

Respiratory Tract Infections Learning Guide

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Module 1: Etiology and pathophysiology

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Preface

The Thermo Fisher Scientific series of learning guides seek to present comprehensive but carefully curated information on the most common infections, with a focus on material that is most relevant to laboratory professionals. Infectious disease specialists and other frontline healthcare providers may also find the series useful.

The body of scientific literature on respiratory tract infections is as vast as the diversity of microorganisms it seeks to describe. This learning guide aims to present currently accepted scientific facts on respiratory tract infections while appreciating that this knowledge, like the pathogens central to our discussion, is constantly evolving.

How to use this learning guide

This Learning Guide comprises four modules of educational content regarding various respiratory pathogens, and an appendix of supplementary material. Each module begins with learning objectives for the reader. After each module, the reader will find a self assessment to test their knowledge. Complete the self assessment and move on to the end of the document to find the correct answers.

The primary objectives of this learning guide are twofold. First, it presents foundational knowledge regarding viral, bacterial, fungal, and parasitic respiratory infections before shifting to more in-depth discussion of these infections, in a format of four modules: Etiology and Pathophysiology, Clinical Practice, Testing Strategies and Initial Workup, and Public Health Surveillance. Second, it serves as an overview of the most important topics to professionals involved in laboratory testing for various respiratory infection diagnosis, screening, and surveillance.

Although designed with the clinical laboratorian in mind, this learning guide provides valuable content for diverse stakeholders such as healthcare advisors, healthcare providers, bacteriologists, virologists, epidemiologists, and public health officials who are managing respiratory infections.

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Module 1: Etiology and pathophysiology

Introduction

- Module 1 gives an overview of the pathogens that cause respiratory tract infections and the conditions associated with them
- Module 2 describes the clinical presentation of respiratory infections and how these infections are managed by clinicians
- Module 3 presents an overview of testing for respiratory tract infections, including how tests are typically used in patient care
- Module 4 details surveillance of respiratory infections for public health purposes and how surveillance data are disseminated

Module 1: Etiology and pathophysiology

Chapter 1. Overview of respiratory pathogens

- 1.1 Classification and characteristics of pathogens
- 1.2 Common pathogens
- 1.3 Other important pathogens

Chapter 2. Introduction to respiratory infections

- 2.1 Upper and lower respiratory tract
- 2.2 Mechanisms of pathogenicity
- 2.3 Transmissibility
- 2.4 Modes of transmission
- 2.5 Populations at-risk of severe infections



Chapter 1. Overview of respiratory pathogens

By the end of this chapter, you will be able to

- Name the major classifications of respiratory pathogens
- 2 Describe characteristics of common respiratory pathogens



According to the World Health Organization (WHO), respiratory infections are the leading cause of disease burden worldwide, measured by years lost through death or disability.



1.1 Classification and characteristics of pathogens

 Viruses cause the majority of respiratory tract infections worldwide, including the common cold and influenza

Respiratory viruses are a significant global health concern:

- In the 1918 influenza pandemic, an estimated 500 million people or one-third of the world's population at that time became infected with an H1N1 influenza virus, leading to more than 50 million deaths worldwide
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As of February 2022, the SARS-CoV-2 virus had led to more than 380 million cases of COVID-19 with an estimated 5.7 million deaths



During the 1918 influenza pandemic, street car riders wore masks as a precaution against infection. Seattle, Washington (ca.1918).

1.1 Classification and characteristics of pathogens

Bacterial pathogens tend to cause more severe illnesses of the respiratory tract, namely pneumonia and tuberculosis.

Certain bacterial respiratory infections become severe on the bases of other **chronic lung diseases** such as asthma, cystic fibrosis, and chronic obstructive pulmonary disease (COPD).

Tuberculosis is a **chronic disease** caused by the bacillus *Mycobacterium tuberculosis* while most pneumonias are **acute infections**

These infections commonly include Haemophilus influenzae, Streptococcus pneumoniae, Staphylococcus aureus, and Pseudomonas aeruginosa.

Respiratory illnesses may also result from **fungal and parasitic infections**, particularly among immunocompromised individuals.

1.2 Common viral pathogens

There are many common viral pathogens that can cause severe respiratory infections.



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These viruses are significant globally because of high mutation rates, seasonal variation, and a limited window of treatment in which anti-viral therapies are effective.

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1.2 Common bacterial pathogens

Bacterial pathogens can also cause severe respiratory infections.





Mycoplasma pneumoniae



Legionella



<u>Mycobacterium</u> <u>tuberculosis</u>



Methicillin-resistant Staphylococcus aureus

1.3 Other important pathogens





<u>Fungi</u>

Aspergillus, cryptococcus, pneumocystis, and endemic fungi are the major pulmonary fungal pathogens. The primary parasites affecting the respiratory system are **helminthic** and **protozoal** pathogens.

Parasites

Chapter 2. Introduction to respiratory infections

By the end of this chapter, you will be able to

- Identify differences in disease severity between the two regions of the respiratory tract
- 2 Describe the four stages of pathogenesis
- 3 Name factors that influence the transmissibility of respiratory infections
- 4 Define the populations who are most at-risk of severe infections



Worldwide, an average adult may have between two and five respiratory tract infections each year and a child may have as many as six to eight episodes annually.

2.1 Upper and lower respiratory tract

- The respiratory tract allows for airflow during ventilation, starting from the nose and mouth and extending to the end of the alveolar sacs
- The respiratory tract can be subdivided into the upper respiratory tract and the lower respiratory tract



Upper respiratory tract infections such as the common cold are usually mild and self-limiting. A small percentage of cases can progress to more severe lower respiratory tract infections such as bronchiolitis and pneumonia.

Lower respiratory tract infections are the third leading cause of death in the world after heart disease and stroke. They are the leading cause of death in countries of low economic status.

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2.2 Mechanisms of pathogenicity

Pathogens go through six stages of pathogenesis as they attempt to establish a respiratory infection:



1. Encounter new host



2. Adhere to host surface



3. Invade host tissues



4. Damage host cells and tissues



5. Navigate host's immune response

If the host's immune response does not deter the pathogen





6. Establish infection

2.3 Transmissibility

Transmissibility is a measure of how easily a pathogen spreads from person to person. It is determined by many factors, including the five shown below:



The **amount** of transmitted "infectious units", where the **amount** is the sum of the transmitted pathogens; an infectious unit correlates to the infectivity of the pathogen



The **contagiousness** of the infected individual, which correlates to the amount of transmitted "infectious units"



3

The **contact patterns** between the infected individual and the exposed individual, including the efficiency of pathogen transfer and the duration of transfer



The susceptibility of the exposed individual



The **environmental stress** exerted on the pathogen during transmission, such as UV radiation or ventilation

2.3 Transmissibility

The transmissibility of respiratory pathogens varies seasonally and geographically, which also depends upon seasonal behavior, such as indoor activities during colder months:

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Darker color saturation correlates to the peak times of transmissibility.

2.4 Modes of transmission

Most commonly, viruses and bacteria involved in respiratory tract infections are transmitted between host organisms via **four major modes of transmission**:

DIRECT CONTACT

Physical interactions between infected and healthy individuals

RESPIRATORY

AEROSOLS

Fine particles



RESPIRATORY DROPLETS

Large particles

INDIRECT CONTACT

Exposure to fomites on contaminated surfaces

Bacterial respiratory tract infections can also be transmitted via microaspiration of contaminated water or direct contact with surgical wounds. **Parasitic infections** of the lung usually occur via ingestion of the parasite or via an insect bite.

In **fungal respiratory infections**, the most common modes of transmission are direct inhalation of fungi into the lung, zoonotic transmission, or by invasion at a wound site.

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2.5 Populations at-risk of severe infections



Very young or elderly individuals

Due to less-developed or age-related decline in immune function



Individuals living in a tropical region or recently traveled

- Hot, humid regions are more conducive to the growth and proliferation of parasites
- Travel creates exposure to pathogens against which the exposed individual has no immune memory



Individuals of low socioeconomic status

- Due to reduced access to health care programs and other medical resources
- Lack of access to potable water, exposure to wastewater, and cramped living conditions increase the risk of infection



Individuals with underlying medical comorbidities

- The patient may have impaired immune response due to underlying conditions or history
- Chronic conditions such as HIV/AIDS, asthma and chronic obstructive pulmonary disease create greater risk for severe respiratory infections

Self-Assessment: Module 1

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1. Which of the following pathogens commonly cause respiratory tract infections?

