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17 Mycoplasma Roles in Disease + Treatment, Prevention

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CONTENTS

Sixteen *Mycoplasma* species are found in humans, but not all may cause human disease. Learn about the many health complications of infection, plus treatment and prevention methods, here.

What is Mycoplasma?

Mycoplasmas are the smallest free-living microorganisms [1, 2].

They belong to a class of bacteria called *Mollicutes*. Their name,

[4].

Mycoplasmas have extremely small genome [5].

Due to these features, *Mycoplasmas* require specific conditions for their growth and depend on the host for survival [6].

Role in Human Disease

More than 200 *Mycoplasma* species have been identified in humans, animals, and plants [7].

16 *Mycoplasma* species are found in humans but only a few have been proven to cause human disease [8].

Several *Mycoplasma* species including *M. salivarium, M. orale, M. buccale, M. faucium,* and *M. lipophilum* are normally found in the mouth and throat without causing disease [8].

Of the *Mycoplasma* species known to infect man, *M. pneumoniae* is the best-known cause of respiratory tract infections [9].

They can also infect organs other than the lungs, including the nervous system, joints, skin, kidneys, heart, muscles, eyes, and blood [10, 11, 12, 13].

These infections can be seen before, during, or after lung disease or can occur without respiratory illness. *Mycoplasma hominis*, *Mycoplasma genitalium,* and *Ureaplasma urealyticum*, commonly found in the urinary and genital tracts, have also been found to cause human disease [14].

1) Respiratory Disease

M. pneumoniae

M. pneumoniae, initially known as “Eaton’s agent,” causes lung infection [15, 16, 17, 18].

Infection is most frequent in children from 5 years of age to young adults [19, 20].

The outbreaks occur in closed communities such as families, military bases, hospitals, and schools because close contact is needed for the spread of infection [7, 21].

Worldwide epidemics occur in children and adults every 3 to 5 years, most commonly in late summer or early fall [4, 7].

Approximately 20% of infected persons have no symptoms. Around 75% have mild respiratory illnesses including chest cold (tracheobronchitis) and inflammation of the windpipe (tracheitis). Only 3 – 10% of patients develop atypical pneumonia, also called “walking pneumonia” [22, 19].

Mycoplasma causes 15% -20% of all pneumonias, and up to 40% of community-acquired pneumonias [23, 20].

People who have walking pneumonia are rarely confined to a bed or need to be hospitalized. Some may even feel well enough to go to work and carry on with other daily activities.

M. pneumoniae is spread through contaminated droplets from person to person by sneezing or coughing [24].

Symptoms include fever, headache, cough, sore throat, chills, muscle aches, and weakness. These symptoms develop slowly

- Vaginal infection (bacterial vaginosis) [53]
- Pelvic inflammatory disease [54, 55, 56, 57]
- Infertility [58]
- Sexually acquired reactive arthritis [51, 59, 60]
- Preterm birth [61, 62]
- Spontaneous abortion [63]
- Postpartum (after childbirth) and postabortion fever [64, 65]

3) Arthritis

Mycoplasma is associated with arthritis, rheumatoid arthritis, and sexually transmitted reactive arthritis [66, 67, 59].

Bone, joint, and muscle complications occur in approximately 14% of patients with acute *M. pneumoniae* infection [68].

U. urealyticum and *M. hominis* also caused septic arthritis in patients with a compromised immune system (hypogammaglobulinemia) [69, 70, 71].

A Canadian study showed an association between *M. pneumoniae* infections and juvenile rheumatoid arthritis in children [72].

causing patients to complain of chest soreness from protracted coughing [25, 26].

Earache occurs in about 30% of patients, but inflammation of the ear canal (otitis externa) and inner ear (otitis media and bullous myringitis) are rare [27, 1].

Children under 5 years of age are most likely to have symptoms of the common cold and wheezing (a whistling sound while breathing) [27].

Older children aged 5 to 15 years are more likely to develop pneumonia [28, 29].

Severe pneumonia, with multiple organ involvement and death, occurs in 0.5 – 2% of all M. pneumoniae pneumonia cases [30].

Children with an impaired immune system have a greater risk of developing more severe pneumonia [31].

Studies suggest that severe disease can also occur in otherwise healthy children and adults of all ages [1, 32].

Almost 50% of severe pneumonia cases occurred in patients aged 20 – 49 years, and 13.5% occurred in people over 70 years old [30].

M. pneumoniae infection may play an important role in the occurrence of asthma.

It can precede the onset of asthma, worsen symptoms, and cause difficulties in controlling asthma [33, 34, 35].

