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An Overview of Psittacosis

AUTHORS DETAIL

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INTRODUCTION

Psittacosis is a zoonotic infection caused by Chlamydia (C.) psittaci (Fig. 1), which is an obligate intracellular bacterium (Hans and Olivia 2016). The term 'psittacosis' originated from the Greek word psittakos, which is used for parrots and was first used by Morange in 1895 (Morange 1895). Direct contact with diseased birds primarily transmits the infection and induces a broad-spectrum of symptoms with varying severity. Psittacosis is also regarded as 'parrot fever' and 'ornithosis' and the birds are considered as a prime epidemiological reservoir for this disease (Fig. 1) Formerly, only the word 'psittacosis' was used but then, another term 'ornithosis' was proposed in order to distinguish the infection in fowls from the infection in psittacine birds.Both of these conditions are now considered similar (Andersen and Vanrompay 2008). Although infection in the birds from the order Psittaciformes (parakeets, parrots, lories, cockatoos, and budgerigars) and Galliformes (chickens, turkeys, pheasants) are more often observed, but the disease can infect every bird species. This has been reported in 467 species from 30 different orders of birds (Stewardson and Grayson 2010). Hence, bird exposure is considered as the major risk factor for its transmission to humans. The bird exposure may occur through direct contact with the diseased birds, or inhalation of aerosolized organisms in faeces, urine, eye, and respiratory secretions. The bird-human contact may happen in veterinary hospitals, pet shops, and bird shows (Halsby et al. 2014), while the person-to-person transmission of psittacosismay also happen but is occasional (Stewardson and Grayson 2010).

Etiology

C. psittaci belongs to family Chlamydiaceae, and order Chlamydiales (Kaleta and Taday 2003). The Chlamydiaceae family comprises of two genera i.e. *Chlamydophila* and *Chlamydia*. Formerly, genus *Chlamydia* was known to have nine species (Laroucau et al. 2009). But according to the revised taxonomy of Chlamydiaceae family, the genus *Chlamydia* now consists of 11 species i.e. *C. psittaci*, *C. pecorum*, *C. felis*, *C. caviae*, *C. abortus*, *C. pneumonia*, *C. suis*, *C. trachomatis* and *C. muridarum* and newly discovered species, *C. avium* and *C. gallinacean* (Sachse et al. 2014). *C. psittaci*, having multiple genotypes, is gram-negative, obligate intracellular bacteria that resides in both, birds and mammals. Successful sequencing of these genotypes by using genotype-specific real-time PCR can help in detection, as well as epidemiological research. Being animal host specific, every genotype can be transmitted to humans and can induce infection (Stewardson and Grayson 2010).

Epidemiology

Generally, psittacosis is considered sporadic (Grayston et al. 1986; Marrie et al. 1987). But, outbreaks of disease may occur as Ritter reported the first outbreak of psittacosis (Jordan and Prouty 1956). He observed seven cases of atypical pneumonia which occurred after contact with parrots and finches at his brother's house. Other early outbreaks that happened in Europe and Faroe Islands were found to have a connection with sick parrots and fulmar petrels (Grayston et al. 1986; Saikku et al. 1985; Palmer 1982). Despite the fact that all groups and genders can be affected by psittacosis, the incidence of this infection is seen to attain a peak in middle-aged people having an age of 35 to 55 years (Yung and Grayson 1988). Still, psittacosis is considered a rare zoonotic infection. Due to this reason, there is no ample awareness regarding this disease among the people and health care providers (de Gier et al. 2018). According to CDC (Centers for Disease Control and Prevention), psittacosis is a notifiable disease in the United States. The estimated reported cases are less than 10 per annum and underdiagnosis and underreporting are thought to be the reasons behind the reporting of such a small number of cases. The individuals who are more likely to have exposure to the birds are generally considered more susceptible of acquiring infection. Bird exposure may occur at veterinary hospitals, pet shops and bird exhibitions and occupational exposure can also occur in the people working in the poultry industry (de Gier et al. 2018).

