Aspergillosis: An Occupational Zoonotic Disease

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ABSTRACT

This chapter provides a comprehensive analysis of Aspergillosis as a major occupational zoonotic disease, examining the complex linkages between human activity, animal relationships, and the spread of Aspergillus species. The zoonotic aspect of the fungal infection, which is mainly brought on by breathing Aspergillus spores, highlights the serious health risk it poses to those who work with animals. The chapter begins with an outline of the epidemiology of Aspergillosis in work contexts and highlights the increased risk faced by professionals in veterinary medicine, agriculture, and other similar industries that involve direct contact with animals. It explores the various work environments where Aspergillus exposure is common, focusing on particular sectors and occupations where people are more vulnerable. In addition, the chapter delves into a variety of risk variables that impact susceptibility, such as immunocompromised states and underlying medical disorders, with a focus on identifying vulnerable groups in industrial settings. The difficulties in diagnosing Aspergillosis in these environments are explored, emphasising the need for improved surveillance and diagnostic instruments designed to address the unique difficulties of zoonotic transmission. The text provides information on control tactics and preventive measures, including the use of personal protective equipment, appropriate immunization regimens, and environmental management. By utilising an interdisciplinary approach, this chapter seeks to bridge the gap between veterinary and human health considerations by offering insightful information on diagnosing, treating, and preventing Aspergillosis in occupational settings. In the end, it remains an invaluable tool for scholars, medical practitioners, and legislators attempting to understand the complexities of Aspergillosis as a zoonotic illness in work environments.

Keywords: Zoonosis, zoonotic aspergillosis, occupational risk, public health, respiratory

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1. INTRODUCTION

Aspergillosis is a fungal infection caused by a specie of fungi known as Aspergillus which can affect the both humans and animals.. Occupational exposure is the main cause for occurrence of this disease especially working with contaminated material such as agriculture, construction, healthcare as Aspergillus spores are found in soil, decaying vegetation, and animal droppings from which these can be inhaled by humans and animals (Malik et al. 2003, Williams et al. 2004, Wild 2010). Aspergillosis is considered a zoonotic disease as it can be transmitted from animals to humans and humans to animals. It also affects the animals particularly birds, but it is more common in domesticated animals like dogs and horses. In humans, it possesses high risk for development in those individuals having weak immune systems such as those undergoing chemotherapy, transplant recipients or those infected with HIV/AIDS. Workers in the industries like agriculture, construction, healthcare, food processing have chances of Aspergillus spores inhalation while working with contaminated material such as hay, grain or compost or may be while cleaning or maintaining contaminated environments. However, there are some occupational groups which are at high risk of developing aspergillosis such as farmers and veterinarians as they both have maximum exposure to Aspergillus contaminated material (Malik et al. 2003, Williams et al. 2004). The symptoms may vary from case to case as in some cases it can cause respiratory infections, allergic reactions, or invasive disease that can lead to serious health complications because it is the most severe form of disease that can affect lungs, brain, kidneys (Morris et al. 2000, Falvey 2007).

Aspergillosis can be prevented by proper hygiene and safety measure in the workplace to prevent occupational exposure, use of personal protective equipment, and prompt diagnosis and treatment of infections. Aspergillosis can be cured by using antifungal medication if the case is complicated then surgery may be necessary (Azie et al. 2012, Blot et al. 2012).

In this chapter, we will discuss different types of aspergillosis and the occupational and zoonotic aspects of Aspergillosis. Besides this, we will also contribute towards prevention and treatment of Aspergillosis as well as proper hygienic conditions to prevent occupational exposure. Impact of Aspergillosis on public health and challenges faced in managing this disease will also be discussed in this chapter.

