Infection

Infection Biology, Treatment and Prevention

Thesis Program for the Curriculum of “Doctor of Philosophy” (N094)

COORDINATORS

Julia Walochnik, PhD, MSc, Assoc Prof
T: +43 (0)1 40 160-38240
julia.walochnik@meduniwien.ac.at

David Leitsch, PhD, MSc, Assoc Prof
T: +43 (0)1 40 160-38211
david.leitsch@meduniwien.ac.at

Institute of Specific Prophylaxis and Tropical Medicine

Medical University of Vienna

Kinderspitalgasse 15, 1090 Vienna

www.meduniwien.ac.at/tropenmedizin

1. Short description

Infectious diseases have been a scourge of humanity since the beginning of times and the present COVID-19 pandemic reminds us again how vulnerable we are to pathogens, even in the age of modern medicine and hygiene. Indeed, communicable diseases still cause a large proportion of annual deaths, especially in low-income countries which carry the largest burden. Lower respiratory tract infections, diarrheal diseases, tuberculosis, malaria, and HIV/AIDS are claiming millions of lives every year and disable even more. But also a very large number of other infectious diseases, often neglected by scientific research and the pharmaceutical industry, pose considerable challenges to societies. Furthermore, the increasing number of resistant pathogens, mainly bacteria but also fungi and parasites, make the treatment of diseases, long believed to be overcome, difficult. Especially in hospitals, the rise of nosocomial infections with multiply resistant microbes has become a major challenge.

It is therefore timely and highly relevant to offer a PhD program specializing on the biology of pathogens and infectious diseases. The program will encompass the whole spectrum of microorganisms, i.e. viruses, bacteria, fungi, and parasites and will cover multiple aspects such as basics in microbiology, pathogen-host interactions, virulence, prevention and hygiene, antimicrobial resistance, vaccine development, and the microbiome. Nosocomial infections as well as community infections will be covered so that a thorough training of PhD candidates enlisting in the program in the field of infection biology can be provided.

2. Scope

General aspects of infection (Walochnik/Leitsch)

Respiratory Viruses (Redlberger-Fritz)

Persistent human viruses (Görzer)

Viral Zoonoses (Camp)

Entry and assembly of enveloped viruses (Stiasny)

Bacterial Pathogens and Diagnostic Methods (Makristathis)

Clinical Mycobacteriology (Veletzky/Winkler)

Fungal Pathogens (Willinger)

Clinical Parasitology (Veletzky/Winkler)

Protist Pathogens (Walochnik)

Malaria (Lell)

Helminthic human pathogens (Köhsler)

Host-parasite interactions of parasitic worms (Schabussova)

Arthropod vectors of human pathogens (Kniha/Camp)

Ticks and Tick-Borne Pathogens (Wijnveld)

Water Hygiene (Sommer/Reiter)

Water-transmitted Pathogens (Reiter/Sommer)

Health-Related Water Microbiology (Kirschner)

Environmental Pathogen Surveillance for Public Health (Bergthaler)

Infection Epidemiology (Schmid)

Sexually transmitted infections (Handisurya)

Infection and women's health (Farr)

Infection prevention and control of the transmission of infectious agents (Presterl/Diab-Elschahawi)

Disinfection (Suchomel)

Pharmacokinetics of antiinfective Drugs (Vossen)

Antiparasitic Chemotherapy (Leitsch)

Vaccines and Vaccination (Inić-Kanada/ Wagner)

Animal models of microbial infections - opportunities and limitations (Knapp)

Post-infection disorders (Untersmayr-Elsenhuber)

3. CONTENTS

3.1. Courses

3.1.1. Basic Course

(2 semester hours/ semester, 1st-2nd semester)

Chapter: General aspects of infection (Walochnik/Leitsch)

Since there was life on earth, there have been extensive interactions of organisms, of cells, of molecules. Indeed, the earliest emergence of life was already driven by infection processes, by early RNA and subsequently also DNA molecules incorporating themselves into other molecules as group I introns, later in the form of single strand and double strand RNA viruses, retrons and group II introns and finally DNA viruses and plasmids. Early evolution was characterized by extensive genetic exchange, conditioning the formation of barriers to keep foreign material out, early compartments evolving into the first cells (progenotes) covered with membranes, in the case of bacteria even with cell walls. The last universal common ancestor (LUCA) is believed to have lived around 3.5 Gya or even 3.8 Gya and may in fact rather have been a community of different progenotes with RNA genomes. The RNA to DNA transition could have resulted independently for Bacteria and for Archaea/Eukarya from two viral invasions. Finally, also the various endosymbiotic events that led to the evolution of the different eukaryotic groups, including metazoans (and thus humans), can be understood as infection processes. Infection is one of the major driving forces for evolution, but infection may also result in disease and eventually death of the host cell/organism.