A study found that *M. pneumoniae* was the cause of asthma attacks in 50% of hospitalized children, and was a worsening

6) Heart Disease

Heart complications associated with *M. pneumoniae* occur in 1 – 8.5% of people with infection [90].

The most frequent cardiovascular complications of *Mycoplasma* infection include inflammation of the heart (myocarditis) and a sac surrounding the heart (pericarditis), heart failure, and accumulation of fluid around the heart (pericardial effusion) [68, 91, 90].

In addition, patients following heart surgery developed inflammation of the inner lining of the heart (endocarditis), including heart valves, caused by *M. hominis* [92, 93, 94].

Mycoplasma infection can also lead to a heart attack in rare cases [95].

7) Fatigue

Mycoplasma infection has been detected in about 50% of patients with chronic fatigue syndrome (CFS) and/or fibromyalgia [96, 97].

In a European study, 68.6% of patients with CFS were infected with *Mycoplasma*, compared to 5.6% healthy subjects [98].

Most patients recover after long-term antibiotic therapy, and the infection cannot be detected after recovery [99].

One study suggested that *Mycoplasma* could be responsible for a large number of cases among veterans [101].

In studies on hundreds of veterans, approximately 40-50% of Gulf War Illness patients show evidence of *Mycoplasma* infections compared to 6-9% in non-deployed, healthy subjects [102].

Gulf War Illness was also transmitted from veterans with Gulf War Illness to immediate family members. 77% of spouses and 65% of children had similar health complaints as the veterans [103].

9) Lyme Disease

Around 75% of chronic Lyme disease patients appear to have *Mycoplasma* infections, and yet *Mycoplasma* is often overlooked in the diagnosis and treatment of this condition [104].

Most symptoms that occur due to Lyme disease – such as fever, chills, headache, neck, muscle and joint pain, neurological symptoms, conjunctivitis, rash, and sleep problems – may also be caused by *Mycoplasma* [105].

10) Kidney Disease

Kidney complications associated with *M. pneumoniae* are rare and usually present as acute tubulointerstitial nephritis, kidney failure, and IgA nephropathy [106, 107, 108].

M. hominis is involved in approximately 5% of cases of acute pyelonephritis in humans [109, 110, 111].

U. urealyticum can induce the formation of kidney stones [112, 113].

11) Gut Disease

12-44% of patients with *M. pneumoniae* pneumonia have poor appetite, nausea, vomiting, or diarrhea [27, 114].

Rarely, inflammation of the liver (hepatitis) and pancreas

M. fermentans has been found in the throats of 16% of children with community-acquired pneumonia [39].

It has also been detected in previously healthy adults who presented with an influenza-like illness that sometimes progressed into respiratory distress syndrome [40].

2) Genital Tract Infections

Infections caused by *M. hominis*, *M. genitalium*, and *U. urealyticum* are sexually transmitted infections [41, 42].

According to the study, *M. genitalium* infection was more common in people who had at least 4 new sexual partners in the past year compared to people who had 1 or less [43].

M. genitalium and *U. urealyticum* cause inflammation of the urethra (urethritis) in men [44, 45, 46].

Men with infection experience burning, painful urination and discharge from the penis [44, 47, 48].

In women, *M. genitalium* is associated with cervical and urethral infection [49, 50].

40 – 75% of women with infection do not have any symptoms [50, 51].

Women experiencing symptoms have abnormal vaginal discharge, painful urination or urgency to urinate, and rarely, bleeding between menstrual periods or after sexual intercourse [50, 51, 52].

12) Blood Disease

M. pneumoniae has been linked to hemolytic and aplastic anemia, thrombotic thrombocytopenic purpura, arterial thrombosis, and Reynaud's syndrome [68, 88].

Severe infection leading to fatal disseminated intravascular coagulation has also been reported [118].

13) Eye Disease

Eye infections caused by *Mycoplasma* are occasionally seen in children, and include conjunctivitis, anterior uveitis, optic neuropathy, retinitis, iritis, and optic disk swelling, with or without permanent damage of vision [68].

14) Infection in Patients with Compromised Immune System

Patients with disorders of antibody production appear to be the most susceptible to *Mycoplasma* infections [100, 119].

M. hominis causes suppurative arthritis in individuals with hypogammaglobulinemia Reduced number of antibodies in the blood) [120].

Also, patients who undergo organ transplantation or treatment of malignant diseases have an increased risk for *Mycoplasma* infections [100, 121, 122].

Mycoplasma may cause deep wound infections that occurred shortly after kidney transplantation [123].