2. ZOONOTIC TRANSMISSION

There are different ways for humans to be affected with *Aspergillus* species such as handling with infected living birds, poor management and hygienic conditions, inhalation of spores from contaminated feed and litter, examination of dead infected carcasses as well as consumption of raw cooked contaminated poultry carcasses (Fig. 1). Birds of all ages are susceptible to this infection but mostly very young or old birds are affected. During growth of the chick, colonization of conidia occurs in the caudal air sacs because birds get infected due to conidia inhalation. This infection basically occurs in the hatchery where cracked eggs shell gets infected with *Aspergillus* spores and infect the embryos during the hatching process in hatchery or during the brooding time and commonly called as “brooder pneumonia”. Stressors also increase the susceptibility to aspergillosis like poor ventilation, high level of humidity of litter, overcrowding, warm temperature, antibiotic use, vitamin A deficiency. Besides of these all, wild birds are also involved in transmission of *Aspergillus* species. Presence of conidia in bird’s dropping is also a source of infection. So, humans can be infected either directly or indirectly (Small and Nicholls 2003).

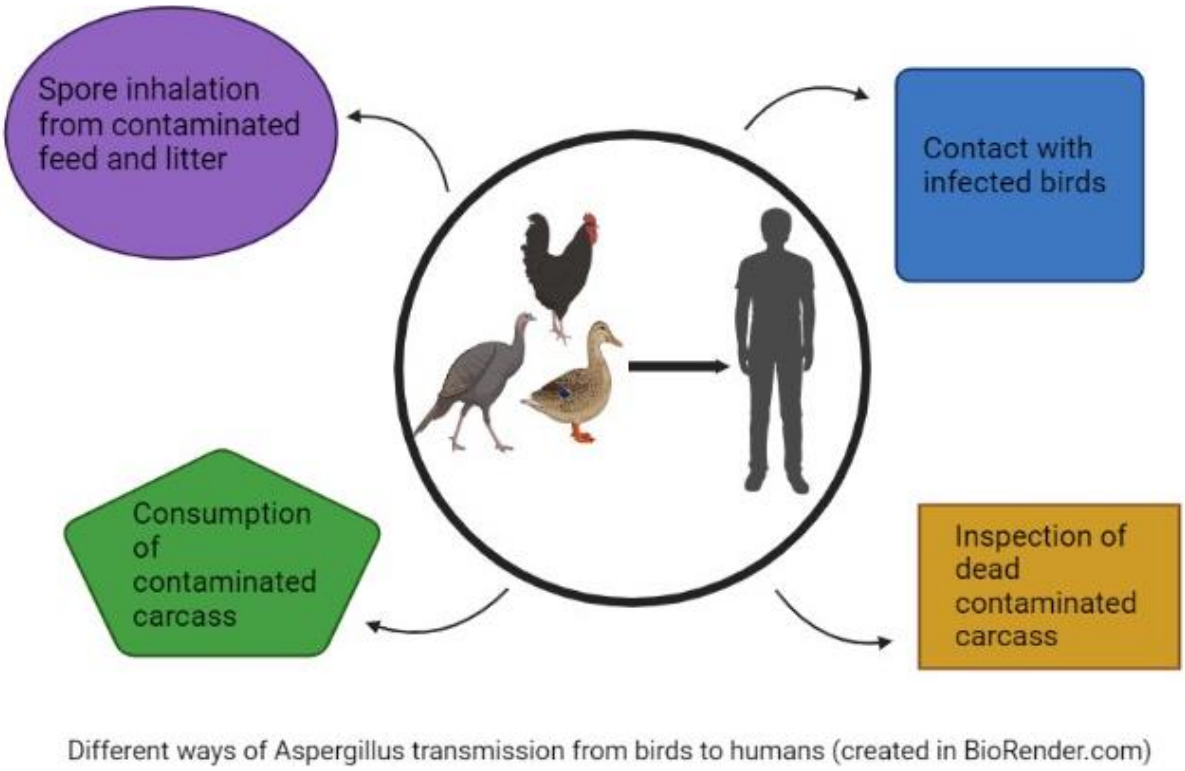

Fig. 1: Methods of *Aspergillus* transmission from animals to humans.