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- Streptococcus pneumoniae
- Plasmodium falciparum
- Hepatitis C virus
- Clostridium tetani

2. Which of the following are parts of the upper respiratory tract?

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- Bronchioles
- Alveoli
- Throat
- Diaphragm

- Pathogens can release nutrients that nourish the host's cells and tissues
- Pathogens can trigger a cytokine storm
- Pathogens can have capsules that protect them from the host immune response and antibiotics
- Gram negative bacteria can release LPS, a toxin that can induce septic shock

- 4. Which of the following is not one of the four major modes of respiratory pathogen transmission?
 - Direct contact
 - Indirect contact
 - Blood transfusion
 - Respiratory aerosols

5. Which of the following individuals would be considered at-risk for severe respiratory illnesses?

- A mid-thirties male with moderate comorbidities
- A child with a healthy immune system and no other comorbidities
- A healthy adult of high socioeconomic status
- An elderly resident of a nursing care facility

6. Which of the following is not known to influence pathogen transmissibility in respiratory tract infections?

- Time of the year
- Hot, humid conditions
- Gender of the transmitting individual
- Environmental stress



Module 2: Clinical practice

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Module 2: Clinical practice

Introduction

- Module 1 gives an overview of the pathogens that cause respiratory tract infections and the conditions associated with them
- Module 2 describes the clinical presentation of respiratory infections and how these infections are managed by clinicians
- Module 3 presents an overview of testing for respiratory tract infections, including how tests are typically used in patient care
- Module 4 details surveillance of respiratory infections for public health purposes and how surveillance data are disseminated

Module 2: Clinical practice

Chapter 3. Clinical presentations of respiratory tract infections

- 3.1 Symptoms of respiratory tract infections
- 3.2 Signs of respiratory tract infections
- 3.3 Conditions associated with respiratory tract infections
- Chapter 4. Clinical management of respiratory tract infections
 - 4.1 Prevention
 - 4.2 Clinical management
 - 4.3 Supportive care
 - 4.4 Specific treatments



Chapter 3. Clinical presentations of respiratory tract infections

By the end of this chapter, you will be able to:

- Describe the symptoms and signs of respiratory tract infections
- Identify conditions associated with respiratory tract infections



According to the World Health Organization's 2017 report on the Global Impact of Respiratory Disease, more than 1 billion people worldwide suffer from either acute or chronic respiratory conditions.

3.1 Symptoms of respiratory tract infections

A symptom is a health issue reported by the patient. The patient's description of their symptoms can assist the doctor in diagnosing an infection.



 The symptoms of a respiratory tract infection depend on many factors

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- Causative agent
- Whether the infection is primary or secondary
- Patient's age, general health, comorbidities, and immunity

3.2 Signs of respiratory tract infections

A sign is a health issue that can be observed. Medical professionals can observe and measure signs in order to assist in diagnosis of infections.

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3.3 Conditions associated with respiratory tract infections

Conditions associated with respiratory tract infections are divided according to the regions they affect, the **upper respiratory tract** or the **lower respiratory tract**.



- Generally, lower respiratory tract infections are more severe, while upper respiratory tract infections tend to be mild and self-limiting
- Conditions associated with **lower respiratory tract** infections are more common in infants, young children, elderly, and in patients with compromised immune systems or chronic medical conditions

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3.3 Conditions associated with respiratory tract infections

Some respiratory infections typically affect both the upper and lower respiratory tract



 Conditions that affect both the upper and lower respiratory tract tend to be highly contagious and can be severe, especially in patients who are very young, elderly, immunocompromised, or have medical comorbidities

Chapter 4. Clinical management of respiratory tract infections

By the end of this chapter, you will be able to

- Describe ways to deter and prevent respiratory infections
- 2 Identify measures for supportive care during respiratory infections
- Oescribe approaches to specific treatments for respiratory infections



In 2019, there were 17.2 billion incident cases of upper respiratory tract infection worldwide, making up about 43% of the total global burden of diseases and injuries.
4.1 Prevention

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Several measures can reduce susceptibility to respiratory infections in adults



Regular exercise



Smoking cessation



4.1 Prevention

Good respiratory hygiene practices can help prevent the spread of respiratory infections.

Reduce social contact with others.

Wear a mask during periods of increased respiratory infection activity in the community.



Open windows to increase ventilation.

Cover the mouth and nose with a tissue when coughing or sneezing and dispose in the nearest waste receptacle.

Perform frequent hand hygiene, such as hand washing with non-antimicrobial soap and water, alcohol-based hand rub, or antiseptic handwash.

4.2 Clinical management of respiratory tract infections







Most respiratory tract infections are **self-diagnosed** and can be self-treated with supportive care at home. More severe infections may require clinical management and/or hospital-based supportive care. Specific treatments are

appropriate for patients who are at-risk for severe infections or who have chronic lung conditions.



Please consult a physician for personalized medical advice.

4.2 Clinical management of respiratory tract infections

Certain patient populations require special considerations in clinical management of respiratory infections.

Patients who are at risk for severe infections	Patients with chronic lung conditions
Immunocompromised patients	 Asthma Bronchiectasis Chronic obstructive pulmonary disease (COPD)
Children Relderly	 Emphysema Cystic fibrosis

For more severe respiratory infections, supportive care in the hospital may be required, such as supplemental oxygen and mechanical ventilation.

4.3 Supportive care

The purpose of **supportive care** is to provide symptom relief and improve quality-of-life while the disease persists, rather than to treat infection.

 Most upper respiratory tract infections are self-diagnosed and can be self-treated with supportive care at home



4.4 Specific treatments

Specific treatment should be directed to the type of pathogen suspected or known to cause the infection.

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4.4 Specific treatments

Overuse or misuse of medical treatments such as antivirals and antibiotics can raise medical costs, induce side effects, and potentially increase drug resistance of pathogens.

Tests for specific pathogens can help target specific treatments to the causative agent.



Mycobacterium tuberculosis drug susceptibility test

Testing can also help to direct specific treatments in certain scenarios.



When patients are immunocompromised





During disease outbreaks





If a patient is at-risk for severe illness

More information on testing is provided in Module 3

Self-Assessment: Module 2

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1. Which of the following is a common symptom of a respiratory tract infection?

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- Cough
- Diarrhea
- Leg pain
- Vomiting

2. What condition is most strongly associated with respiratory syncytial virus infection?

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- Rhinitis
- Pneumonia
- Bronchiolitis
- Sinusitis

3. Which of the following conditions are appropriately treated with antibiotics?

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- COVID-19
- Influenza
- Bacterial pneumonia
- Malaria

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- Bacterial
- Fungal
- Viral
- Parasitic

- 5. Which of the following does *not* deter or prevent respiratory infections?
 - Stress management
 - Frequent handwashing
 - Increasing social contact
 - Use of bacterial and viral vaccines



Module 3: Testing strategies and initial workup

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Module 3: Testing strategies and initial workup Introduction

- Module 1 gives an overview of the pathogens that cause respiratory tract infections and the conditions associated with them
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- Module 4 details surveillance of respiratory infections for public health purposes and how surveillance data are disseminated



Module 3: Testing strategies and initial workup

Chapter 5. Overview of testing strategies

- 5.1 Testing purposes
- 5.2 Testing considerations

Chapter 6. Testing for respiratory tract infections

- 6.1 Initial workup
- 6.2 Clinical specimens
- 6.3 Testing methodology



Chapter 5. Overview of testing strategies

By the end of this chapter, you will be able to

Identify the three strategic purposes of testing

2 Describe testing considerations



According to the World Economic Forum, inaccurate diagnostic tests are one of the most expensive and logistically difficult challenges in healthcare in low- and middle-income countries.

5.1 Testing purposes

Here are the three strategic purposes for which respiratory infection testing modalities have been developed:



Diagnostic

Identify the causative pathogen(s) of a symptomatic infection and help determine treatment and prognosis. Also used for cohorting and isolation decisions for inpatients. Important for infection control and prevention.



Screening

Detect whether a high-risk asymptomatic person is likely to have or develop an infection. May be important for infection control and prevention, cohorting, and epidemiology for inpatients. Important for patients at-risk for severe infections.



Surveillance

Monitor temporal and geographic circulation patterns of infections, locally or globally. Important for monitoring outbreaks, variants, and drug resistance (active or passive surveillance).

5.1 Testing purposes

There are many additional ways that testing can be strategically implemented, including to support precision medicine, clinical/translational research, and population health.

Precision medicine is a holistic way of stratifying patients based on large-scale data, such as patient characteristics and test results. It can support antimicrobial and antiviral stewardship.



Clinical/translational research

takes scientific discoveries and transforms them into **new approaches to medical care and treatments.** Test data can direct research priorities, monitor efficacy of treatments, and help test hypotheses.

Population health is a partnership between healthcare systems, agencies, and organizations that connects practice to policy to achieve **positive health outcomes**. Test data can be used to guide intervention selection, monitoring, and evaluation.

There are many considerations when choosing a testing strategy, including the following:

Patient's clinical presentation or risk stratification



Trajectory of the disease

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Current public health challenges



Community in which the patient resides

Will the test result affect patient care?