After completion of this chapter, the PhD student will:

1. be familiar with the relevant terminology and definitions

2. understand the basics of infection biology

3. understand the basics of the evolution of pathogens

Chapter: Respiratory Viruses (Redlberger-Fritz)

Annually, respiratory viruses circulate within the human population and cause numerous viral infections of the upper and/or lower respiratory tract. At present, well over 200 viral pathogens are known to cause respiratory infections, most of them (e.g. influenza, respiratory syncytial virus or coronaviruses) show seasonal patterns in their annual appearance. However, this seasonality does not only occur with the typical colds during the winter months, but we can also observe it with a large number of other viral diseases. As an example, the "summer flu" - which is caused by enteroviruses - or the periodically observed parvovirus or varicella activity during spring should be mentioned. Knowledge of the regional and temporal epidemiological activity of the circulating viruses can therefore represent an aid in diagnostics/differential diagnostics that should not be underestimated. In addition to the clinical examination and the just discussed consideration of the epidemiology of the circulating viruses, a thorough anamnesis is also indispensable.

In this chapter we will not only discuss the characteristics of the most common respiratory viruses but we will also give an better insight into their epidemic activity, the clinical differences, the severity and also the possible prophylaxes.

After completion of this chapter, the PhD student will be able to:

1. know the characteristics of the most common respiratory viruses like influenza, SARS CoV2, RSV, etc…

2. know the epidemiological pattern of circulating viruses

3. have an insight of the reciprocal influences of the different dynamics of viral spread of different respiratory viruses

4., have knowledge on the possible prophylaxes in preventing respiratory viral infections

Chapter: Persistent human viruses (Görzer)

A number of human viruses persists lifelong in the human host after infection. Well-known examples are herpesviruses, retroviruses or anelloviruses. In recent years the extent and complexity of persistent human viruses have become more and more evident due to large scale virus genome sequencing approaches. Since then, numerous studies deciphered the human virome in different life style and clinical settings. The coexistence of a complex virus community seems to range from beneficial to disease-causing.
This lecture will provide an overview of the complexity of persistent viruses, their multiple different strategies to efficiently infect the human host and to successfully evade the immune control. Moreover the direct and indirect involvements of persistent viruses into pathogenic processes which often only occur under certain circumstances, such as a congenital cytomegalovirus infection or a potential role of EBV in triggering multiple sclerosis, will be discussed. Finally, latest knowledge on the interplay between antiviral prophylactic and therapeutic options and emergence of viral resistance will be given. The themes will be exemplified by commensal (e.g. anelloviruses) and pathogenic (e.g. herpesviruses) viruses.

After completion of this chapter, the PhD student will be able to:
1., know the major types of persistent human viruses and their prevalence
2., describe major strategies to persist and evade the immune control
3., learn about current detection methods
4., understand the pathogenic potential and main options of treatment

Chapter: Viral Zoonoses (Camp)

Over half of the zoonotic pathogens affecting humans are viruses, and most of these are specifically RNA viruses. These comprise a large part of what are considered emerging pathogens, but also include re-emerging and some persistent infectious diseases. The viruses are maintained in natural foci of (often complex) transmission involving specific animal hosts, some of them acting as reservoir hosts, maintenance hosts, amplifying hosts, and/or bridge vectors. Emergence of the viruses in the human population is related to specific ecological or anthropogenic factors that affect host populations or bring humans in close physical/temporal proximity to natural (enzootic) foci, assisted by some intrinsic properties of RNA viruses to adapt and overcome host barriers. Understanding and predicting spillover events remains a difficult task, but controlling and preventing these events is of utmost importance. The success of zoonotic viruses in the human population varies widely: from dead-end transmission (highly-pathogenic avian influenza A(H5N1) virus, hantaviruses, and arboviruses such as West Nile virus or Tick-borne encephalitis virus); to limited human-to-human transmission (Crimean-Congo hemorrhagic fever virus, MERS-coronavirus, Zaire ebolavirus); to successful and continued human-to-human transmission (SARS-CoV-2, A(H1N1)pdm09

influenza virus, HIV); as well as successful incorporation of humans into transmission networks (arboviruses such as Zika virus, Dengue virus, and Chikungunya virus).

Rather than a taxonomic overview, this chapter will provide a conceptual overview of major themes in the ecological maintenance, spillover, and control of zoonotic viruses currently affecting humans. The themes will be exemplified by "local" zoonotic viruses, including examples from arthropod-borne viruses (flaviviruses and bunyaviruses), rodent-borne viruses (hantaviruses), and some other important zoonotic viruses (coronaviruses, rabies virus, and filoviruses).