A study has shown the affection of humans in a way that about 15 million people can be infected by aspergillosis with more than 1 million deaths annually (Global Action Funds for Fungal Infections 2020). *Aspergillus Fumigatus* is the most commonly found specie of *Aspergillus* in case of humans (Lamoth 2016). In most of the countries, fungal cause of invasive and allergic infection in humans is *Aspergillus* flavus (Chakrabarti et al. 2008; Hadrich et al. 2010, 2013). However, in other affected areas different species have been reported such as *Aspergillus lentulus*, *Aspergillus thermomutatus*, *Aspergillus pseudofischeri* and *Aspergillus felis* (Barrs et al. 2013; Howard 2014; Negri et al. 2014). *Aspergillus* infection has been characterized in 4 ways depending upon clinic spectrum like invasive aspergillosis, chronic pulmonary aspergillosis, *Aspergillus* bronchitis and allergic bronchopulmonary aspergillosis (Kosmidis and Denning 2015). The severity of fungal infection depends mainly on two things fungal extension in tissues and immune response. After inhalation of spores, macrophages detect these spores in lungs alveoli and engulf and destroy them and if the human is immunocompromised then severe allergy with systemic disorder may occur (Brakhage et al. 2010; Milos et al. 2011). Immunocompromised humans are more susceptible to these infections with severe clinical picture and mortality rate (Bassetti et al. 2015). COVID associated pulmonary aspergillosis, invasive aspergillosis, influenza associated pulmonary aspergillosis and chronic pulmonary aspergillosis have been reported.

3. OCCUPATIONAL EXPOSURE

Aspergillosis is an infection caused by various *Aspergillus* species like *Aspergillus Fumigatus*. As aspergillosis can be developed by anyone, due to higher exposure of *Aspergillus* spores' certain occupations are there to be considered at high risk (Malik et al. 2003, Wild, 2010). However, here are the commonly associated occupations with higher risk of aspergillosis such as farmers and agricultural

workers, veterinarians and animal handlers, construction workers, woodworkers, gardeners and horticulturist, waste handlers and compost workers (Malik et al. 2003). Organic materials such as moldy hay, straw, grain and compost harbour *Aspergillus* spores which can lead to respiratory infection upon inhalation of these spores (Malik et al. 2003). Therefore, farmers are at high risk or aspergillosis due to exposure to these organic materials. Farmers with weakened immune system or pre-existing lung conditions are more susceptible to aspergillosis (Wild 2010). Veterinarians and other animal handlers are found at increased risk of aspergillosis due to their close contact with animals especially birds as in bird droppings, decaying organic matter and contaminated bedding material *Aspergillus* spores can be found (Williams et al. 2004). There are two veterinary procedures which can increase the risk of exposure such as handling contaminated materials or performing surgeries because during these procedures inhaled spores can cause respiratory aspergillosis (Malik et al. 2003, Williams et al. 2004). Buildings with dampness, water damage or poor ventilation can provide a favourable environment to molds for their growth as spores need high humidity to grow and demolition of renovation of such type of buildings provide chance to these spores to be released in the air increasing the risk of inhalation (Reddy et al. 2009, Viegas et al. 2013). So, working in molds contaminated environments may increase the risk of exposure to construction workers which can lead to aspergillosis (Reddy et al. 2009). Wood can be moldy when stored in damp conditions or exposed to water damage may encounter *Aspergillus* spore for woodworkers such as carpenters and furniture makers working with wood contaminated with molds (Malik et al. 2003, Siruguri et al. 2012) Manipulation of such type of wood by cutting, sanding or any other way can lead to release of spore increasing the risk of inhalation (Siruguri et al. 2012). *Aspergillus* spores are also present in soil, compost, decaying plant matter or rotting wood. So, professional gardeners and horticulturists mag be exposed to *Aspergillus* spores working in gardening, landscaping and horticulture (Malik et al. 2003, Williams et al. 2004, Wild and Gong 2010) During gardening activities or handling plants when these materials are disturbed there is a chances to spores release into the air leading to inhalation causing respiratory aspergillosis (Wild 2010, Siruguri et al. 2012). The most important source of *Aspergillus* spores is waste. So, waste handlers and compost workers involved in waste management may face increased exposure to *Aspergillus* spores from moldy organic waste such as rotting vegetation, food waste or compost piles having high concentration of *Aspergillus* fungi (Reddy et al. 2009, Viegas et al. 2013). Working in proximity to contaminated materials can result in respiratory infections.