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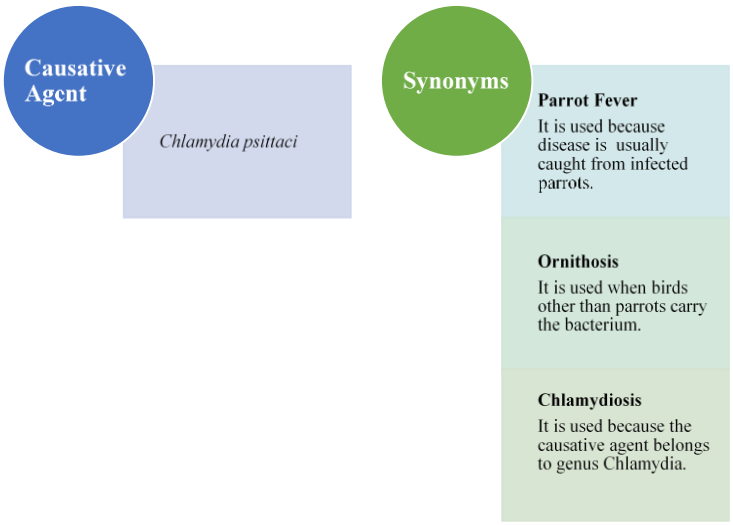

Fig. 1: Facts regarding Psittacosis.

Modes of Transmission

Bird to Bird

Psittacosis is regardedas "Avian Chlamydiosis" (AC) in birds. *C. psittaci* is found in nasal discharges and faeces of birds which harbors the infection. Sickbirds, as well as, asymptomatic birds may give out the bacteria alternatively for many months. Birds don't develop immunity against it and so, there is a chance to acquire the infection again (Balsamo et al. 2017).

Bird to Humans

C. psittaci is transmitted through the air passageway. Apart from the direct transmission through droplets, the indirect transmission of bacteria may occur by inhaling the aerosol of faeces of infected birds (Saito et al. 2005). It is reported that some patients experienced the symptoms without having ahistory of bird exposure (Ito et al. 2002) and even momentary exposures can cause symptomatic infection (Rehn et al. 2013).

Person to Person

It is believed that psittacosis is hardly transferred via direct human-to-human contact because none of the studies show evidence regarding its transmission among individuals (Hughes et al. 1997; Ito et al. 2002; McGuigan et al. 2012; Wallensten et al. 2014; Ojeda Rodriguez et al. 2022).

Other Animals to Human

Parrots and ornamental birds are usually considered as the source of psittacosis. However, some other birds and animals, like pigeons, poultry species and even mammals, have also been observed as the source of infection in humans (Haag-Wackernagel and Moch 2004; Fenga et al. 2007; Verminnen and Vanrompay 2009; Deschuyffeleer et al. 2012). *C. psittaci* transmission to humans from non-avian sources is probably not known, however, it has been reported in the case studies of some pregnant women who had a history of exposure to abortion products from sheep, abattoir workers, shepherds, and laboratory staff members (Barnes and Brainerd 1964; Anderson et al. 1978; Hyde and Benirschke 1997; Meijer et al. 2004). There are also some case reports in which humans who hadcontact with ill foals were infected with psittacosis (Chan et al. 2017). Fig. 3 shows various routes from where human may get the infection.

Pathogenesis

According to recent research employing a bovine model, C. *psittaci* initiates infection of the alveolar epithelial cells upon inoculation to the host (Knittler et al. 2014). The infection spreads due to the multiplication of bacteria within the host's epithelial cells. This elicits a host immune response resulting in a large inflow of neutrophils along with the release of chemokine and interleukin-8 (Knittler et al. 2014).