After completion of this chapter, the PhD student will be able to:

1., know the major types of zoonotic RNA viruses and their maintenance in nature
2., describe major modes of spillover of zoonotic viruses into humans, citing major barriers to spill-over and continued transmission, and provide examples.
3., understand current methods in surveillance, prevention and/or mitigation of zoonotic RNA viruses and spillover events.

Chapter: Entry and assembly of enveloped viruses (Stiasny)

Many animal and human viruses are surrounded by a lipid membrane (enveloped viruses), which is acquired usually at a late stage of particle assembly. The viral membranes is decorated with virus-encoded envelope proteins that are important for host cell entry and thus infection. In this chapter, the different structures of these proteins as well as the mechanisms of virus entry and assembly will be discussed using influenza viruses, coronaviruses (particularly SARS-CoV-2) and flaviviruses as examples. In addition, because of their important functions in virus entry, these envelope proteins are the major targets of neutralizing antibodies and therefore important components of virus vaccines, another topic that will be addressed.

After completion of this chapter the PhD student will be able to:

1. describe the different structural classes of viral envelope proteins and their functions
2. different mechanisms of virus entry and how it can be blocked by neutralizing antibodies
3. describe different assembly pathways of enveloped viruses

Chapter: Bacterial Pathogens and Diagnostic Methods (Makristathis)

The body is constantly exposed to a variety of bacterial species, including beneficial commensals, but also pathogenic bacteria that have mechanisms to overcome the body's normal defences. The latter is especially true for obligate pathogenic species. However, the vast majority of bacterial infections are caused by facultative pathogens, which are often part of the resident or transient colonising flora and cause local or systemic infections under certain circumstances.

Bacterial infections can range from being asymptomatic and self-limiting to life-threatening situations requiring rapid diagnosis. This chapter presents the arsenal of microbiological laboratory diagnostics for the

most important bacterial infectious agents, which has expanded greatly in recent years. New mainly molecular methods for rapid identification of the pathogen and its resistance mechanism to the most important antibiotics are presented and their reasonable use in combination with conventional methods is discussed.

After completion of this chapter the PhD student will be able to:

1., understand the challenges of laboratory diagnostics of bacterial infectious diseases
2., recognise the potential but also the limitations of existing technologies
3., identify areas where there is still a need for new diagnostic procedures

Chapter: Clinical Mycobacteriology (Veletzky/Winkler)

Mycobacterial infections and especially those due to *Mycobacterium (M.) tuberculosis* are responsible for a major proportion of the worldwide infectious disease burden. Nearly one third of the world population is considered infected with *M. tuberculosis* and more than 1 Million tuberculosis deaths are counted annually. While tuberculosis mainly affects the lungs, all other organs might be the target of the disease. The complete spectrum of interaction between the human host and mycobacteria, with its often devastating clinical sequelae, are not yet fully understood. This course will provide an insight into host-mycobacterial interaction and its clinical consequences, thus providing an understanding of the biology of mycobacterial disease.

After completion of this chapter the PhD student will be able to:

1., understand the biological and clinical relevance of mycobacterial infections

2., explain the manifestations caused by mycobacterial disease in humans

3., identify open research questions in clinical mycobacteriology

Chapter: Fungal Pathogens (Willinger)

For many years, fungi were believed to be clinically insignificant, but an increased incidence of invasive fungal infections in recent decades has created a major challenge for healthcare professionals. More than 600 different fungi, yeasts, and filamentous fungi, including molds and dermatophytes, have been reported to infect humans, ranging from common to very serious infections, including those of the mucosa, skin, hair, and nails, and other ailments. Particularly, invasive fungal infections are found in patients at risk and are frequently fatal. This chapter will address the changing epidemiology of fungal infections and will deal with well-known, but also with emerging fungal pathogens.

Diagnosing fungal infections, especially invasive fungal infections, remains a problem. However, early diagnosis and prompt initiation of antifungal therapy are essential steps in the management of patients with invasive fungal infections. None of the currently available tests provide sufficient sensitivity and specificity alone; thus, the optimal approach relies on a combination of various testing strategies. This underscores the

need for the development of new techniques of detecting fungal pathogens. Also, the importance of antifungal susceptibilities and their determination will be discussed.