Tests can be used to



Detect infections that can become serious if left untreated



Direct the course of treatment



Inform decisions about the patient management process, such as hospitalization and follow-up



Is the patient at-risk for a severe illness?

Tests can help



Detect bacterial, viral, and fungal coinfections



Increase the likelihood of an early diagnosis



Distinguish between infectious and noninfectious agents





Is the community experiencing greater than moderate disease prevalence?

Tests can facilitate



Understanding of pathogen transmission dynamics and virulence characteristics



Monitoring of disease prevalence, for example by using tests for screening asymptomatic persons



Informed decision-making regarding public health measures (when test results are aggregated)



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Chapter 6. Testing for respiratory tract infection

By the end of this chapter, you will be able to

- Describe the pathway to diagnosis of respiratory tract infections
- 2 Identify clinical specimens used in diagnostic testing
- 3 Describe the different testing modalities



As of March 2022, there are more than 680 commercially available diagnostic tests for COVID-19.

6.1 Initial workup for respiratory tract infections

The initial workup for respiratory tract infections can have many different components. The healthcare provider determines which components are required, according to the patient's presentation.

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6.2 Clinical specimens

Clinical specimens are collected to identify the causative agent in a respiratory tract infection.



Each respiratory pathogen requires a unique set of specimen types, collection methods, and transport conditions to optimize diagnostic yield.

Manufacturer instructions for specimen collection devices should be followed.



6.3 Testing methodology

The main testing modalities are culture, rapid antigen detection tests, multiplex nucleic acid amplification tests, and serological tests.

	Advantages	Challenges
Sample Culture	Culture is the oldest method of diagnosis of the causative pathogen in respiratory infections and is widely used .	Long TAT (1-30 days), moderate sensitivity, not available as a kit, laborious, highly technical, and prone to contamination-related errors.
Rapid Antigen Detection Test	TAT of ≤15 minutes , amenable to point-of-care testing, requires little technical expertise, and is inexpensive .	Is less sensitive and can be less specific than other modalities, such as culture or molecular methods.
Multiplex Nucleic Acid Amplification Test	Highly sensitive and specific, can test many pathogens at once, and can screen for large numbers of specimens.	Investment in equipment and training is required and TATs vary (rapid 1-3 hours; batch 1-3 days).
Serological Test	May differentiate between active and historical	Interpretation can be limited by specificity of the
(Assess IgM or IgG antibody)	convalescent specimens.	antigens and there is a time lag between infection onset and development of antibodies.

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Self-Assessment: Module 3

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1. Which of the following is not one of the three strategic purposes of testing?

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- Imaging
- Surveillance
- Diagnostic
- Screening

- Tests do not help direct the course of treatment
- Tests do not help monitor disease prevalence
- Tests do not increase the likelihood of an early diagnosis
- Tests distinguish between infectious and non-infectious diseases

3. Which of the following is not a part of the initial workup for respiratory infection?

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- History of present illness
- Physical examination
- Medical history
- Payment of fees

4. Which of the following is an upper respiratory tract clinical specimen?

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- Nasopharyngeal swab
- Sputum
- Tracheal aspirate
- Pleural fluid

- 5. Which of the following test types is *most* commonly used to test for multiple pathogens at once?
 - Multiplex nucleic acid amplification test
 - Sample culture
 - Rapid antigen detection test
 - Serological tests

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Module 4: Public health surveillance

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Module 4: Public health surveillance

Introduction

- Module 1 gives an overview of the pathogens that cause respiratory tract infections and the conditions associated with them
- Module 2 describes the clinical presentation of respiratory infections and how these infections may be managed
- Module 3 presents an overview of testing for respiratory tract infections, including how tests are typically used in patient care
- Module 4 details surveillance of respiratory infections for public health purposes and how surveillance data are disseminated



Module 4: Public health surveillance

Chapter 7. Viral surveillance

- 7.1 Overview of surveillance
- 7.2 The role of viral surveillance
- 7.3 Viral surveillance systems
- 7.4 Challenges to viral surveillance

Chapter 8. Bacterial surveillance

- 8.1 The role of bacterial surveillance8.2 Bacterial surveillance systems
- 8.3 Challenges to bacterial surveillance

Chapter 9. Other public health concerns

- 9.1 Surveillance of fungal infections
- 9.2 Surveillance of parasitic infections
- 9.3 Antimicrobial resistance
Chapter 7. Viral surveillance

By the end of this chapter, you will be able to

- 1 Recognize the role of viral surveillance in public health
- 2 Describe examples of viral surveillance systems
- 3 Describe the challenges to viral surveillance



The World Health Organization is the global public health organization established to unite countries in the common goal of achieving better health. There are also local, regional, and national public health agencies.

7.1 Overview of surveillance

Public health disease surveillance is the ongoing, systematic collection, analysis, and interpretation of outcome-specific health-related data.

Most viral surveillance tracking, including screening, is for symptomatic individuals based on report of an influenza-like illness. Data are collected on the distribution of respiratory viruses to **inform trends and to guide** prevention efforts.

Data from surveillance should be **quickly disseminated** to support the prevention and control of disease.



7.1 Overview of surveillance

No agency can confront global health challenges alone. Some of the largest public health agencies are shown below, with their geographic areas indicated in red.

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7.2 The role of viral surveillance

The global impact of emerging viruses – especially SARS-CoV-2 – has resulted in an increasingly important role for viral surveillance in public health.

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According to the World Health Organization, the objectives of viral surveillance are as follows:



7.2 The role of viral surveillance

The collection, analysis, and dissemination of surveillance data is critically important to the work of public health agencies, supporting a variety of interrelated tasks:



Detect emerging public health threats



Improve health security



Inform decision-making



Perform risk assessment and management



Track cases



Forecast & contain outbreaks

7.3 Viral surveillance systems

The World Health Organization has many public health systems in place to monitor respiratory viruses.



National, regional, and local public health organizations also have surveillance systems for respiratory viruses, particularly for viruses of public health importance which include influenza, RSV, and SARS-CoV-2.

7.3 Viral surveillance systems

Crowdsourced data collection has been successfully used for viral surveillance, in which a large group of volunteers (10,000+) report information using internet-based platforms.

There are many successful recent examples of crowdsourced viral surveillance:







The FluWatchers Program Global Public Health Intelligence Network Program for Monitoring Emerging Infectious Diseases



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7.4 Challenges to viral surveillance

There are many challenges to surveillance, particularly in resource-limited settings:



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7.4 Challenges to viral surveillance

Timely data integration is a major challenge that needs to be overcome as surveillance moves into the modern era.

There is need for more real-time, automated data analysis pipelines with **data visualization outputs** that are regularly and automatically updated.





Existing **global data quality issues** must be overcome to ensure the findings are useful to different regions in the world.

7.4 Challenges to viral surveillance

To overcome the challenges of surveillance, there are certain key elements that are necessary to create successful and effective surveillance programs:



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Successful surveillance of viral infections can detect outbreaks, prevent and control infections, direct public health programs and policies, and monitor the impact of interventions.

Chapter 8. Bacterial surveillance

By the end of this chapter, you will be able to

- 1 Identify the role of bacterial surveillance in public health
- 2 Describe examples of bacterial surveillance systems
- 3 Describe the challenges to bacterial surveillance



Pneumonia caused by *Streptococcus* pneumoniae continues to be the most common cause of vaccine-preventable death in children worldwide, underscoring the importance of bacterial surveillance.

8.1 The role of bacterial surveillance

Surveillance of bacterial infections is necessary to formulate strategies to improve patient outcomes.



8.2 Bacterial surveillance systems

The World Health Organization (WHO) monitors bacterial infection rates and incidence worldwide. Some examples of WHO bacterial surveillance programs are described below:



The Global Tuberculosis Programme, part of the World Health Organization, works towards the goal of a world free of tuberculosis. Data are collected from regional networks to estimate the global tuberculosis burden and support improvements in patient care.

The **PSERENADE project** was commissioned in 2021 by the World Health Organization to assess the impact of pneumococcal conjugate vaccines on invasive pneumococcal disease (IPD).



8.2 Bacterial surveillance systems

Surveillance of tuberculosis (TB) is one of the oldest disease surveillance systems in the world and is now one of the most high-functioning surveillance systems for infectious diseases.

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8.2 Bacterial surveillance systems

In the US, the Centers for Disease Control and Prevention has established the Active Bacterial Core surveillance (ABCs) program.