The acute-phase reaction brought about by chemokines causes the activation of an inflammatory cascade and reactive oxygen species. This further results in the recruitment and aggregation of immune cells and phagocytes from the bloodstream to the site of infection. This is considered to cause the hematogenous spread of *C.* Psittacithrough the disintegration of the alveolar-capillary membrane and tissue damage (Knittler et al. 2014). This inflammatory cascade and infection hinder the transfer of oxygen within the alveoli resulting in hypoxemia and

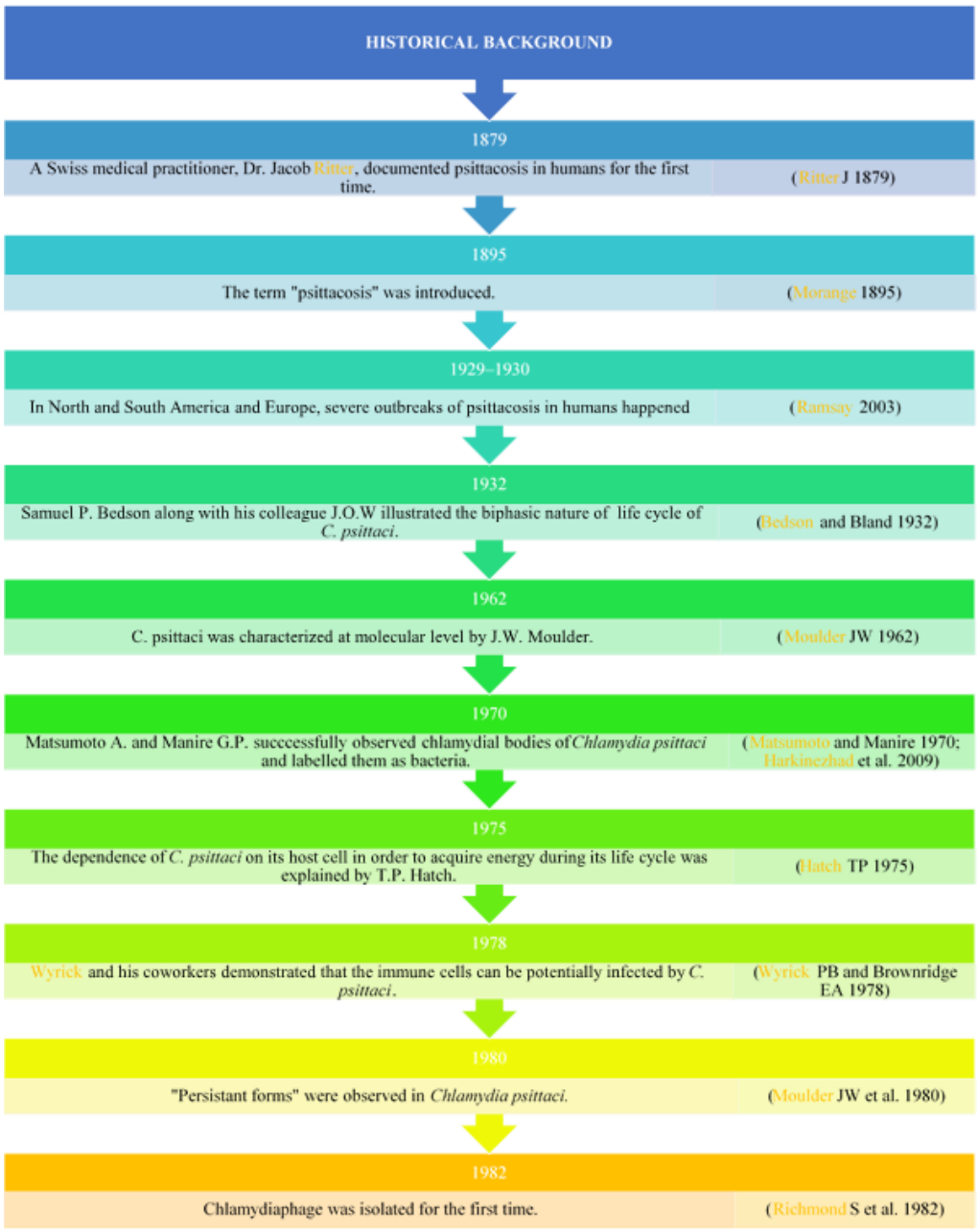

Fig. 2: A bird eye view of historical background is described.

alveolar hypoventilation (Knittler et al. 2014). The hematogenous spread of *C. psittaci* which resulted in various pathological changes in the body have been shown in Fig. 4.