After completion of this chapter the PhD student will be able to:

1. understand the epidemiology of fungal pathogens
2. know the most important techniques for diagnosis, identification of fungal pathogens and their resistance mechanisms
3. name the most important antifungal agents
4. develop an understanding for resistance mechanisms in fungi

Chapter: Clinical Parasitology (Veletzky/Winkler)

Parasitic diseases are still responsible for a major part of the worldwide disease burden. While parasites are part of the ecosystem, they have bothered mankind, fauna and flora for thousands of years and have co-evolved simultaneously. The complete spectrum of interaction between mammalian and specifically human parasites and their hosts, including negative effects (disease) and possible positive effects (immunomodulation e.g. protection from autoimmune disease), is not yet fully understood. Comprising a heterogenous group of pathogens, parasites cause a variety of clinical syndromes, from rather chronic, asymptomatic infections to rapidly evolving, life threatening or debilitating syndromes. This course will provide an insight into caused diseases, their manifestations and damage, and thus provide an understanding of the clinical impact of these diseases on the individual and on populations.

After completion of this chapter the PhD student will be able to:

1., understand the clinical relevance of parasitic infections

2., explain the manifestations caused by parasites in humans

3., identify open research questions in clinical parasitology

Chapter: Protists as human pathogens (Walochnik)

Around 100 protist species can be parasites of humans, less than half of them are significantly harmful to their hosts. Nevertheless, some of these microorganisms are of prime importance for human health, being the causative agents of malaria, sleeping sickness, leishmaniasis, amoebic dysentery, amoebic encephalitis or giardiasis, just to give a few examples. Moreover, quite a number of protists are opportunistic, causing more severe disease in immunocompromised individuals.

Many parasitic protists have complicated life cycles with several different developmental stages. Their sizes vary from <5 µm (amastigote *Leishmania* spp.: 2–4 µm) up to 150 µm (the ciliate *Balantioides coli*), they can inhabit almost all body sites and they are often difficult to identify by morphological means. Nevertheless, in many cases, identification to the species or even genotype level is essential not only to understand the epidemiology of these infections, but also because treatment schemes vary depending on species. In this chapter, the most important pathogenic protists will be introduced, including their morphologies and

phylogenies, their modes of infection, their locations within the human body, pathomechanisms and the signs and symptoms these infections cause.

After completion of this chapter the PhD student will be able to:

1., describe the protist agents of infectious diseases of humans
2., identify the modes of infection and locations of protist pathogens within the human body
3., explain the pathomechanisms of and manifestations caused by protist pathogens
4., understand host-parasite interactions in protist pathogens

Chapter: Malaria (Lell)

Malaria is still one of the most important infectious diseases in humans and remains endemic in many low and middle income countries, causing over 200 Million cases and around 500,000 deaths annualy. Rapid and accurate diagnosis and treatment without delay are essential for reducing morbidity and mortality, particularly in malaria tropica, caused by *Plasmodium falciparum*.

After completion of this chapter the PhD student will be able to:

1., describe the *Plasmodium* species causing malaria in humans
2., describe the mode of infection and the factors relevant for malaria epidemiology
3., explain the pathomechanisms of and manifestations caused by *Plasmodium* spp. in humans
4., understand the concept of semi-immunity
5., describe the most important anti-malarials and understand the concept of malaria prophylaxis

Chapter: Helminthic human pathogens (Köhsler)

Approximately 1.5 billion people are infected with helminthic parasites worldwide, making it the most common infection in the world. Generally, pathogenic helminths belong to three different groups - trematotes or flukes, nematodes or flat worms and cestodes or tape worms. They are most common in tropical areas, where people regularly suffer from more than one parasitic helminth.

The most fatal helminthic disease is schistosomiasis causing more than 200.000 deaths per year. Intestinal helminths, most importantly *Ascaris lumbricoides*, *Trichuris trichiura* or hookworms lead to less fatalities, however are responsible for 5 million disability-adjusted life years. Many helminthic pathogens have complicated life cycles including one or more intermediate hosts.

There are several strategies how helminthic pathogens enter the hosts body. Some helminths penetrate the skin, some are ingested with contaminated food and others enter the human host via uptake of their cyst forms in meat from intermediate hosts. They can be found in almost all organs, most importantly in the intestine, but also in the muscles, skin, liver or in the brain, often leading to life-threatening diseases.

In this chapter, the most important pathogenic helminths will be introduced. The morphology, mode of infection, location in the hosts body, and symptoms of these infections will be discussed and also the pathomechanisms of these parasites will be elucidated.