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Group A Streptococcus Group B Streptococcus **ABCs monitors five pathogens** determined to be of public health importance in the United Haemophilus influenzae States due to their prevalence and potential to cause severe illnesses. Neisseria meningitidis Streptococcus pneumoniae

8.3 Challenges to bacterial surveillance

There are various challenges to bacterial infection surveillance:







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The **symptoms** of most bacterial and viral respiratory infections **are similar**, making differentiation between causative pathogens difficult. **Tests** that could determine whether an infection is viral or bacterial **are not always available or clinically necessary**, so test results data do not always exist or can be limited. If a diagnostic test is performed, the **identified bacteria may be part of the patient's normal flora (colonization)** rather than a pathogen, so the test result can be difficult to interpret.

8.3 Challenges to bacterial surveillance

Surveillance in low and middle-income countries has unique challenges, but is important because these regions account for a disproportionate (approximately 90%) burden of the deaths due to bacterial infections worldwide.

Challenges to surveillance in low- and middle-income countries

- Lack of laboratory facilities
- Limited laboratory supplies
- Limited testing capacity
- Lack of standardized testing approaches
- Gaps in quality assurance
- Non-standardized data management
- Few skilled personnel
- Inadequate funding



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8.3 Challenges to bacterial surveillance

To overcome the challenges to bacterial surveillance, a key element to success is **strong international collaboration** and sharing of resources, data, and education between these groups:

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Chapter 9. Other public health concerns

By the end of this chapter, you will be able to

- 1 Describe the surveillance of fungal and parasitic pathogens
- 2 Explain the challenges in surveillance of fungal and parasitic pathogens
- 3 Describe the importance of antimicrobial resistance and how it is surveilled



Antimicrobial resistance is important because according to the World Health Organization, people with methicillinresistant *Staphylococcus aureus* (MRSA) infections are 64% more likely to die than people with methicillinsusceptible *S. aureus* infections.

9.1 Surveillance of fungal infections

The Global Action Fund for Fungal Infections estimates that over 300 million people worldwide are afflicted with a serious fungal infection, and 25 million are at high risk of dying or losing their sight.

- The World Health Organization is undertaking a comprehensive review of fungal infections of public health importance, but has not yet identified a plan for global surveillance of fungal infections
- An increase in the number of immunocompromised individuals has contributed to an escalation of the prevalence of respiratory fungal infections
- Therefore, fungal surveillance and public health efforts are essential, particularly among immunocompromised individuals



Surveillance of fungal and drug-resistant fungal infections is challenging because funding for fungal disease research and public health efforts is low.

9.2 Surveillance of parasitic infections

The Parasitic Diseases Task Force of the World Health Organization estimates the global burden of parasitic disease using regional public health records.

- Parasitic data availability was assessed in 2015 for 194 countries
- For the five most populous countries, the number of parasitic data gaps is called out
- Global data specific to respiratory parasitic infections are not available, but estimates suggest that 5-20% of parasitic infections affect the respiratory system in some way



Global Data Gaps for Parasitic Infections

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9.2 Surveillance of parasitic infections

Parasitic disease surveillance is challenging because these diseases often have their highest impact in low- and middle-income countries.

• In these settings



Hospital treatment is less available

Health data collection and reporting is frequently lacking



Surveillance of malaria, caused by five different species of plasmodium parasites, is one of the three pillars of the WHO's global technical strategy for malaria 2016–2030.



9.3 Antimicrobial resistance

Antimicrobial-resistant pathogens cause at least 700,000 deaths globally each year, constituting a grave public health threat.



In 2019, the WHO collected data from 114 countries on bacterial resistance or decreased susceptibility to treatment; **reported resistance ranged from 0-96%**.



Increasing levels of resistance have important economic implications since second- and third-line regimens are much more expensive than first-line drugs.



Second- and third-line regimens can also have more side effects and can be less effective in treatment.



Antimicrobial susceptibility testing can help to determine what therapies are likely to be successful.

9.3 Antimicrobial resistance

The increasing prevalence of drug-resistant fungi and parasites is a significant threat to public health, particularly in low- and middle-income countries.

The prevalence of drug-resistant parasitic and fungal infections continues to rise and is leading to critical health challenges:



Increased difficulty in treating infections



Longer hospital

stays



More expensive treatment options



9.3 Antimicrobial resistance

In 2015, the World Health Organization launched the Global Antimicrobial Resistance and Use Surveillance System (GLASS). The purpose of GLASS is to collect, analyze, interpret, and share worldwide data related to antimicrobial resistance in four key areas:

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Self-Assessment: Module 4

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- 1. Which of the following is not one of the objectives of viral surveillance?
- Monitor infection incidence
- Track epidemiological changes and new variants
- Guide the implementation of disease control measures
- Withhold information until the disease mechanism is fully understood

2. Which of the following is considered a barrier to effective surveillance?

- Well-maintained infrastructure and equipment
- Lack of access to necessary equipment
- Healthcare personnel is fully staffed
- Timely validation of laboratory protocols

- 3. Which of the following programs surveils invasive pneumococcal disease?
- The FluWatchers Program
- WHO Global Influenza Surveillance and Response System
- The PSERENADE project
- WHO Global Respiratory Syncytial Virus Surveillance

- 4. Which of the following is not one of the areas of GLASS surveillance?
- Prevalence of human parainfluenza viruses
- Antimicrobial resistance in humans
- The use of antimicrobial medicines
- Antimicrobial resistance in the environment

5. Which of the following is a consequence of the increasing prevalence of drug-resistant fungal infections?

- Shorter hospital stays
- Less expensive treatment options
- Easier to treat infections
- Treatment failures



Our Editors

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Michael Kann, MD

Module 1 – Etiology and Pathophysiology

- Dr. Kann is a Professor of Clinical Virology in the Department of Infectious Diseases at the Institute of Biomedicine at the University of Gothenburg/Sahlgenska University Hospital in Sweden
- Currently, he is the President of the European Society for Virology and a member of International Committee on Taxonomy of Viruses
- He served for many years as a physician in the Virological Diagnostic Department at the University Hospitals of Bordeaux, France

Carolina Garcia-Vidal, MD, PhD

Module 2 – Clinical Practice

- Dr. Garcia-Vidal is an Infectious Diseases Consultant in the Infectious Disease Department at the Hospital Clinic of Barcelona in Spain
- She is past president of the Grupo Español de Micología Médica (Medical and Experimental Mycology Research Group) at the Universidad Pontificia Bolivariana
- In 2015, she received the European Society of Clinical Microbiology and Infectious Diseases
 Young Investigator Award for Research in Clinical Microbiology and Infectious Diseases

Donna Wolk, MHA, PhD

Module 3 – Testing Strategies and Initial Workup

- Dr. Wolk is the Division Chief of Molecular and Microbial Diagnostics and Development at Geisinger Medical Laboratories and a Clinical Professor at the Geisinger Commonwealth School of Medicine in the United States
- She is also the Director of the Infectious Disease Research Laboratory at the Weis Research Center, a diplomate of the American Board of Medical Microbiology, and a board-certified medical laboratory scientist
- In 2016, she received the Becton-Dickinson Research Award for Clinical Microbiology from the American Society for Microbiology

Catherine Hogan, MD, CM, MSc

Module 4 – Public Health Surveillance

- Dr. Hogan is a Medical Microbiologist at the British Columbia Centre for Disease Control Public Health Laboratory in Canada and is a Clinical Assistant Professor within the Department of Pathology and Laboratory Medicine at The University of British Columbia
- She holds a master's degree in epidemiology from the London School of Hygiene and Tropical Medicine and serves as an associate editor for the Journal of Clinical Virology
- In 2020, she was granted a Global Health Diagnostics Fellowship in the Department of Pathology at the Stanford University School of Medicine in the United States
Self Assessment Answers

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Module 1

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1. Which of the following pathogens commonly cause respiratory tract infections?

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- Streptococcus pneumoniae
- Plasmodium falciparum
- Hepatitis C virus
- Clostridium tetani

2. Which of the following are parts of the upper respiratory tract?

Thermo Fisher

- Bronchioles
- Alveoli
- Throat
- Diaphragm

3. Which of the following is not one of the mechanisms of pathogenicity?

- Pathogens can release nutrients that nourish the host's cells and tissues
- Pathogens can trigger a cytokine storm
- Pathogens can have capsules that protect them from the host immune response and antibiotics
- Gram negative bacteria can release LPS, a toxin that can induce septic shock

- Direct contact
- Indirect contact
- Blood transfusion
- Respiratory aerosols

5. Which of the following individuals would be considered at-risk for severe respiratory illnesses?

- A mid-thirties male with moderate comorbidities
- A child with a healthy immune system and no other comorbidities
- A healthy adult of high socioeconomic status
- An elderly resident of a nursing care facility

6. Which of the following is not known to influence pathogen transmissibility in respiratory tract infections?

- Time of the year
- Hot, humid conditions
- Gender of the transmitting individual
- Environmental stress



Module 2

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1. Which of the following is a common symptom of a respiratory tract infection?