Histopathology

The developmental cycle of *C. psittaci* involves two forms. The organism comprises of a larger metabolically active intracellular reticulate body and an extracellular infectious elementary body (Chu et al. 2022).

The extracellular infectious elementary body is endocytosed into the cell when it comes in contact with the cell membrane receptor of the host cell, dodging the host immune response. As a result, a metabolically active reticulate body is formed when the endocytosed elementary body increases in size (Grimes 1987; Peeling and Brunham 1996).

The reticulate bodies use host cells' ATP and form further new reticulate bodies upon binary fission. These inclusion reticulate bodies reorganize to form an intermediate state. Ultimately, elementary bodies are formed and released by

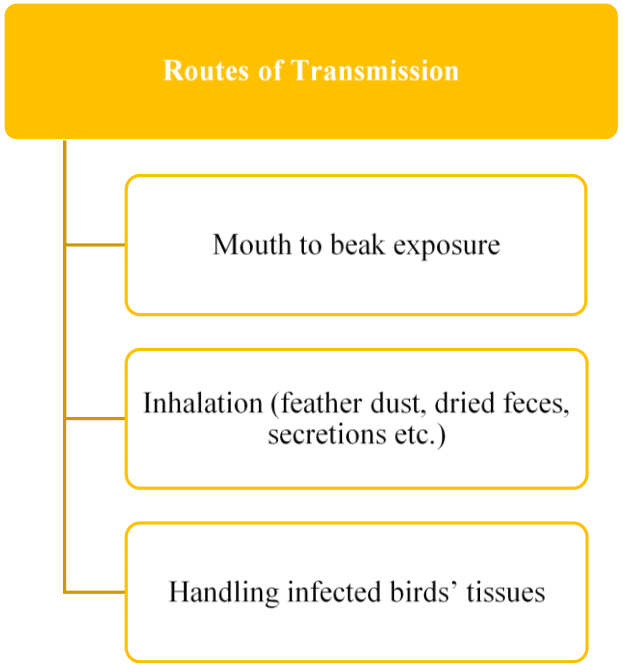

Fig. 3: Possible routes of infection transmission to humans

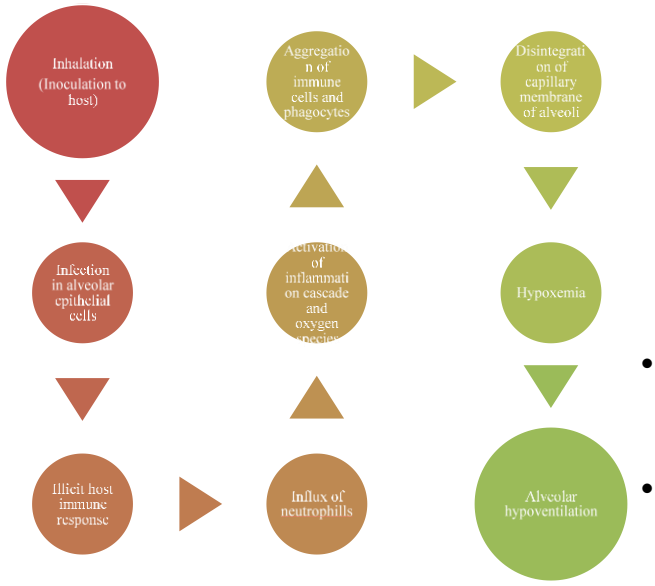

Fig. 4: Hematogenous spread of *C. psittaci* resulting in various pathological changes in the host body

cell lysis and reverse endocytosis and this release of elementary bodies are considered as a cause of silent and chronic infection (Peeling and Brunham 1996).

New host cells are infected with these released elementary bodies. In this way, the disease cycle propagates and spreads to other organ systems of the body via a hematogenous route (Vanrompay et al. 1995; Knittler and Sachse 2015). The infectious cycle of *C. psittaci* involving the formation of reticulate and elementary bodies have been shown in Fig. 5.