15) Autoimmune Disease

According to some researchers, the similarity between the *Mycoplasma* and human cell membranes may promote the production of autoantibodies that attack the host and result in autoimmune disease [124].

Mycoplasma infections have been linked to the progression of

However, a causal link has not yet been established between *Mycoplasma* and autoimmunity.

16) AIDS

M. fermentans, *M. penetrans,* and *M. pirum* are the most common species of *Mycoplasma* associated with AIDS.

These microorganisms may accelerate the progression of HIV infection [128, 129].

A study showed that African women who are infected with *M. genitalium* are two times more likely to acquire HIV infection [130].

M. fermentans may also cause kidney and neurological complications in patients with AIDS [131, 132].

M. penetrans is linked to Kaposi's sarcoma in homosexual men with AIDS [133].

17) Cancer

Experimental studies showed that *Mycoplasma* can cause changes in chromosomes and cells [100], potentially leading to cancer development.

Mycoplasma infection has also been linked to prostate cancer [134, 135, 136].

Studies suggest a possible role of *Mycoplasma* infection in childhood leukemia, kidney, ovarian, and breast cancer [137, 138, 139, 140, 141].

Mycoplasma was present in 55% of cases of gut carcinoma, including colon and gastric carcinoma [142].

Pathogenesis of *Mycoplasma* Infections

Development of *Mycoplasma* infection includes several factors:

Neurological complications include inflammation of the brain (encephalitis), spinal cord (myelitis), nerve roots (polyradiculitis), and membranes lining the brain and spinal cord (meningitis), psychosis, coma, and cerebellar syndrome [10, 75].

Also, cranial nerve palsy, brachial plexus neuropathy, ataxia, choreoathetosis, and ascending paralysis (Guillain-Barre syndrome) have been described [76, 77, 78].

In addition, acute transverse myelitis and acute disseminated encephalomyelitis can result in some of the most severe complications associated with *Mycoplasma* infection [79].

Studies also reported cases of neonatal meningitis and brain abscess caused by *M. hominis* [80, 81, 82, 83].

5) Skin Disease

Skin complications occur in approximately 25% of patients with *M. pneumoniae* infections [4].

Rashes (erythematous maculopapular, vesicular rashes), Stevens-Johnson syndrome, erythema nodosum, and ulcerative stomatitis commonly occur [4, 84, 85, 86].

In a study, *M. pneumoniae* caused 42.1% of erythema multiforme cases [87].

Some studies suggest that 7% of cases of *M. pneumoniae*

M. genitalium are the best-studied adhesins in *Mycoplasma* [143, 144].

This close attachment prevents bacteria from being removed by the normal clearance mechanisms of the host's respiratory and genitourinary tract [145, 146].

Toxic Metabolic Products

The close association of the *Mycoplasma* cells and the host cells increases the production of toxic products (hydrogen peroxide and superoxide) that damages host tissues [145].

Mycoplasma also inhibits the host cell enzyme catalase, further increasing peroxide concentrations [147].

M. pneumoniae produces a unique community-acquired respiratory distress syndrome (CARDS) toxin that is important in developing lung disease [148].

Immune System Changes

Mycoplasma can activate macrophages, B-cell differentiation, and antibody production (149, 145, 150).

They can cause white blood cells to produce cytokines IL-1, IL-2, IL-4, IL-6, and TNF-alpha, which leads to either increased or decreased function of the immune system [145, 147, 151].

Mycoplasma can also avoid detection by the immune system by changing the composition of its cell membrane to imitate the host cell membrane [152].

The similarity between the *Mycoplasma* and human cell membranes may cause the body to make autoantibodies that attack the host and produce autoimmune disease [124].

Diagnosis of Mycoplasma Infections

Patient symptoms, physical examination, radiology procedures and laboratory findings along with additional serologic and culture tests lead to an accurate diagnosis [1, 153].

urogenital specimens [154].

A culture of ***M. pneumoniae*** from clinical samples such as nose and throat swabs or sputum was considered standard for diagnosis several years ago [155].

However, the organism usually takes 2 to 3 weeks to grow, it requires specialized and expensive growth media, and the sensitivity of cultures may be as low as 60-70% [156].

Therefore, the culture method is rarely used for routine diagnosis of *M. pneumoniae* infections in specialized laboratories and should be done for epidemiological reasons [156].

Culture is rarely successful for ***M. genitalium*** [154].

Serology

Serologic tests are simple and very often used to diagnose ***M. pneumoniae*** respiratory infections [157].

Serologic tests measure **antibodies** specific for *M. pneumoniae* to show the presence of infection [157].