It is important to note that not only the above discussed occupations are at the risk of aspergillosis. Instead of these, mill workers, textile workers, bakers and those working in laboratories are also at the high risk of aspergillosis depending upon the specific tasks and presence of *Aspergillus* in their working environment. Along with the presence of *Aspergillus* infection, there is a need to prevent this infection. Preventive measures can be the use of personal protective equipments, proper ventilation, regular cleaning, and maintenance of work environments can reduce the risk of exposing the people to the *Aspergillus* spores in occupational areas. People working in high risk occupations should take special measures like potential hazards, maintain good respiratory hygiene and if they experience any type of respiratory symptom or suspect exposure to *Aspergillus* they should take medical attention.

4. SOURCES OF EXPOSURE

Most of the nosocomial aspergillosis outbreaks have been reported due to air contamination (Fig. 2). In 1970s and 1980s, the outbreaks were due to the sources existing outside the hospitals with inadequate ventilation systems (Maschmeyer et al. 2007, Warnock 2007). A study has shown that pigeon excreta has been the source in two outbreaks (Maschmeyer et al. 2007, Warnock 2007).

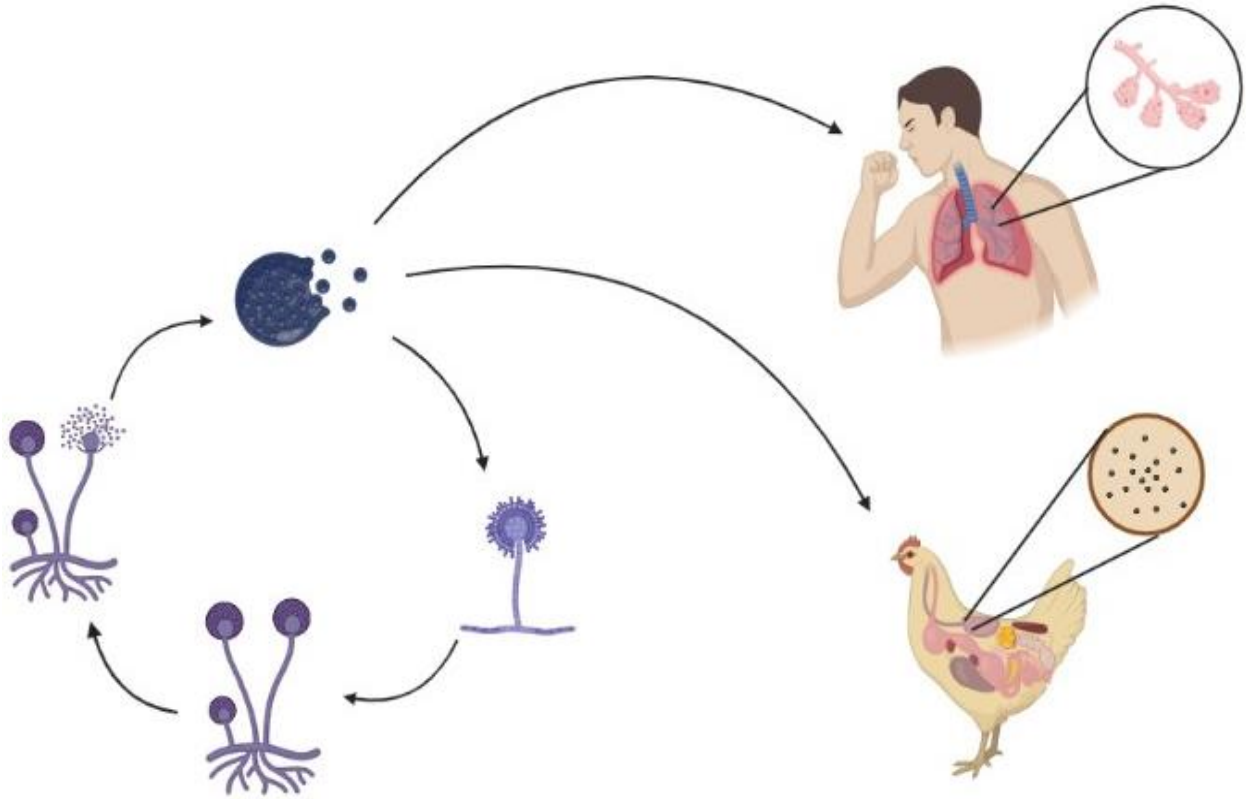

Fig. 2: Sources of exposure to *Aspergillus* for humans.