History of Patient

Although there is a strong connection between bird exposure and psittacosis, yet it is not compulsory for diagnosis. This is considered accuratefor areas where there is an abundance of undomesticated birds. In Australia, two outbreakshappened in the areas that were located amidst large avian flora (Williams et al. 1998; Telfer et al. 2005). Diagnosis mostly dependson taking adetailed history involving the medical history, travel history, occupation andhobbies of the patient, along withstrong suspicion of infection (Chu et al. 2022).

Clinical Manifestations

Despite the respiratory symptoms of *C.psittaci* infection in humans, there can be other clinical manifestations that can extremely differ. Infection can influence multiple organ systems as it spreads after replicating in the respiratory system. The average incubation period of infection is about 5-14 days (Beeckman and Vanrompay 2009).

The onset of symptoms is usually sudden. Headache is usually mentioned along with fever, nausea, diarrhea, cough and myalgias (Yung and Grayson 1988). Other signs of psittacosis include disoriented mental condition, photophobia, mild stiffness in the neck, hepatomegaly, splenomegaly and pharyngitis (Stewardson and Grayson 2010). Fig. 6 shows the clinical manifestation of psittacosis infection in the host.

Diagnosis

Lab Investigations

- *White Blood Cell Differential count*: Slight decrease inleukocyte count manifest initial phase of infection. Leukopenia can be noticedin the acute phase of infection (Longbottom and Coulter 2003).
- *Red Blood Cell Count*: During the course of infection, hemolysismay lead to anemia (Longbottom and Coulter 2003).
- *Liver Function Tests*: Sometimes, there can be high levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), besides gamma-glutamyltranspeptidase (GGT) (Longbottom and Coulter 2003). Elevated levels of CRP (C- reactive protein) can also be observed (Longbottom and Coulter 2003).
- *Culture*: *C. psittaci* is isolated from respiratory tract secretions (sputum, throat swab etc.) and can be cultured on Minimum Essential Medium (MEM) (Favaroni et al. 2021).
- *Serology*: This method is usually applied to confirm psittacosis. Following serological tests are available for diagnosis of psittacosis:

Microimmunofluorescence Test: IgG-specific and IgM-specific antibodies are detected by MIF test.