After completion of this chapter the PhD student will be able to:

1., describe the most important helminthic pathogens of humans

2., identify the modes of infection and locations of helminthic pathogens within the human body

3., explain the pathomechanisms of and manifestations caused by helminthic pathogens

Chapter: Host-parasite interactions of parasitic worms (Schabussova)

Parasitic worms, helminths, are multicellular organisms of medical importance that can infect humans and animals. They can be classified into three groups: flukes (Trematoda), tapeworms (Cestoda), and roundworms (Nematoda), often with very different and often highly complicated parasitic cycles. For example, (i) they may be transmitted by transdermal route (Ancylostoma, Necator, Schistosoma, etc.), orally (Trichuris, Ascaris, Echinococcus etc.) by an arthropod vector (Onchocerca, Wuchereria, Dirofilaria, etc.) or by a predator-prey transmission (Dracunculus, Taenia, Diphyllobothrium, etc.); (ii) their definitive and intermediate hosts can range from mammals, birds, reptiles, fish, molluscs to arthropods; and (iii) they may be localized in gut, liver, lung, heart, lymphatic vessels, etc.

Helminths cause a wide spectrum of diseases, from mild to potentially deadly. If left untreated, most helminth infections result in chronic inflammatory disorders that cause pathology such as anaemia, growth stunting, fatigue, poor cognitive development, blindness, bladder cancer, or in extreme cases, they may cause death.

The majority of hosts tend to harbour a few parasites and only the minority are heavily infected hosts. This extraordinary equilibrium of the immune defence of the host and the immune evasion of the parasite was established during long-term coevolution. Helminths have developed several means of escaping the host immune responses and they have been called “masters of immunomodulation”. Helminths can interfere with inflammatory and immune mechanisms in other parasitic infections, and other immune-mediated diseases such as allergy or autoimmunity or with responses to vaccines.

This course will provide students with an understanding of important human parasitic diseases, including their life cycles, vectors of transmission, distribution and epidemiology, pathophysiology and clinical manifestations, treatment, and prevention and control. Additionally, the hygiene hypothesis will be discussed.

After completion of this chapter, the PhD student will be able to:

1. Describe the various types and infection routes of medically important worm parasites
2. Understand the life cycles of several medically important worm parasites
3. Understand the principles of interaction of the worm parasites with the human immune system

Chapter: Arthropod vectors of human pathogens (Kniha/ Camp)

Hematophagy (feeding on the blood of a vertebrate host) has evolved multiple times in arthropods, and remains a very successful strategy for some extant taxa. In addition to the nuisance of blood-feeding, many

human pathogens have co-evolved with blood-feeding arthropods, allowing the arthropod to act as a vector. It is estimated that over 700 million people contract a mosquito-borne illness each year; among them, malaria causes over 200 million cases and 0.5 million deaths per year (despite the existence of successful mosquito control measures, anti-malarial treatment and prophylaxis, and the ever-nearing development of a successful vaccine). Ticks are also commonly known to transmit a variety of bacterial and viral pathogens to humans, however there exist many more hematophagous arthropods that are vectors of pathogens to humans, including blackflies (onchocerciasis), fleas (plague), lice (typhus), sandflies (leishmaniasis and sandfly fever), reduviid "kissing" bugs (American trypanosomiasis) and tsetse flies (African trypanosomiasis). Global climate change, human global transportation, and anthropogenic habitat alteration has had drastic effects on the abundance and geographic distribution of some major arthropod vectors, and has mostly increased the risk of humans contracting vector-borne diseases.

Understanding the biology of hematophagous arthropods has long been the focus of research, and quite a lot is understood about their role as biological vectors (or reservoirs) of disease. This chapter will discuss the major groups of arthropod vectors, identifying the major pathogens they transmit and the biological mechanisms that allow pathogen transmission. The epidemiology of vector-borne diseases will be discussed as it relates to vector biology, focusing on examples of emerging and persistent pathogens, and how emergence (or persistence) relates to human activities.

After completion of this chapter the PhD student will be able to:

1., know the major types of arthropod vectors and the pathogens they transmit;

2., describe the physiological barriers to biological transmission of pathogens by vectors;

3., understand how humans encounter vector-borne diseases and existing vector control measures.

Chapter: Ticks and Tick-Borne Pathogens (Wijnveld)

Ticks are the main vector of pathogens in the northern hemisphere and pose risks to human and animal health worldwide. Being a hematophagous arthropod, ticks require several bloodmeals during their active life stages. The best-known pathogen transmitted by ticks is *Borrelia burgdorferi* sensu lato (the causative agent of Lyme borreliosis). However, this is not the only pathogenic microbe associated with ticks. Ticks can transmit a large range of bacterial, viral, protozoal, and fungal pathogens. This chapter aims to give further insight into human biting ticks in Austria and the medically relevant pathogens associated.

After completion of this chapter the PhD student will be able to:

1. Recognise ticks of human medical relevance in Austria.
2. Explain the life cycle of hard ticks.
3. Know which tick-borne pathogen genera affect human health in Austria
4. Describe the infection route of tick-borne microbes and how the colonisation of ticks differs between microorganisms.
5. Give examples of how tick-borne pathogens try to evade the host immune system.