Internal construction or renovation with failure to control spread of contaminated dust or debris has been the main source of most outbreaks of nosocomial aspergillosis (Almyroudis et al. 2005, Ballard et al. 2008). Especially the main point of outbreaks was the renovation or construction of that floor where infected patients were housed (Almyroudis et al. 2005, Ballard et al. 2008). Hospital location's renovations have been a great source of infection especially where ancillary procedures were performed such as radiology (Meerssemam et al. 2004). Contaminated air vents or filters have been a great source of aspergillosis (Maschmeyer et al. 2007, Warnock 2007). Other objects like syringes and spinal needles, a liquid nitrogen tank near the operating room (Kronman et al. 2007), gauze used to cover venepuncture sites (Laarkin et al. 1996), dressing supplies, latex finger stalls (Menotti et al. 2005), and electronic equipment in the operating room (Heinemann et al. 2004) can be the source of infection. Water exposure has been a great source of infection (Laarkin et al. 1996). Now at this time dust above acoustical ceiling tiles has been a source of infection when acoustical ceiling tiles have been removed or damaged, allowing airborne dissemination of fungal spores (Almyroudis et al. 2005). Aspergillosis is also caused by inhalation of fungal spores resulting in pulmonary disease. Dissemination from pulmonary site is well described with more than 500 cases of post-operative aspergillosis (Pasquolotto 2006). From these, most cases are due to airborne infection during surgical procedure such as cardiac surgery, ophthalmological surgery, and dental surgery. Cutaneous aspergillosis has been reported due to contaminated dressing materials (Laarkin et al. 1996). Besides above mentioned sources, animals have also been a source of aspergillosis for veterinarians and farmers as well such as poultry birds, cat, dog, etc.

5. PATHOGENESIS AND CLINICAL MANIFESTATIONS

The life cycle of *Aspergillus* infection begins with conidia production which are asexual spores that are dispersed to maintain the indoor and outdoor environment ubiquity (Falvey 2007). Humans get infected with these conidia spores via inhalation of these spores which then deposit in the bronchioles or alveolar spaces. Conidia are not removed by the primary resident phagocytes (mucociliary clearance encounter epithelial cells or alveolar macrophages) of the lungs as alveolar macrophages are responsible for conidia phagocytosis and neutrophils initiation to the site of infection. Conidia that survive from macrophage killing, germinate and become the target of infiltrating neutrophils that are responsible to destroy hyphae and infection occurs due to dysfunction in these host defences and *Aspergillus Fumigatus* growth in pulmonary environment (Morris et al. 2000).

Humans can be infected from different *Aspergillus* species from transmitted from animals. Clinical manifestations of aspergillosis in humans vary with site of infection and immune status. Respiratory aspergillosis is common when transmitted zoonotically. The manifestations range from mild allergic reactions to invasive infections like allergic bronchopulmonary aspergillosis, aspergilloma, invasive pulmonary aspergillosis (Barnes 2006). Allergic Bronchopulmonary Aspergillosis is an allergic hypersensitivity response noticed by wheezing, shortness of breath, coughing, recurrent episodes of bronchitis or asthma which leads to the lung tissue damage if not treated well (Barnes 2006). Aspergilloma is a fungal ball develops in lung cavities or damaged lung tissue and discovered on chest imaging asymptomatically (Singh 2005). Symptomatically, it appears with chest pain, chronic cough, hemoptysis and respiratory distress (Singh 2005, Barnes 2006). Invasive pulmonary aspergillosis mostly affects immunocompromised individual that's why this is called life threatening infection which can lead to pleuric chest pain, cough, fever, shortness of breath.