Thermo Fisher

- Cough 🗸
- Diarrhea
- Leg pain
- Vomiting

2. What condition is most strongly associated with respiratory syncytial virus infection?

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- Rhinitis
- Pneumonia
- Bronchiolitis
- Sinusitis

3. Which of the following conditions are appropriately treated with antibiotics?

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- COVID-19
- Influenza
- Bacterial pneumonia 🤡
- Malaria

4. Anthelminthics can be used as a specific treatment for which type of infection?

Thermo Fisher

- Bacterial
- Fungal
- Viral
- Parasitic

- 5. Which of the following does *not* deter or prevent respiratory infections?
 - Stress management
 - Frequent handwashing
 - Increasing social contact
 - Use of bacterial and viral vaccines

Module 3

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1. Which of the following is not one of the three strategic purposes of testing?

Thermo Fisher

- Imaging
- Surveillance
- Diagnostic
- Screening

2. Which of the following statements about testing of respiratory tract infections is true?

- Tests do not help direct the course of treatment
- Tests do not help monitor disease prevalence
- Tests do not increase the likelihood of an early diagnosis
- Tests distinguish between infectious and non-infectious diseases \checkmark

3. Which of the following is not a part of the initial workup for respiratory infection?

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- History of present illness
- Physical examination
- Medical history
- Payment of fees

4. Which of the following is an upper respiratory tract clinical specimen?

Thermo Fisher

- Nasopharyngeal swab
- Sputum
- Tracheal aspirate
- Pleural fluid

- 5. Which of the following test types is *most* commonly used to test for multiple pathogens at once?
 - Multiplex nucleic acid amplification test
 - Sample culture
 - Rapid antigen detection test
 - Serological tests

Module 4

- 1. Which of the following is not one of the objectives of viral surveillance?
- Monitor infection incidence
- Track epidemiological changes and new variants
- Guide the implementation of disease control measures
- Withhold information until the disease mechanism is fully understood \checkmark

2. Which of the following is considered a barrier to effective surveillance?

- Well-maintained infrastructure and equipment
- Lack of access to necessary equipment
- Healthcare personnel is fully staffed
- Timely validation of laboratory protocols

- 3. Which of the following programs surveils invasive pneumococcal disease?
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- The PSERENADE project
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- Avendaño Carvajal L, Perret Pérez C. Epidemiology of Respiratory Infections. Pediatric Respiratory Diseases. 2020:263-72.
- Azziz Baumgartner E, Dao CN, Nasreen S, Bhuiyan MU, Mah EMS, Al Mamun A, et al. Seasonality, timing, and climate drivers of influenza activity worldwide. J Infect Dis. 2012;206(6):838-46.
- Bakaletz LO. Viral-bacterial co-infections in the respiratory tract. Curr Opin Microbiol. 2017;35:30-5.
- Ball M, Hossain M, Padalia D. Anatomy, Airway. StatPearls. Treasure Island (FL): StatPearls Publishing LLC; 2022.
- Benito N, Moreno A, Miro JM, Torres A. Pulmonary infections in HIV-infected patients: an update in the 21st century. European Respiratory Journal. 2012;39(3):730-745.
- Bouchez V, Guiso N. Bordetella pertussis, B. parapertussis, vaccines and cycles of whooping cough. Pathogens and Disease. 2015;73(7).
- Branche AR, Falsey AR. Parainfluenza Virus Infection. Semin Respir Crit Care Med. 2016;37(4):538-54.
- Cannell JJ, Vieth R, Umhau JC, Holick MF, Grant WB, Madronich S, et al. Epidemic influenza and vitamin D. Epidemiol Infect. 2006;134(6):1129-40.
- Cascella M, Rajnik M, Aleem A, Dulebohn SC, Di Napoli R. Features, Evaluation, and Treatment of Coronavirus (COVID-19). Treasure Island (FL): StatPearls Publishing LLC; 2022 Jan.
- Charlton CL, Babady E, Ginocchio CC, Hatchette TF, Jerris RC, Li Y, et al. Practical Guidance for Clinical Microbiology Laboratories: Viruses Causing Acute Respiratory Tract Infections. Clin Microbiol Rev. 2019;32(1).
- Choe YJ, Smit MA, Mermel LA. Seasonality of respiratory viruses and bacterial pathogens. Antimicrob Resist Infect Control. 2019;8:125.
- Collaborators GLRI. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990-2016: a systematic analysis
 for the Global Burden of Disease Study 2016. Lancet Infect Dis. 2018;18(11):1191-210.
- Corman VM, Lienau J, Witzenrath M. Coronaviruses as the cause of respiratory infections. Internist (Berl). 2019;60(11):1136-45.
- Crowe JJE. Common Viral Respiratory Infections. In: Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, editors. Harrison's Principles of Internal Medicine, 20e. New York, NY: McGraw-Hill Education; 2018.
- Cunha BA, Burillo A, Bouza E. Legionnaires' disease. Lancet. 2016;387(10016):376-85.
- Eccles R. Understanding the symptoms of the common cold and influenza. Lancet Infect Dis. 2005;5(11):718-25.
- El-Sherbini GT, Abosdera MM. Risk factors associated with intestinal parasitic infections among children. J Egypt Soc Parasitol. 2013;43(1):287-94.

- Fact Sheet: Influenza (Seasonal), Switzerland: World Health Organization. Updated 6 November 2018. Available from: https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal)
- Fact Sheet: Pneumonia Geneva, Switzerland: World Health Organization. Updated 11 November 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/pneumonia.
- Fact Sheet: Tuberculosis, Switzerland: World Health Organization. Updated 14 October 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/tuberculosis.
- Fogel N. Tuberculosis: a disease without boundaries. Tuberculosis (Edinb). 2015;95(5):527-31.
- Friedman DZP, Schwartz IS. Emerging Fungal Infections: New Patients, New Patterns, and New Pathogens. Journal of Fungi. 2019;5(3):67.
- Fuhrimann S, Winkler MS, Pham-Duc P, Do-Trung D, Schindler C, Utzinger J, et al. Intestinal parasite infections and associated risk factors in communities exposed to wastewater in urban and peri-urban transition zones in Hanoi, Vietnam. Parasit Vectors. 2016;9(1):537.
- Garber G. An overview of fungal infections. Drugs. 2001;61 Suppl 1:1-12.
- Ghoneim HE, Thomas PG, McCullers JA. Depletion of alveolar macrophages during influenza infection facilitates bacterial superinfections. J Immunol. 2013;191(3):1250-9.
- Gilsdorf JR. Hib Vaccines: Their Impact on Haemophilus influenzae Type b Disease. J Infect Dis. 2021;224(12 Suppl 2):S321-s30.
- Goldstein EJC, Murphy TF, Parameswaran GI. Moraxella catarrhalis, a Human Respiratory Tract Pathogen. Clinical Infectious Diseases. 2009;49(1):124-31.
- Greenberg SB. Human Rhinovirus Infections. Human Respiratory Viral Infections. 1st ed: CRC Press; 2014. p. 353–76.
- Greenberg SB. Update on Human Rhinovirus and Coronavirus Infections. Semin Respir Crit Care Med. 2016;37(4):555-71.
- Guitor AK, Wright GD. Antimicrobial Resistance and Respiratory Infections. Chest. 2018;154(5):1202-12.
- Hao Y-W, Wang Q, Cao C-L, Tian T, Zhu Z-L, Xu J, et al. Chapter Eleven Construction and application of surveillance and response systems for parasitic diseases in China, led by NIPD-CTDR. In: Engels D, Wang Y, Zhou X-N, editors. Advances in Parasitology. 110: Academic Press; 2020. p. 349-71.
- Hirai J, Kinjo T, Koga T, Haranaga S, Motonaga E, Fujita J. Clinical characteristics of community-acquired pneumonia due to Moraxella catarrhalis in adults: a retrospective single-centre study. BMC Infectious Diseases. 2020;20(1):821.
- Jain S, Self WH, Wunderink RG, Fakhran S, Balk R, Bramley AM, et al. Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults. N Engl J Med. 2015;373(5):415-27.
- Khemasuwan D, Farver C, Mehta AC. Parasitic Diseases of the Lung. Diseases of the Central Airways. 2016:231-53.