Chapter: Water Hygiene (Sommer/ Reiter)

Water hygiene comprises a holistic strategy and measures to prevent water-associated diseases, in particular infections by water transmittable pathogens. Infections can be caused by contaminated drinking water (public and private water supply, bottled water), recreational water (surface water, pool water), water in health care facilities (nosocomial infections), water for medical purposes, water for haemodialysis, water in cooling facilities, water in food production and wastewater. Preventive strategies are protection of water resources, water treatment and water disinfection by chemical and physical technologies.

The surveillance and control of water quality includes an on-site inspection, a detailed sampling strategy and instructions followed by chemical, physical and microbiological methods. Direct determination of pathogens is not fast and reliable enough to intervene in time in case of contamination. Thus, a set of faecal indicators are used for water quality monitoring. To ensure reliable results, international standard methods are established and - connected to these methods, limit values for safe water have been laid down in regulations. Important examples are the EU directive for the quality of water for human consumption, the EU directive on Bathing water quality or the EU regulation on the minimum quality for water reuse.

After completion of this chapter the PhD student will be able to:

1. comprehend the most important preventive strategies of water associated infections
2. explain suitable methods for the disinfection of drinking water, pool water, waste water
3. understand the process and methods to assess the microbiological water quality in terms of human health
4. have an overview of the essential regulations, standards and guidelines for water quality

Chapter Water-transmitted Pathogens (Reiter/ Sommer)

Water associated infections belong to the main health burdens worldwide accounting for 8 million deaths per year according to WHO. There are two main pathways for acquiring infections caused by water-transmitted pathogens.

On the one hand, water serves as carrier for faecally excreted pathogens, comprising bacteria, viruses, protozoa and other parasites. On the other hand, indigenous water microorganisms including facultative pathogens may cause human infections. Routes of infections are by oral consumption, contact, aerosol inhalation and intravenous.

Prevention strategies include protection of water resources from faecal pollution, management and disinfection. Knowledge of the concentrations occurring in the different water sources is a prerequisite for the selection of target-oriented measures and quantitative microbial risk assessment.

Detection and quantification of pathogens in water samples are challenging and can be performed by different techniques. Prerequisite for reliable results are the application of concentration methods, followed by cultivation-based analytics, microscopic or molecular-biological methods. For reliable interpretation of the results, it is critical to take the method chosen into account.

After completion of this chapter the PhD student will be able to:

1. understand the most significant water transmittable pathogens
2. comprehend the different routes of infection in context with exposition to water

3. to gain an understanding of the concentrations of pathogens that can occur in different water sources (drinking water, surface water, waste water).
4. understand the various methods for analysing pathogens in water samples and know how to interpret the results

Chapter: Health-Related Water Microbiology (Kirschner)

The quality of water is of fundamental importance for human health in all areas of life. According to the World Health Organization (WHO), unsafe water or lack of sanitation accounts for up to nearly 10% of global health impacts, especially in developing regions. Besides chemical-toxicological issues, problems with microbiological water quality are of most prominent importance. Naturally, each water resource contains a high number of (beneficial) microbes that are completely harmless concerning human health. However, the natural equilibrium can be impaired by allochthonous microbial pollution or unwanted autochthonous microbial growth such as fecal pollution based transmission of intestinal pathogens (waterborne infections) or the growth of opportunistic pathogens in water systems under specific situations (e.g. "emerging" water based pathogens such as *Legionella spp. or Vibrio spp.*). In addition, the water cycle is also increasingly discussed as a potential vector (or reservoir) to spread antimicrobial resistance. This course will provide a basic understanding on microbiological water quality and health issues: problems and health relevance, WHO framework for the safe water use, basic analytical/diagnostic methods, and available hazard and risk assessment and management tools to identify and prevent the spread of infectious diseases via the water cycle (in natural and technical systems).

By the end of this course students will be able to …

1. explain and describe the most important concepts of health-related water microbiology
2. explain and describe the basic diagnostic methods to detect microbes in water
3. define and describe essential microbial aspects of assessment/prevention/control strategies for safe water use

Chapter: Environmental Pathogen Surveillance for Public Health (Bergthaler)

Public health surveillance is the continuous systematic collection, analysis and interpretation of health-related data. According to the WHO, disease surveillance serves multiple aims such as an early warning system for impending outbreaks that could become public health emergencies; monitoring and evaluation of the impact of interventions and tracking progress towards specific goals; and clarifying the epidemiology of health problems, guiding priority-setting and planning of public health policy and strategies.