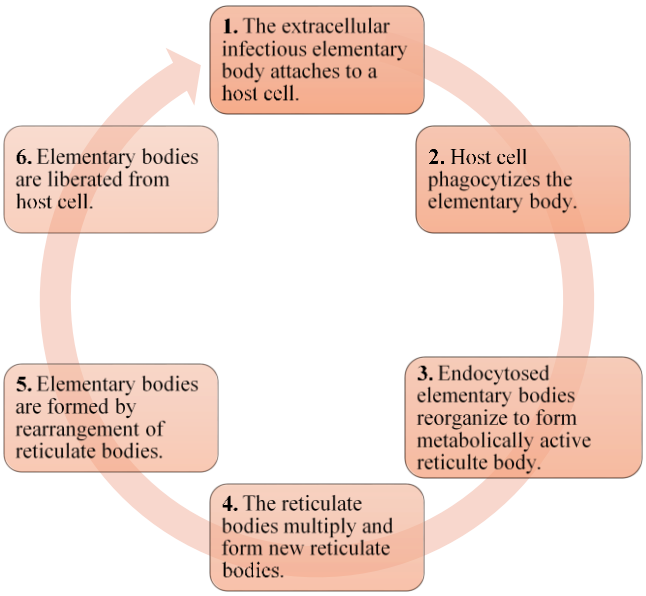

Fig. 5: Infectious cycle of *C. psittaci*

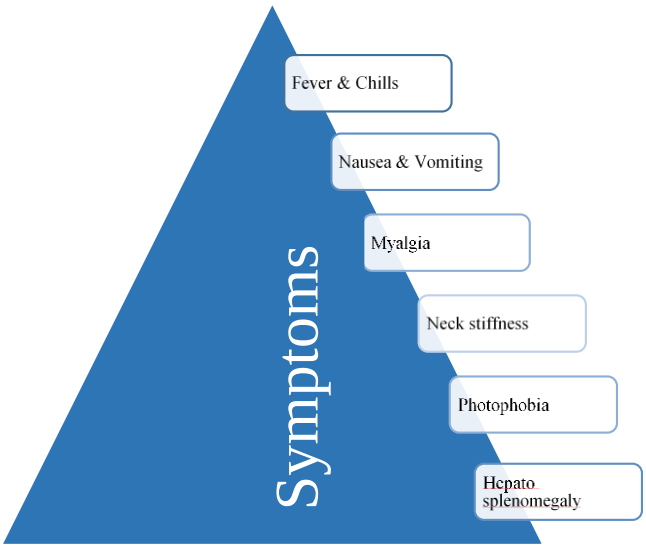

Fig. 6: Clinical manifestation of psittacosis infection

In the initial stage of diagnosis, there is a positive result of IgM. The positive rate may reach up to 80–95 % (Mi et al. 2015).
Complement-fixation test (CFT): If paired serum titers elevate at a four-time speed while detecting specific antibodies then a diagnosis is required (Mi et al. 2015).
Microimmunofluorescence (MIF) is considered more sensitive than the complement-fixation test (CFT) (Mi et al. 2015).

Imaging:

- *Chest X-Ray*: Around 80% to 90% of patients exhibit abnormal chest x-rays. These involve migratory infiltrates and pleural effusions (Yamato et al. 1992).

Magnetic Resonance Imaging (MRI): MRI is usually advisedfor diagnosing neurological issues associated with psittacosis (Mi et al. 2015).

Nucleic Acid Amplification

PCR helps in the rapid detection of psittacosis patients as it allows us to find out the source of infectionby genotyping. It is highly sensitive only in the acute phase and is mild in chronic cases (Nieuwenhuizen et al. 2018).

Prognosis

The prognosis of psittacosis may be influenced by the severity of clinical disease and the comorbidities of the patient. In addition to this, prognosis also relies on the duration of treatment and management. (Hogerwerf et al. 2017). The mortality rate is approximately 1%, despite of antibiotics treatment (Chin 2000).

Treatment

Psittacosis is primarily treated by antibiotics. Tetracycline and doxycycline are two antibiotics that are usually recommended and considered effective against this disease without contraindications. Most patients show improvement within48 hours (Yung and Grayson 1988). Intravenous doxycycline can be used in cases where antibiotics cannot be administered orally. The recommended dosage of doxycycline is 100 mg PO or IV for 10 to 14 days. Azithromycin can also be used ininfants. Erythromycin and azithromycin are recommended for pregnant patients and can also be used in cases where doxycycline is contraindicated (Chu et al. 2022).
Fluoroquinolonescan also be prescribed at times but these are less effective than tetracyclines and azithromycin (Chu et al. 2022).

Differential Diagnosis

There aremany disorders which may have similar symptoms as psittacosis or parrot fever. A comparison can be beneficial for differential diagnosis. The differential features of psittacosis infection have been mentioned in Table 1.

Complications

The psittacosis-infected patients may present several manifestationsas a consequence of its hematogenous spread after the first inoculation. *C. psittaci* infection may lead to respiratory failure, hepatitis, pneumonia, pancreatitis, endocarditis, DIC (Disseminated Intravascular Coagulation) and encephalitis. The fulminant course of psittacosis may lead to multiple organ failures (Chu et al. 2022).