- Kim EH, Bae JM. Seasonality of tuberculosis in the Republic of Korea, 2006-2016. Epidemiol Health. 2018;40:e2018051.
- Koch A, Mizrahi V. Mycobacterium tuberculosis. Trends Microbiol. 2018;26(6):555-6.
- Krammer F, Smith GJD, Fouchier RAM, Peiris M, Kedzierska K, Doherty PC, et al. Influenza. Nat Rev Dis Primers. 2018;4(1):3.
- Kuzucu A. Parasitic diseases of the respiratory tract. Curr Opin Pulm Med. 2006;12(3):212-21.
- Lakhundi S, Zhang K. Methicillin-Resistant Staphylococcus aureus: Molecular Characterization, Evolution, and Epidemiology. Clin Microbiol Rev. 2018;31(4).
- Lange C, Dheda K, Chesov D, Mandalakas AM, Udwadia Z, Horsburgh CR, Jr. Management of drug-resistant tuberculosis. Lancet. 2019;394(10202):953-66.
- Lee AS, de Lencastre H, Garau J, Kluytmans J, Malhotra-Kumar S, Peschel A, et al. Methicillin-resistant Staphylococcus aureus. Nature Reviews Disease Primers. 2018;4(1):18033.
- Leung NHL. Transmissibility and transmission of respiratory viruses. Nature Reviews Microbiology. 2021.
- Li Z, Lu G, Meng G. Pathogenic Fungal Infection in the Lung. Front Immunol. 2019;10:1524.
- Lynch JP, 3rd, Kajon AE. Adenovirus: Epidemiology, Global Spread of Novel Serotypes, and Advances in Treatment and Prevention. Semin Respir Crit Care Med. 2016;37(4):586-602.
- Mermel LA, Machan JT, Parenteau S. Seasonality of MRSA infections. PLoS One. 2011;6(3):e17925.
- Moriyama M, Hugentobler WJ, Iwasaki A. Seasonality of Respiratory Viral Infections. Annu Rev Virol. 2020;7(1):83-101.
- Obando-Pacheco P, Justicia-Grande AJ, Rivero-Calle I, Rodríguez-Tenreiro C, Sly P, Ramilo O, et al. Respiratory Syncytial Virus Seasonality: A Global Overview. J Infect Dis. 2018;217(9):1356-64.
- Paul M. Seasonality in infectious diseases: does it exist for all pathogens? Clin Microbiol Infect. 2012;18(10):925-6.
- Pertussis: Summary of Vaccine Recommendations: Centers for Disease Control and Prevention. Updated 22 January 2020. Available from: https://www.cdc.gov/vaccines/vpd/pertussis/recs-summary.html.
- Popper H. Pathology of Lung Disease: Morphology Pathogenesis Etiology. 1st ed. Berlin, Germany: Springer; 2017.
- Ramirez P, Fernández-Barat L, Torres A. New therapy options for MRSA with respiratory infection/pneumonia. Curr Opin Infect Dis. 2012;25(2):159-65.
- Romero F, Cazzato S, Walder F, Vogelgsang S, Bender SF, van der Heijden MGA. Humidity and high temperature are important for predicting fungal disease outbreaks worldwide. New Phytol. 2021.

- Rowe HM, Meliopoulos VA, Iverson A, Bomme P, Schultz-Cherry S, Rosch JW. Direct interactions with influenza promote bacterial adherence during respiratory infections. Nat Microbiol. 2019;4(8):1328-36.
- Saraya T. Mycoplasma pneumoniae infection: Basics. J Gen Fam Med. 2017;18(3):118-25.
- Shaman J, Kohn M. Absolute humidity modulates influenza survival, transmission, and seasonality. Proc Natl Acad Sci U S A. 2009;106(9):3243-8.
- Shi T, McAllister DA, O'Brien KL, Simoes EAF, Madhi SA, Gessner BD, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. Lancet. 2017;390(10098):946-58.
- Simasek M, Blandino DA. Treatment of the common cold. Am Fam Physician. 2007;75(4):515-20.
- Stefani S, Chung DR, Lindsay JA, Friedrich AW, Kearns AM, Westh H, et al. Meticillin-resistant Staphylococcus aureus (MRSA): global epidemiology and harmonisation of typing methods. Int J Antimicrob Agents. 2012;39(4):273-82.
- van Doorn HR, Yu H. Viral Respiratory Infections. Hunter's Tropical Medicine and Emerging Infectious Diseases. 2020:284-8.
- Wang Y, Grunewald M, Perlman S. Coronaviruses: An Updated Overview of Their Replication and Pathogenesis. Methods Mol Biol. 2020;2203:1-29.
- Yi L, Xu X, Ge W, Xue H, Li J, Li D, et al. The impact of climate variability on infectious disease transmission in China: Current knowledge and further directions. Environmental Research. 2019;173:255-61.

- Abraham T, Sistla S. Trends in Antimicrobial Resistance Patterns of Group A Streptococci, Molecular Basis and Implications. Indian Journal of Medical Microbiology. 2018;36(2):186-91.
- Avendaño Carvajal L, Perret Pérez C. Epidemiology of Respiratory Infections. Pediatric Respiratory Diseases. 2020:263-72.
- Azoulay E, Russell L, Van de Louw A, Metaxa V, Bauer P, Povoa P, et al. Diagnosis of severe respiratory infections in immunocompromised patients. Intensive Care Med. 2020;46(2):298-314.
- Battisti AS, Modi P, Pangia J. Sinusitis: StatPearls; 2021. Available from: <u>https://www.statpearls.com/ArticleLibrary/viewarticle/29061</u>.
- Bergeron C, Cantin AM. Cystic Fibrosis: Pathophysiology of Lung Disease. Semin Respir Crit Care Med. 2019;40(6):715-26.
- · Best S. Pharyngitis: Johns Hopkins Medicine; 2022. Available from: https://www.hopkinsmedicine.org/health/conditions-and-diseases/pharyngitis.
- Bouchez V, Guiso N. Bordetella pertussis, B. parapertussis, vaccines and cycles of whooping cough. Pathogens and Disease. 2015;73(7).
- Bronchitis: Mayo Clinic; 2022. Available from: www.mayoclinic.org/diseases-conditions/bronchitis.
- Buchy P, Badur S. Who and when to vaccinate against influenza. Int J Infect Dis. 2020;93:375-87.
- Cascella M, Rajnik M, Aleem A, Dulebohn SC, Di Napoli R. Features, Evaluation, and Treatment of Coronavirus (COVID-19). Treasure Island (FL): StatPearls Publishing LLC; 2022 Jan.
- Chiappini E, Regoli M, Bonsignori F, Sollai S, Parretti A, Galli L, et al. Analysis of different recommendations from international guidelines for the management of acute pharyngitis in adults and children. Clin Ther. 2011;33(1):48-58.
- Dunning J, Baillie JK, Cao B, Hayden FG. Antiviral combinations for severe influenza. Lancet Infect Dis. 2014;14(12):1259-70.
- Eccles R. Understanding the symptoms of the common cold and influenza. Lancet Infect Dis. 2005;5(11):718-25.
- Epiglottitis 2021. Updated 23 June 2021. Available from: <u>https://www.nhs.uk/conditions/Epiglottitis/</u>.
- Fact Sheet: Immunization coverage Geneva, Switzerland: World Health Organization. Updated 15 July 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/immunization-coverage.
- Fact Sheet: Influenza (Seasonal) Geneva, Switzerland: World Health Organization. Updated 6 November 2018. Available from: https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal).
- Fact Sheet: Pneumonia Geneva, Switzerland: World Health Organization. Updated 11 November 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/pneumonia.
- Fact Sheet: Tuberculosis, Switzerland: World Health Organization. Updated 14 October 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/tuberculosis.

- Fogel N. Tuberculosis: a disease without boundaries. Tuberculosis (Edinb). 2015;95(5):527-31.
- Forum of International Respiratory Societies. The Global Impact of Respiratory Disease Second Edition. Sheffield, UK: European Respiratory Society; 2017.
- Foucher G, Pillon F. What is nasopharyngitis? Actualités Pharmaceutiques. 2016;55(556):55-6.
- Grief SN. Upper respiratory infections. Prim Care. 2013;40(3):757-70.
- Hand RM, Snelling TL, Carapetis JR. Group A Streptococcus. Hunter's Tropical Medicine and Emerging Infectious Diseases. 2020:429-38.
- Hayden FG, Whitley RJ. Respiratory Syncytial Virus Antivirals: Problems and Progress. The Journal of Infectious Diseases. 2020;222(9):1417-21.
- Hirai J, Kinjo T, Koga T, Haranaga S, Motonaga E, Fujita J. Clinical characteristics of community-acquired pneumonia due to Moraxella catarrhalis in adults: a retrospective single-centre study. BMC Infectious Diseases. 2020;20(1):821.
- Hoare Z, Lim WS. Pneumonia: update on diagnosis and management. BMJ. 2006;332(7549):1077-9.
- Ison MG. Antiviral Treatments. Clin Chest Med. 2017;38(1):139-53.
- Jin X, Ren J, Li R, Gao Y, Zhang H, Li J, et al. Global burden of upper respiratory infections in 204 countries and territories, from 1990 to 2019. E Clinical Medicine. 2021;37:100986.
- Kacmarek RM, Stoller JK, Heuer AJ. Egan's Fundamentals of Respiratory Care. 12th ed: Mosby; 2020 March 23, 2020.
- Karampatsas K, Kong J, Cohen J. Bronchiolitis: an update on management and prophylaxis. Br J Hosp Med (Lond). 2019;80(5):278-84.
- Khemasuwan D, Farver C, Mehta AC. Parasitic Diseases of the Lung. Diseases of the Central Airways. 2016:231-53.
- Kuchar E, Miśkiewicz K, Nitsch-Osuch A, Szenborn L. Pathophysiology of Clinical Symptoms in Acute Viral Respiratory Tract Infections. Adv Exp Med Biol. 2015;857:25-38.
- Kurnatowski P, Kurnatowska AK. Treatment of fungal infections of upper respiratory tract and ear. Otolaryngol Pol. 2007;61(3):280-5.
- Laryngitis: NHS UK. Updated 29 December 2020. Available from: <u>https://www.nhs.uk/conditions/laryngitis/</u>.
- Liu Q, Zhou YH, Ye F, Yang ZQ. Antivirals for Respiratory Viral Infections: Problems and Prospects. Semin Respir Crit Care Med. 2016;37(4):640-6.
- Matthay MA, Aldrich JM, Gotts JE. Treatment for severe acute respiratory distress syndrome from COVID-19. Lancet Respir Med. 2020;8(5):433-4.
- Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med. 2019;200(7):e45-e67.