Technological advances in sequencing techniques have empowered the monitoring of one or more pathogens not only in individual persons but also in environmental samples. This includes the surveillance of wastewater, which has undergone a renaissance during the SARS-CoV-2 pandemic and became a cornerstone of national monitoring of the pandemic virus in many countries. Population-level based surveillance of pathogens allows non-invasive monitoring with the benefit of reduced sampling bias and cost effectiveness. Important limitations relate to the need for sophisticated data interpretation and the lack of

resolution for individual cases. In the future, environmental pathogen surveillance is expected to play an increasingly important role for public health.

After completion of this chapter the PhD student will be able to:

1. describe key principles of pathogen surveillance on a population-level,
2. understand the basics of next-generation sequencing techniques, and
3. contextualize both the opportunities as well as the limitations of environmental pathogen surveillance.

Chapter: Infection Epidemiology (Schmid)

The descriptive and analytical infectious disease epidemiology (IDE) is a practical science, concerned with the complex relationships among infectious agents (bacteria, viruses, fungi, protozoans, worms), their hosts (people, animals) and shared environment to minimize the impact of infectious agents on public health. The field of IDE cooperates with disciplines such as hygiene, clinical infectiology, medical microbiology, veterinary medicine, environmental and social science; furthermore, it makes use of molecular typing methods to give a highly resolved picture of transmission over the short term of outbreaks, and the longer term of international spread; and it makes use of mathematical models for understanding infectious disease dynamics and evaluating the impact of interventions to prevent or control.

After completion of this chapter, the PhD student has been introduced to the

- Investigation of food-born outbreaks
- epidemiological surveillance – the continuous monitoring and evaluation of the epidemiology of infectious diseases
- Epidemiological study designs: cohort study, case-control study, cross-sectional studies
- Development and evaluation of prevention and control strategies

Chapter: Sexually transmitted infections (Handisurya)

Sexually transmitted infections (STIs) encompass bacterial, viral and parasitic diseases, which are predominantly transmitted by sexual activity, such as vaginal, anal and oral intercourse. Some STIs can spread from mother to child during pregnancy, childbirth and breastfeeding.

The most common bacterial STIs are chlamydia (caused by *Chlamydia trachomatis serotypes D-K*), gonorrhoea (caused by *Neisseria gonorrhoeae*), and syphilis (caused by *Treponema pallidum*). An estimated 218 million people worldwide become infected each year with one of these three pathogens. While these bacterial STIs are generally curable with the existing antibiotics, severe complications, such as pelvic inflammatory disease and infertility in women, can arise from not or inadequately treated gonorrhoea and chlamydia infections. Infections with human papillomavirus (HPV), hepatitis B virus (HPB), human immunodeficiency virus (HIV) and herpes simplex virus (HSV) represent the most common viral STIs. Antivirals can modulate the course of HIV, HBV and HSV infections, although complete cure cannot yet be achieved. However, vaccination can confer protection against HPV and HBV infections, which otherwise

could lead to development of anogenital, most notably cervical, cancers and subset of oropharyngeal cancers or hepatocellular carcinoma, respectively. Parasitic STIs include trichomoniasis (caused by *Trichomonas vaginalis*), which affects about 156 million worldwide. Other ectoparasitic STIs are infestations with *Pthirus pubis*, which leads to Pediculosis pubis, and *Sarcoptes scabiei*, the cause of scabies.

After completion of this chapter the PhD student will be able to:

1. describe the causative agents of the most common STIs

2. explain the most important clinical manifestations and complications of STIs in afflicted humans

3. understand the most important key points in therapy and prevention

Chapter: Infection and women's health (Farr)

The microbiome of the female reproductive tract is physiologically composed by millions of germs. However, infectious diseases are responsible for more than half of urgent consultations in gynaecologic offices, with potentially enormous consequences on each individual patient. Proper diagnostics, screening and consequent treatment are crucial to avoid long-term effects including infertility and preterm birth. Currently, there is a number of emerging candidates that focus on precision medicine rather than undirected antimicrobial chemotherapy. In this chapter, common infectious diseases in women's health are bei ng discussed, with special emphasis on pregnancy, as well as on preterm prevention, diagnostic tools and treatment. Further, the intrauterine and placental microbiome will be discussed, as well as multidisciplinary neonatal care.

After completion of this chapter the PhD student will be able to:

1., understand the basic principles of the female microbiome

2., name the most important infectious diseases in women's health

3., develop an understanding for ante-, peri- and postpartum care

Chapter: Infection prevention and control of the transmission of infectious agents (Presterl/ Diab-Elschahawi)

Infectious diseases have always been a threat to civilizations. Hygiene and infection prevention and control are prerequisites for successful civilisations and their prosperity. Prevention of transmission and control of the spread of infectious agents are important in general life and particularly in the hospital. The COVID-19 pandemic has impressively demonstrated that the first and fundamental way of protection from infectious diseases is the establishment of infection control measures including general and personal protection, e.g. safe conduct and/or attire. To know the pathways and mechanisms of transmission of infectious agents, i.e. bacteria, fungi, viruses etc. together with the principles of hygiene is pivotal for infection control and prevention. Implementation of the infection control and protection measures will be sustainable using the multimodal strategy according to the World Health Organisation.

