA and protein synthesis. It has narrow spectrum and fungistatic action. It can be used to treat Candida, C.neoformans infection. 5-FC treatment can cause bone marrow suppressions manifested by leukopenia, thrombocytopenia and/or pancytopenia. Hepatotoxicity, Nephrotoxicity, GI disturbances are also some of the side effects associated with the use of these antifungals.

The fourth type of antifungals is Griseofulvin. It acts by disorganizing the spindle microtubules. It also affects cytoplasmic microtubules. It is fungistatic in action and is used to treat dermatophytosis. Some of the locally acting antifungals are Iodine, Copper preparations, dyes like crystal violet, organic acids like benzoic and salicylic acids used in Whitefield's ointment (3% salicylic acid; 6% benzoic acid) etc. Some of the essential oils are also known to have some antifungal actions like Thyme, Lavender etc.

Conclusion

Fungal infections are generally very difficult to treat because, unlike bacteria, fungi are eukaryotes and antifungals that kill fungi also harm the eukaryotic host. Antibiotics only target prokaryotic cells, whereas compounds that kill fungi also harm the eukaryotic animal host. Fungal infections tend to be of chronic nature requiring prolonged treatment with antifungal drugs. Antifungal resistance and host-related adverse reactions further limit the development of antifungals against fungal pathogens. Moreover emergence of antifungal resistance among fungus has further complicated the challenge in developing antifungal drugs in the future.

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Shortcommunication Article

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COVID-19: A Real Killer Disease

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Abstract

Knowledge of COVID-19 is changing almost daily through numerous scientific reports. We have been hearing new information regularly, sometimes contradictory due to constantly changing the scientific findings and results. At the commencement of the COVID-19 we were learnt that cough and fever were the unambiguous signs of COVID-19. Now we know that the disease can cause a wide variety of symptoms and even no symptoms at all. Many accurate facts about the disease remain unknown. Scientists do not have enough time to analyze the data and symptoms as they are busy in saving lives. Scientists are going too fast to understand the pandemic, causing more confusion to say whether Covid-19 is a killer disease.

Keywords: COVID-19; Killer Disease.

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Introduction

COVIDd-19 is a very complicated disease as half of those infected don't develop symptoms, and most patients have only mild symptoms. It has been reported that several patients died due to uncontrolled reaction of the immune system, called cytokine storm that can damage most vital organs (Li et al., 2020). The new coronavirus can attack the nervous system (Wu et al., 2020). In some cases, respiratory failure is related to neurological failure, not pneumonia. It's not certain when recovered patients stop being contagious. There are doubts about how long immunity lasts after the disease (Li et al., 2020).

COVID-19

Coronavirus infected cells generate an uncontrolled inflammatory response, not only in lungs but can be widespread in the body (Chen et al., 2020). Indeed, there have been reports of kidney, intestinal, or coronary damage (Madjid et al., 2020). It is not known which factors influence patients to

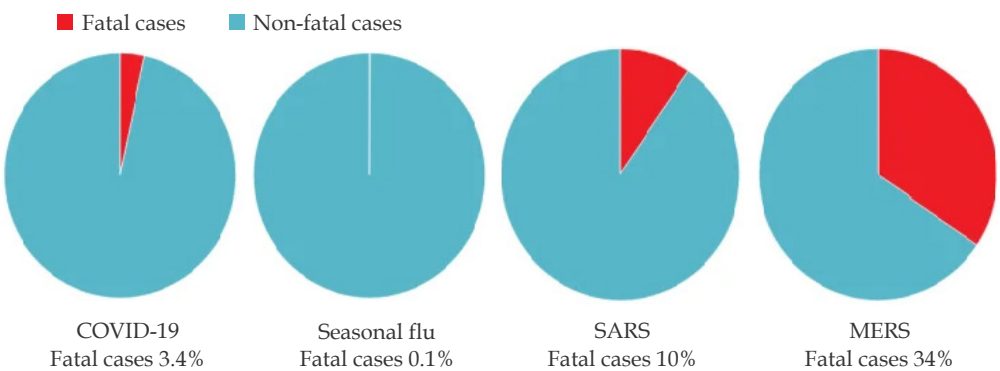

Fig. 1: COVID-19, Seasonal flu, SARS, and MERS fetal cases total to date (Source: CDC and WHO)

develop the syndrome. Regarding COVID-19, age is very significant. The key is to understand who are the most susceptible, it will take long time to understand.

The latest statistics indicate a fatality rate of new coronavirus is about 3.4 % (WHO, 2020). The SARS virus killed about 10% of all infected individuals (del Rey Calero J, 2004), while the MERS outbreak had a fatality rate of around 35% (Lin et al., 2018). There are 19, 345,57 confirmed cased of Covid-19 and has caused 1,20,438 deaths across the world of April 14, 2020 (Worldometer). The mortality rate of the virus has fluctuated. In the past few decades, we have seen a session of other pandemics: SARS, H1N1 and MERS, to name a few (fig.1 and 2).

SARS (severe acute respiratory disease) was flung in 2002. SARS came out in a way somewhat close to Contemporary Covid-19. It has been infiltrated in 29 countries. There were just over 8,000 confirmed incidents of the virus and Almost 800 persons were killed, putting the death rate close to 10%. Not to be alarming, but COVID-19 already has more confirmed cases and has claimed more lives April 14,2020. More lives. In 2009, H1N1, deemed the swine flu, broke out and hit more than 210 countries and approx. 3 lakhs people were died according to the CDC. Three years later, in 2012, MERS (Middle East respiratory syndrome) spread to a total of 27 countries. According to the World Health Organization, MERS killed 34% of people who had it.

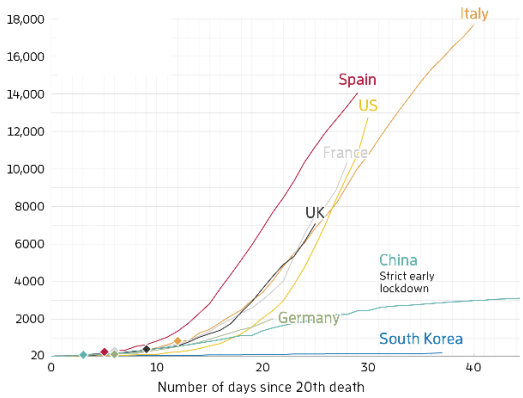

Fig. 2: COVID-19 cumulative deaths as of 8th April, 2020 (Source: Johns Hopkins University, USA).

At least so far, Covid-19 does seem to be more lethal than the seasonal flu or SARS or MERS (Wang et al.,2020). In the last four months, the virus has taken the world by storm and already claimed around 1,20,438 lives. The latest data suggests that it's less deadly than either SARS or MERS. Only time will tell how covid-19 will ultimately compare to other worldwide pandemics. It will take several weeks to be confident about how the virus behaves, including its mortality rate.

Conclusion

It is a very hard task to identify the reason or the reasons for infection containment, but nevertheless each and every variable and the confounding factors need to be addressed and analyzed. Tropical countries encounter a lot of pathogens resulting in infectious diseases. These infectious diseases may mask the milder symptoms of COVID-19 which may go undetected and thus unscreened and unreported. Lack of infrastructure and resources is a limiting factor for disease control and hence may create hot spots from where the virus can continually spread. This is a dynamically unfolding pandemic that will require the concerted efforts of counties around the world to control.

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