- Nahid P, Dorman SE, Alipanah N, Barry PM, Brozek JL, Cattamanchi A, et al. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. Clin Infect Dis. 2016;63(7):e147-e95.
- Nokso-Koivisto J, Marom T, Chonmaitree T. Importance of viruses in acute otitis media. Curr Opin Pediatr. 2015;27(1):110-5.
- O'Donnell AE. Medical management of bronchiectasis. J Thorac Dis. 2018;10(Suppl 28):S3428-s35.
- Pertussis (Whooping Cough): Centers for Disease Control and Prevention. Updated 25 October 2019. Available from: <u>https://www.cdc.gov/pertussis/clinical/treatment.html</u>.
- Plotkin SA, Orenstein WA, Offit PA. Vaccines. 6th ed. Philadelphia, PA, USA: Elsevier Saunders; 2013.
- Respiratory Hygiene/Cough Etiquette in Healthcare Settings: Centers for Disease Control and Prevention. Updated 1 August 2009. Available from: <u>https://www.cdc.gov/flu/professionals/infectioncontrol/resphygiene.htm</u>.
- Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, Brook I, Ashok Kumar K, Kramper M, et al. Clinical practice guideline (update): adult sinusitis. Otolaryngol Head Neck Surg. 2015;152(2 Suppl):S1-s39.
- Rost LM, Nguyen MH, Clancy CJ, Shields RK, Wright ES. Discordance Among Antibiotic Prescription Guidelines Reflects a Lack of Clear Best Practices. Open Forum Infect Dis. 2021;8(1):ofaa571.
- Schuchmann S, Hauck S, Henning S, Grüters-Kieslich A, Vanhatalo S, Schmitz D, et al. Respiratory alkalosis in children with febrile seizures. Epilepsia. 2011;52(11):1949-55.
- Shahan B, Barstow C, Mahowald M. Respiratory Conditions: Upper Respiratory Tract Infections. FP Essent. 2019;486:11-8.
- Simasek M, Blandino DA. Treatment of the common cold. Am Fam Physician. 2007;75(4):515-20.
- Somerville VS, Braakhuis AJ, Hopkins WG. Effect of Flavonoids on Upper Respiratory Tract Infections and Immune Function: A Systematic Review and Meta-Analysis. Adv Nutr. 2016;7(3):488-97.
- Thomas M, Bomar PA. Upper Respiratory Tract Infection. Treasure Island (FL): StatPearls Publishing LLC; 2022 Jan.
- Yoon YK, Park CS, Kim JW, Hwang K, Lee SY, Kim TH, et al. Guidelines for the Antibiotic Use in Adults with Acute Upper Respiratory Tract Infections. Infect Chemother. 2017;49(4):326-52.
- Zarei AE, Almehdar HA, Redwan EM. Hib Vaccines: Past, Present, and Future Perspectives. J Immunol Res. 2016;2016:7203587.

- Aring AM, Chan MM. Current Concepts in Adult Acute Rhinosinusitis. Am Fam Physician. 2016;94(2):97-105.
- Azoulay E, Russell L, Van de Louw A, Metaxa V, Bauer P, Povoa P, et al. Diagnosis of severe respiratory infections in immunocompromised patients. Intensive Care Med. 2020;46(2):298-314.
- Banerjee S, Ford C. Clinical Decision Rules and Strategies for the Diagnosis of Group A Streptococcal Infection: A Review of Clinical Utility and Guidelines [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health, CADTH Rapid Response Reports; 2018 May 23.
- Besser J, Carleton HA, Gerner-Smidt P, Lindsey RL, Trees E. Next-generation sequencing technologies and their application to the study and control of bacterial infections. Clinical Microbiology and Infection. 2018;24(4):335-41.
- Chiappini E, Regoli M, Bonsignori F, Sollai S, Parretti A, Galli L, et al. Analysis of different recommendations from international guidelines for the management of acute pharyngitis in adults and children. Clin Ther. 2011;33(1):48-58.
- Collaborators GLRI. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Infect Dis. 2018;18(11):1191-1210.
- Das S, Dunbar S, Tang Y-W. Laboratory Diagnosis of Respiratory Tract Infections in Children the State of the Art. Frontiers in Microbiology. 2018;9.
- Diagnostics for Better Health: Considerations for Global Implementation. World Economic Forum; 2021.
- Garg M, Prabhakar N, Gulati A, Agarwal R, Dhooria S. Spectrum of imaging findings in pulmonary infections. Part 1: Bacterial and viral. Pol J Radiol. 2019;84:e205-e13.
- Grief SN. Upper respiratory infections. Prim Care. 2013;40(3):757-70.
- Guitor AK, Wright GD. Antimicrobial Resistance and Respiratory Infections. Chest. 2018;154(5):1202-12.
- Hayward AC. Use of point-of-care testing for respiratory viruses in hospital. Lancet Respir Med. 2021;9(4):324-6.
- Hirai J, Kinjo T, Koga T, Haranaga S, Motonaga E, Fujita J. Clinical characteristics of community-acquired pneumonia due to Moraxella catarrhalis in adults: a retrospective singlecentre study. BMC Infectious Diseases. 2020;20(1):821.
- Kelly-Cirino CD, Nkengasong J, Kettler H, Tongio I, Gay-Andrieu F, Escadafal C, et al. Importance of diagnostics in epidemic and pandemic preparedness. BMJ Global Health. 2019;4(Suppl 2):e001179.
- Kuzucu A. Parasitic diseases of the respiratory tract. Curr Opin Pulm Med. 2006;12(3):212-21.
- Madran B, Keske Ş, Uzun S, Taymaz T, Bakır E, Bozkurt İ, et al. Effectiveness of clinical pathway for upper respiratory tract infections in emergency department. International Journal
 of Infectious Diseases. 2019;83:154-9.

- Mahashur A. Management of lower respiratory tract infection in outpatient settings: Focus on clarithromycin. Lung India. 2018;35(2):143-9.
- Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med. 2019;200(7):e45-e67.
- Mustafa Hellou M, Górska A, Mazzaferri F, Cremonini E, Gentilotti E, De Nardo P, et al. Nucleic acid amplification tests on respiratory samples for the diagnosis of coronavirus infections: a systematic review and meta-analysis. Clin Microbiol Infect. 2021;27(3):341-51.
- Noviello S, Huang DB. The Basics and the Advancements in Diagnosis of Bacterial Lower Respiratory Tract Infections. Diagnostics (Basel). 2019;9(2).
- Petruzzi G, De Virgilio A, Pichi B, Mazzola F, Zocchi J, Mercante G, et al. COVID-19: Nasal and oropharyngeal swab. Head Neck. 2020;42(6):1303-4.
- Prakash S, Prakash O, Mishra H, Khan DN, Shukla S, Pandey A, et al. Feasibility, efficiency & effectiveness of pooled sample testing strategy (pooled NAAT) for molecular testing of COVID-19. Indian J Med Res. 2021;153(1 & 2):227-32.
- Prinzi A. Screening Versus Diagnostic Tests for COVID-19, What's the Difference? American Society for Microbiology. 2020.
- Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, Brook I, Ashok Kumar K, Kramper M, et al. Clinical practice guideline (update): adult sinusitis. Otolaryngol Head Neck Surg. 2015;152(2 Suppl):S1-s39.
- Specimen Collection Guidelines: Centers for Disease Control and Prevention; 2021. Available from: <u>https://www.cdc.gov/urdo/downloads/speccollectionguidelines.pdf</u>.
- Spencer S, Thompson MG, Flannery B, Fry A. Comparison of Respiratory Specimen Collection Methods for Detection of Influenza Virus Infection by Reverse Transcription-PCR: a Literature Review. J Clin Microbiol. 2019;57(9).
- Thomas M, Bomar PA. Upper Respiratory Tract Infection. Treasure Island (FL): StatPearls Publishing LLC; 2022 Jan.
- van Doorn HR, Yu H. Viral Respiratory Infections. Hunter's Tropical Medicine and Emerging Infectious Diseases. 2020:284-8.
- Yamamoto K, Ohmagari N. Microbiological Testing for Coronavirus Disease 2019. JMA J. 2021;4(2):67-75.
- Zheng T, Finn C, Parrett CJ, Dhume K, Hwang JH, Sidhom D, et al. A Rapid Blood Test To Determine the Active Status and Duration of Acute Viral Infection. ACS Infect Dis. 2017;3(11):866-73.
- Zoch-Lesniak B, Ware RS, Grimwood K, Lambert SB. The Respiratory Specimen Collection Trial (ReSpeCT): A Randomized Controlled Trial to Compare Quality and Timeliness of Respiratory Sample Collection in the Home by Parents and Healthcare Workers From Children Aged <2 Years. J Pediatric Infect Dis Soc. 2020;9(2):134-41.
References