Cutaneous aspergillosis occurs due to direct contact of spores into the skin through burns, wounds. It results in local skin infections like ulcers, abscesses, bruises (Lee et al. 2004). In immunocompromised individuals, infection spreads from the initial site. Ocular aspergillosis occurs due to either direct inoculation of spores or dissemination from the infected site with the manifestation of keratinitis, endophthalmitis, uveitis, or orbital cellulitis with symptoms like eye redness, pain etc (Fig. 3) (Lee et al. 2004, Barnes 2006). If *Aspergillus* infection spreads from primary infection site to other organs, it is called disseminated aspergillosis. It commonly affects liver, heart, brain, kidneys, bones and it can be life threatening.

6. DIAGNOSIS AND TREATMENT

Diagnosis of every disease depends upon history, signs and lesions. The history like poor environmental conditions, severe respiratory signs or bird carcasses are indications for aspergillosis. Clinically Aspergillosis is not specific as the other infections (Dahlhausen et al. 2004). Affected birds may have white granulomatous nodules or cheesy plaques in the lungs, air sacs or other organs as diagnostic sign. Definitive diagnosis of aspergillosis is possible (Jones and Orosz 2000, Charlton et al. 2008, Beernaert et al. 2010). Different staining methods can be used to detect fungal hyphae such as Periodic Acid-Schiff, Bauer's and Gridley's, Methanamine Silver and Grocott's and Gomori stain. Furthermore, lactophenol cotton blue stain can be used to detect fungal hyphae if wet smear from specific nodules fixed with 20% potassium hydroxide stained with lactophenol cotton blue stain. Use of Parker's India ink is another way to detect fungal hyphae. Affected organs showed different structures under histopathological examination like granulomatous foci with central depressed coagulative necrosis surrounded by inflammatory cells and congestion of pulmonary and perialveolar blood vessels with perivascular edema was also diagnosed (Girma et al 2016). Samples for diagnostic purpose can be