In all serologic tests, two blood specimens are collected 2 – 4 weeks apart, one taken in the acute and one in the convalescent stage of the illness. A fourfold rise in antibody level (titer) indicates recent infection [158].

Serologic tests include:

- **Complement fixation test**

Antibody levels do not peak until 4 – 6 weeks after infection. Since antibodies may persist for up to 1 year, a sustained high level of antibodies does not necessarily indicate a current infection [155].

- **Cold agglutinin test** (frequently used to confirm the diagnosis)

pneumoniae infection, a presumptive diagnosis can be made [159].

- **ELISA** (Enzyme-Linked Immuno Assay) and **IFA** (immunofluorescence assays)

ELISA is used for the detection of IgM (shows the presence of acute infection) and IgG (shows prior exposure, remains positive for years) antibodies [160].

Antibodies can be detected after about 1 week of illness, and peaks at 3 – 6 weeks and then declines gradually.

Molecular Methods

Development of molecular methods such as polymerase chain reaction (PCR) assays improved diagnosis of *Mycoplasma* infection in pediatric and adult patients [161, 162].

Many studies have described the use of different molecular methods among which real-time PCR has both high sensitivity (true positive rate) and high specificity (true negative rate) [153].

Real-time PCR may detect *Mycoplasma* in 60 – 100% of people with the infection, and report an absence of infection in 96.7 – 100% of healthy people. In practical terms, this means that the PCR technique is extremely unlikely to report an infection in someone who doesn't have one, but it has up to a 40% chance of reporting no infection in someone who is infected [163].

The PCR technique is practically the only method for detection of *M. genitalium* [164].

Diagnosis is made only through nucleic acid amplification testing (NAAT), but there are no commercially available diagnostic tests [165].

Treatment

Mycoplasma infection is treated with certain types of antibiotics.

depends on the efficacy of the host immune system.

Macrolides, such as erythromycin, clarithromycin, and azithromycin are the treatment of choice for *M. pneumoniae* infections in both adults and children [4, 28, 167].

Resistance to macrolides has been emerging and increasing in *M. pneumoniae* since 2000, especially in Asia [168, 169].

Several Japanese studies have reported that 20 – 40% of strains are resistant to macrolides [153, 168].

Tetracyclines, fluoroquinolones (levofloxacin) and ketolides have also been effective in treating *Mycoplasma* infection [4, 170, 167].

In the past, tetracyclines have been effective against both *M. hominis* and *U. urealyticum*, but resistance has developed. Clindamycin is an alternative to the tetracyclines [171].

Antibiotic therapy typically lasts 10-14 days. **If your doctor prescribes a course of antibiotics, it is extremely important to finish the whole prescription, even if your symptoms disappear after the first few days.** Failure to complete treatment may increase the risk of antibiotic resistance in the pathogen.

Prevention

Different types of vaccines against *Mycoplasma* have been tested but none are presently available [27].

Like many respiratory diseases, *M. pneumoniae* infection may be prevented by taking simple precautions [172]:

- Cover mouth and nose with a tissue when coughing or sneezing.
- Cough or sneeze into upper sleeve or elbow, instead of hands, if a tissue is not available.
- Wash hands often with warm water and soap for at least 20 seconds.
- Use an alcohol-based hand rub if soap and water are not

Parenthood).

- Not having sex until you and your partner have completed antibiotic treatment, if necessary.
- A follow-up test to confirm that treatment has cleared the infection.

As is the case with the discovery of any sexually transmissible disease, all past sexual partners need to be contacted, tested and, if needed, treated.

About the Author

Dr. Puya Yazdi is a physician-scientist with 14+ years of experience in clinical medicine, life sciences, biotechnology, and nutraceuticals.

As a physician-scientist with expertise in genomics, biotechnology, and nutraceuticals, he has made it his mission to bring precision medicine to the bedside and help transform healthcare in the 21st century.He received his undergraduate education at the University of California at Irvine, a Medical Doctorate from the University of Southern California, and was a Resident Physician at Stanford University. He then proceeded to serve as a Clinical Fellow of The California Institute of Regenerative Medicine at The University of California at Irvine, where he conducted research of stem cells, epigenetics, and genomics. He was also a Medical Director for Cyvex Nutrition before serving as president of Systomic Health, a biotechnology consulting agency, where he served as an expert on genomics and other high-throughput technologies. His previous clients include Allergan, Caladrius Biosciences, and Omega Protein. He has a history of peer-reviewed publications, intellectual property discoveries (patents, etc.), clinical trial design, and a thorough knowledge of the regulatory landscape in biotechnology.He is leading our entire scientific and medical team in order to ensure accuracy and scientific validity of our content and products.

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