- 2.3 National TB prevalence surveys, Switzerland: World Health Organization; 2021. Available from: https://www.who.int/publications/digital/global-tuberculosis-report-2021/tb-disease-burden/prevalence-surveys.
- Active Bacterial Core Surveillance (ABCs): Centers for Disease Control and Prevention; 2021. Updated 19 July 2021. Available from: https://www.cdc.gov/abcs/index.html.
- Almas I, Afzal S, Imtiaz H, Shaheen MA, Daud M, Saghir A, et al. Drug Resistance in Hepatitis C Virus: Future Prospects and Strategies to Combat It. Crit Rev Eukaryot Gene Expr. 2020;30(4):323-36.
- Aspergillosis: The Centers for Disease Control and Prevention; 2021. Updated 7 May 2021. Available from: <u>https://www.cdc.gov/fungal/diseases/aspergillosis/index.html</u>.
- Ávila-Ríos S, Parkin N, Swanstrom R, Paredes R, Shafer R, Ji H, et al. Next-Generation Sequencing for HIV Drug Resistance Testing: Laboratory, Clinical, and Implementation Considerations. Viruses. 2020;12(6).
- Bennett JC, Hetrich MK, Garcia Quesada M, Sinkevitch JN, Deloria Knoll M, Feikin DR, et al. Changes in Invasive Pneumococcal Disease Caused by Streptococcus pneumoniae Serotype 1 Following Introduction of PCV10 and PCV13: Findings from the PSERENADE Project. Microorganisms. 2021;9(4).
- Boehm E, Kronig I, Neher RA, Eckerle I, Vetter P, Kaiser L. Novel SARS-CoV-2 variants: the pandemics within the pandemic. Clin Microbiol Infect. 2021;27(8):1109-17.
- Bonney R, Cooper CB, Dickinson J, Kelling S, Phillips T, Rosenberg KV, et al. Citizen science: a developing tool for expanding science knowledge and scientific literacy. BioScience. 2009;59(11):977-84.
- Chen X, Kang Y, Luo J, Pang K, Xu X, Wu J, et al. Next-Generation Sequencing Reveals the Progression of COVID-19. Front Cell Infect Microbiol. 2021;11:632490.
- Cheepsattayakorn A, Cheepsattayakorn R. Parasitic Pneumonia and Lung Involvement. Biomed Res Int. 2014; 2014: 874021.
- Chiolero A, Buckeridge D. Glossary for public health surveillance in the age of data science. J Epidemiol Community Health. 2020;74(7):612-6.
- Dunachie SJ, Day NPJ, Dolecek C. The challenges of estimating the human global burden of disease of antimicrobial resistant bacteria. Current Opinion in Microbiology. 2020;57:95-101.
- Fact Sheet: Antimicrobial Resistance, Switzerland: World Health Organization; 2022. Updated 17 November 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance.
- First meeting of the WHO antifungal expert group on identifying priority fungal pathogens: Meeting Report Geneva, Switzerland: World Health Organization; 2020. Updated 9 June 2020. Available from: <u>https://www.who.int/publications/i/item/9789240006355</u>.

References

- Gandra S, Alvarez-Uria G, Turner P, Joshi J, Limmathurotsakul D, van Doorn HR. Antimicrobial Resistance Surveillance in Low- and Middle-Income Countries: Progress and Challenges in Eight South Asian and Southeast Asian Countries. Clin Microbiol Rev. 2020;33(3).
- Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report: 2021 Geneva, Switzerland: World Health Organization; 2021. Updated 9 June 2021. Available from: <u>https://www.who.int/publications/i/item/9789240027336</u>.
- Global Influenza Surveillance and Response System (GISRS) Geneva, Switzerland: World Health Organization; 2021. Updated 10 October 2021. Available from: <u>https://www.who.int/initiatives/global-influenza-surveillance-and-response-system</u>.
- GOARN: Global Outbreak Alert and Response Network Geneva, Switzerland: World Health Organization; 2020. Available from: https://extranet.who.int/goarn/.
- Jayatilleke K. Challenges in Implementing Surveillance Tools of High-Income Countries (HICs) in Low Middle Income Countries (LMICs). Curr Treat Options Infect Dis. 2020:1-11.
- Lee L, Mukhi S, Bancej C. Crowdsourced disease surveillance success story: The FluWatchers program. Can Commun Dis Rep. 2021;47(9):354-6.
- Lipkin WI, Firth C. Viral surveillance and discovery. Curr Opin Virol. 2013;3(2):199-204.
- List of National Influenza Centres Geneva, Switzerland: World Health Organization; 2022. Updated 3 March 2022. Available from: <u>https://www.who.int/initiatives/global-influenza-surveillance-and-response-system/national-influenza-centres</u>.
- Litwin T, Timmer J, Berger M, Wahl-Kordon A, Müller MJ, Kreutz C. Preventing COVID-19 outbreaks through surveillance testing in healthcare facilities: a modelling study. BMC Infectious Diseases. 2022;22(1):105.
- Lone SA, Ahmad A. Candida auris-the growing menace to global health. Mycoses. 2019;62(8):620-37.
- Madoff LC. ProMED-mail: an early warning system for emerging diseases. Clin Infect Dis. 2004;39(2):227-32.
- Micoli F, Bagnoli F, Rappuoli R, Serruto D. The role of vaccines in combatting antimicrobial resistance. Nature Reviews Microbiology. 2021;19(5):287-302.
- Mykhalovskiy E, Weir L. The Global Public Health Intelligence Network and early warning outbreak detection: a Canadian contribution to global public health. Can J Public Health. 2006;97(1):42-4.
- Pai M, Kasaeva T, Swaminathan S. Covid-19's Devastating Effect on Tuberculosis Care A Path to Recovery. N Engl J Med 2022; 386:1490-1493
- Perez F, Villegas MV. The role of surveillance systems in confronting the global crisis of antibiotic-resistant bacteria. Curr Opin Infect Dis. 2015;28(4):375-83.

References

- Public health surveillance for COVID-19: Interim Guidance. Geneva, Switzerland: World Health Organization; 2022. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-SurveillanceGuidance-2022.1.
- Respiratory Syncytial Virus Surveillance Geneva, Switzerland: World Health Organization; 2022. Available from: https://www.who.int/teams/global-influenza-programme/global-respiratory-syncytial-virus-surveillance.
- Rodrigues ML, Nosanchuk JD. Fungal diseases as neglected pathogens: A wake-up call to public health officials. PLoS Negl Trop Dis. 2020;14(2):e0007964.
- Schwoebel V. Surveillance of tuberculosis. Indian J Tuberc. 2020;67(4S):S33-S42.
- Tarantola D, Dasgupta N. COVID-19 Surveillance Data: A Primer for Epidemiology and Data Science. Am J Public Health. 2021;111(4):614-9.
- Torgerson PR, Devleesschauwer B, Praet N, Speybroeck N, Willingham AL, Kasuga F, et al. World Health Organization Estimates of the Global and Regional Disease Burden of 11 Foodborne Parasitic Diseases, 2010: A Data Synthesis. PLoS Med. 2015;12(12):e1001920.
- Vermicelli S, Cricelli L, Grimaldi M. How can crowdsourcing help tackle the COVID-19 pandemic? An explorative overview of innovative collaborative practices. R&D Management.
 2020.
- Vouga M, Greub G. Emerging bacterial pathogens: the past and beyond. Clin Microbiol Infect. 2016;22(1):12-21.