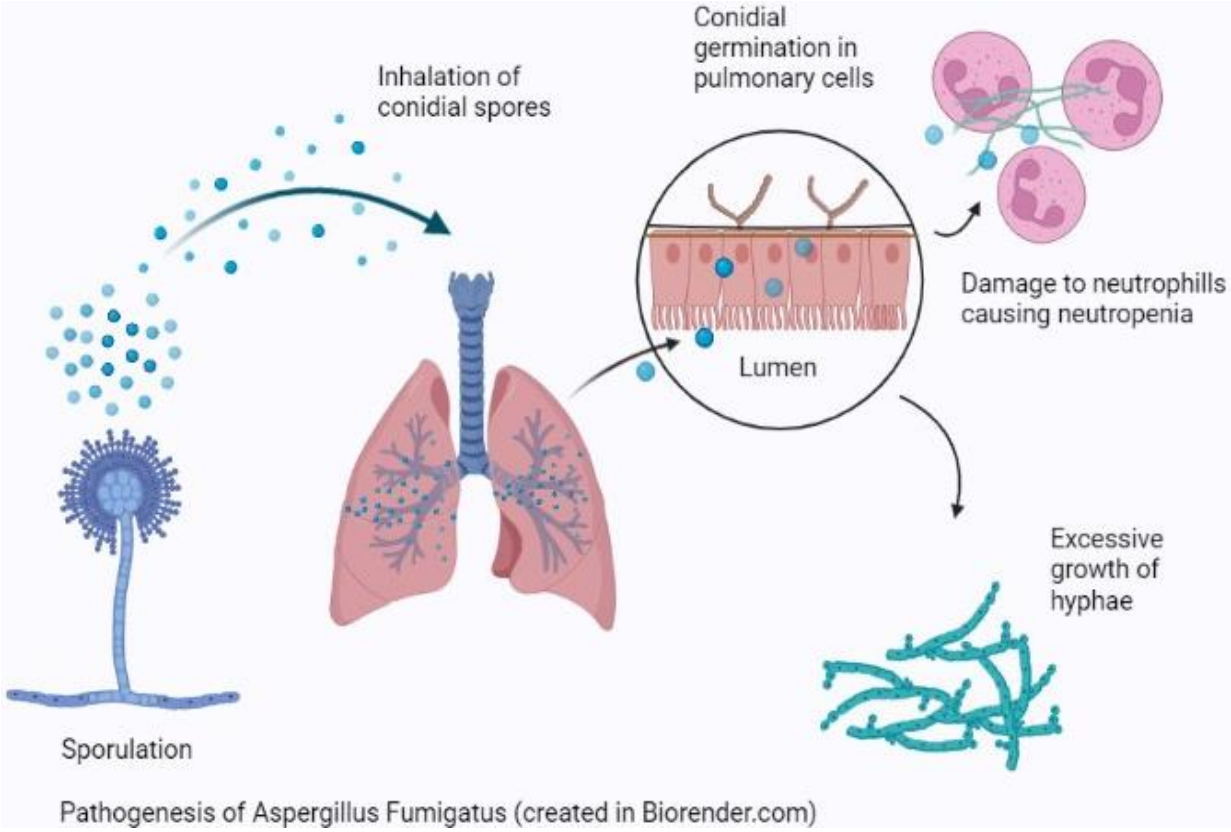

Fig. 3: Pathogenesis of *Aspergillus* infection.

selected from different affected parts of the body such as larynx, trachea, lungs, air sacs and brain and cultured on Sabouraud's dextrose agar or malt agar which are selective specific media for fungal growth and incubated at 37°C for 24 hours. By this method, characteristic conidial head and colony of fungal species can be identified (Dahlhausen et al. 2004). However, the main point should be noted that *Aspergillus* infection still appear in negative culture. Biochemical and haematological parameters are other methods to diagnose *Aspergillus* infection (Jones and Orosz 2000). Serological test can also be performed to diagnose *Aspergillus* infection such as enzyme-linked immunosorbent assay (Le Loc'h et al. 2005, Arca-Ruibal et al. 2006), immunohistochemistry (Beytut et al. 2004, Beytut 2007), galactomannan assay and plasma protein electrophoresis (Cray et al. 2006, 2009a, b). Confirmatory methods to diagnose Aspergillosis are use of monoclonal or polyclonal antibodies. Radiographically, lateral and ventrodorsal views of suspected birds can indicate the aspergillosis (Jones and Orosz 2000). If suspected birds are diagnosed endoscopically then yellowish-white plaques covered with green or grey hyphae of fungal growth can be observed in abdominal air sacs (Dahlhausen et al. 2004). Molecular techniques can also be used to diagnose aspergillosis like molecular beacon technology, polymerase chain reaction (PCR) and nucleic acid sequencing based amplification (Dahlhausen et al. 2004, Balajee et al. 2009, Saleemi et al. 2012, Zhao and Perlin 2013).

7. PREVENTION AND CONTROL

The only way to protect chickens is prevention (Arné et al. 2011). There should be strict hygienic and sanitary conditions at setters, brooders and hatcheries (Beernaert et al. 2010). It is recommended that