Table 1: Differential Features of Psittacosis Infection with Various Other Disorders

References		(Moghadami 2017)	(HamidrezaHonarmand 2012; BiyankaJaltotage et al. 2021)	(Ticona et al. 2021; Jain et al. 2022)	(Penn 1994; Yeni et al. 2021)	(Yagupsky and Baron 2005)
Signs	Pericarditis	✓	✓	✓	✓	✓
	Hepatomegaly	✗	✓	✗	✓	✓
	Leukopenia	✗	✗	✗	✗	✗
Symptoms	Myalgia (muscle pain)	✓	✓	✓	✓	✓
	Malaise	✓	✓	✓	✓	✓
	Fever and chills	✓	✓	✓	✓	✓
	Abdominal pain	✓	✓	✓	✓	✓
	Nausea and vomiting	✓	✓	✓	✓	✓
Differential diagnosis of Psittacosis		Influenza	Q fever	Pneumonia	Tularemia	Brucellosis

Prevention and Control

There are no vaccines available so far against this infection (Stidham et al. 2019). So, for now, strategies for minimizing the spread of these bacteria are the only way to control the disease (Smith et al. 2005). Therefore, people should be guided in dealing with birds and birdhouses in order to restrictthe spread of disease (Schlossberg et al. 1993). The use of personal protective equipment (PPE) such as gloves, masks, etc. must be assured while dealing with diseased birds and their cages. The veterinarians and healthcare providers must be consulted if the birds are doubted for carrying the infection (Chu et al. 2022).

Public Health Significance

Psittacosis, being zoonotic in nature (Gaede et al. 2008; Andersen and Vanrompay 2000; Seth-Smith et al. 2011), has distinct importance in public health, as parrots are kept in our houses, in schools and nursing homes on regular basis (OIE Terrestrial Manual, 2008). Proper knowledge and guidance about the clinical signs and course of the diseaseshould be provided to people who are susceptible of acquiring disease, along with the healthcare professionals (Balsamo et al. 2017). This must cover the public awareness aspect regarding the proper handling of birds, the use of personal protective equipment, and disposable particulate respirator usage. In order to figure out the sources of disease, there should be coordination between the healthcare personnel and the public health department for the guidance of industry and the public in tracking down all the dealings involving birds. The sick birds should be tagged, quarantined and isolated along with the implementation of appropriate cleaning and infection preventive guidelines (Balsamo et al. 2017). All these suggestions highlight the importance of general public awareness and the role of health care providers in the control of this zoonotic disease. So, an initiative involving general public awareness and cooperation between veterinarians and public health authorities is highly required for the prevention of this disease (Chu et al. 2022).

Future Perspectives

On-time reporting of disease and development of commercial vaccines are the biggest challenges related to psittacosis in future, as no human or avian vaccines are developed and commercialized yet. However, immunization with genetically modified DNA plasmid consisting of *C. psittaci* ompA gene induced partial immunity in SPF (specified pathogen free) budgerigars and turkeys. DNA immunization can be done even if maternal antibodies are present which triggershumoral and cell-mediated immune responses similar to those in usual body infections. So, it is high time that safe and effective vaccine against psittacosis must be developed. Studies have also shown the effectiveness of ovotransferrin against *C. psittaci*, when administered in turkeys. It potentially decreased the concentration of bacteria in the air and significantly lowered the mortality rate. So, the administration of ovotransferrin (OvoTF) in poultry is suggested as it can be a groundbreaking antimicrobial approachin near future (Van Droogenbroeck et al. 2011).

Conclusion

Increasing incidence of various zoonotic infections is one of the burning issues around the globe. However, psittacosis as a zoonotic disease is still overlooked. It is regarded as a reportable disease in many countries but still, it is an underreported condition. Even the usual laboratory investigationsdo not involve the diagnostic tests required for psittacosis. Moreover,the serological tests cannot give confirmatory diagnosis if a single serum sample is provided. The proportion of reported cases as compared to the actual ones is very low. So, we can say that the estimated impact of psittacosis on public health is still not clear.The bird-human contact is undeniable as man has been domesticating birds for ages. Moreover, the expansion of poultry industry over the past few years has made this contact more often but bird owners, public, poultry farmers and even medical practitioners have insufficient understanding of this infection. Therefore, raising general awareness for psittacosis is required which will promote the timely

reporting of this disease. Devising effective vaccines and specific diagnostic strategies are the needs of time and required to control this zoonosis.

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