formaldehyde or antifungal compounds as thiabendazole (120-360 g/m3) should be used through cleaning, disinfection and fumigation (Pattisson et al. 2008). Using azoles for environmental disinfection and decontamination of bedding is common (Nawrot et al. 2019). The litter and feed should be free of contamination by controlling environmental conditions. The litter should be free from molds and replaced by clean one. However, antifungal preparations as copper sulphate or nystatin can be used to treat moldy litter. Feeders and drinkers should be cleaned and disinfected (Kunkle et al. 2003). There should be no morbid bird in the flock. In such cases there is no effect of antifungal drugs on fungus as treatment is recommended in mild and early stages of infection. Effective dose of copper sulphate is 1:2000 through water or should be given through feed for 6 days treatment along with one or more antifungal drugs such as itraconazole, miconazole, eniconazole, clotrimazole, ketoconazole, fluconazole, amphotericin B and fungicidin (Dhama et al. 2013). Due to the most of fungistatic drugs, it has been noted that there is an increase in the resistance to the classical antifungal drugs. New trends are being applied to cover such infections such as use of essential oils of some plants that have showed broad spectrum potential antifungal activities in poultry (Pinto et al. 2009, Radwan et al. 2018b, Abed et al. 2021). Different studies have shown the antifungal properties or plants essential oils (Chuang et al. 2007, Kędzia and Holerna-Kedzia 2007, Yang and Clausen 2007, Pinto et al. 2009). Complete inhibition of fungal spores has been shown by a mixture of cinnamon, lavender, rosemary and sage oil at 1% concentration (Cvek et al. 2010). However, strong suppressive activity against *Aspergillus* species have been shown by cinnamon or cinnamon fortified with cinnamaldehyde at low concentration of 0.1% (Abed et al. 2021), or a concentration of 4% (López et al. 2005). There is a study on antifungal activity of thyme essential oil and thymol against molds (Klarić et al. 2007) and the results showed the vaporous phase having long lasting antifungal activity on molds from damp dwelling. It is important to control the conditions in a proper way as wearing gloves and masks during bird handling, ventilation should be proper, and feed should be free from molds (Mubarak 2017). If the infection has been detected at farm, there should be rapid diagnosis, treatment and disposal of dead birds to reduce infection spread (Mubarak 2017).

8. OCCUPATIONAL HEALTH POLICIES

There is a great role of occupational health policies and regulations in securing the health and wellbeing of workers along with reducing the incidence of aspergillosis and other occupational diseases (Azie et al. 2012, Blot et al. 2012). There are few policies and regulations in which employers play an important role in promoting a safe working environment such as risk assessment and prevention, education and training, implementation of control measures, provision of personal protective equipments, health surveillance, and compliance and enforcement (Blot et al. 2012). Occupational health policies need employers to conduct comprehensive risk assessments and identify potential hazards in the workplace especially those related to aspergillosis (Blot et al. 2012). This procedure involves the assessment of certain factors such as ventilation systems, exposure to molds contaminated materials and personal protective equipment requirements (Blot et al. 2012, Azie et al. 2012). When employers identify these risks then they can apply preventive measures in order to minimize workers exposure to *Aspergillus* spores such as improved ventilations, proper waste management, regular cleaning and use of appropriate personal protective equipment (Becker et al. 2003) Along with identifying these risks, employers also have a great responsibility regarding provision of proper education and training to workers about aspergillosis associated risks and necessary preventive measures (Becker et al. 2003, Leeflang et al. 2008). This training includes instructions on proper use of personal protective equipments as well as proper handling, storage and disposal of molds contaminated materials

(Montagna et al. 2012). When workers are well educated then employers tell them to protect themselves from these potential exposures and promote a safe environment in the workplace. Employers are responsible to apply control measures in order to decrease the risks of aspergillosis such as repair of water leaks or damage, regular monitoring of air quality and humidity levels, proper ventilation and proper work areas (Azie et al. 2012, Blot et al. 2012, Montagna et al. 2012). By applying these control measures results in decrease in molds growth ultimate decrease in risk of aspergillosis (Becker et al. 2003, Leeflang et al. 2008, Montagna et al. 2012) . Besides these all steps, employers are also responsible to provide personal protective equipments such as respiratory masks, gloves, protective clothing to workers who exposed to *Aspergillus* spores (Becker et al. 2003, Azie et al. 2012). Personal protective equipments play an important role to create a barrier between workers and harmful materials and reduce the risk of spores inhalation. Employers should make sure the availability of properly maintained personal protective equipments for workers. Besides the implementations of control measures, occupational health policies also need employers to apply health surveillance programs to check health of workers exposed to potential hazards including *Aspergillus* spores by doing regular medical check-ups and identifying early signs or symptoms of aspergillosis for timely treatment (Leeflang et al. 2008, Montagna et al. 2012) Health surveillance also collect the data of occupational diseases for future prevention strategies. Along with other opportunities, occupational health policies and regulations also provide a platform for compliance and enforcement (Becker et al. 2003, Blot et al. 2012). Employers are responsible to follow these regulations making sure the protection of workers from occupational hazards including aspergillosis. Compliance and occupational health policies emerge a safe working environment and decreases the risk of aspergillosis.

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