After completion of this chapter the PhD student will be able to:

1., understand the basic principles of infection prevention and control of transmissible diseases

2. know the mechanisms of transmission of infectious diseases and their agents

3. develop an understanding of the process of implementation of infection prevention and control with the use of a multimodal strategy

Key words for basic lecture: Infection prevention and control, hand hygiene, transmission precautions, general and personal protection measures

Chapter: Disinfection (Suchomel)

Contaminated surfaces and especially hands can play a very important role in the transmission of pathogens. With suitable disinfectants (biocides) and appropriate disinfection procedures, these transmission routes can be effectively interrupted. Unfortunately, the wrong use of disinfectants can favour the emergence of tolerant and resistant pathogens, especially bacteria. In this chapter, the most important biocidal agents and their areas of application are presented, the correct implementation of hand and surface disinfection is discussed and the various possible causes of the development of resistance to biocides are pointed out.

After completion of this chapter the PhD student will be able to:

1., explain the basic principles of disinfection
2., know the most important biocidal agents and their antimicrobial efficacies
3., understand the development of resistance to biocides

Chapter: Pharmacokinetics of antiinfective Drugs (Vossen)

About 30% of patients treated in intensive care units suffer from sepsis. This infection with organ failure is the main driver of morbidity and mortality in the ICU setting. Especially in this patient cohort, antimicrobial agents are life saving therapeutics. Their efficacy hinges on the attainment of sufficient tissue concentration at the point of infection. Thus, understanding antimicrobial drug mode of action and the influence of different dosing strategies is key in ensuring safe and effective therapy with a minimum of induction of bacterial resistance. Pharmacokinetic/pharmacodynamic indices vary between drug classes but highly influence drug dosing regimens and their modification during organ failure and organ replacement therapy.

We will discuss the most important antimicrobial drugs and their pharmacokinetic profiles as well as possible modificators of their plasma levels.

After completion of this chapter the PhD student will be able to:

1., understand pharmacokinetic / pharmacodynamics indices of antiinfective drugs

2., understand the influence of sepsis and organ replacement therapies on pharmacokinetics

3., understand the impact of pharmacokinetics on resistance induction

4., name the most important antibacterial drugs

Chapter: Antiparasitic Chemotherapy (Leitsch)

Parasitic diseases affect billions of people every year but vaccines against parasites have proven notoriously difficult to develop. Consequently, the management of parasitic diseases widely relies on chemotherapy. Although parasites are eukaryotes and therefore much more closely related to humans, numerous biochemical and cytological differences exist between humans and parasites which can be exploited as drug targets. In this chapter, the most important antiparasitic drugs will be introduced and discussed, ranging from antimalarials to anthelmintic drugs and pesticides used for vector control. Further, the mechanism of action of the most important antiparasitic drugs will be detailed as well as pertinent resistance mechanisms which have developed in some parasites.

After completion of this chapter the PhD student will be able to:

1., understand the basic principles of antiparasitic chemotherapy
2., name the most important antiparastic chemotherapeutics
3., develop an understanding for drug resistance mechanisms in parasites

Chapter: Vaccines and Vaccination (Inić-Kanada/ Wagner)

Current vaccinations are among the most significant public health interventions of the past hundred years. Implementing comprehensive vaccination programs and discoveries of new vaccines against different infectious diseases demonstrated how certain contagious diseases have decreased in their incidence. Although vaccination has proven to be the best way of initiating protection against viral and bacterial infections, only 26 vaccines are licensed against infectious diseases. Effective vaccines against many pathogens such as human immunodeficiency virus, Zika virus, hepatitis C virus, *Chlamydia trachomatis*, and *Borrelia burgdorferi* are unfortunately still unavailable for a variety of reasons, which include but are not limited to pathogen complexity, absence of efficient delivery system and adjuvants, and lack of knowledge how to induce a protective immune response against specific pathogens. In this chapter, the different types of vaccines will be introduced and discussed: live-attenuated vaccines; inactivated vaccines; messenger RNA (mRNA) vaccines; subunit, recombinant, polysaccharide, and conjugate vaccines; toxoid vaccines; and viral vector vaccines. Appropriate vaccine adjuvants will also be discussed. Moreover, the initiation of a vaccine response and generation of immune memory after vaccination will be detailed.
After completion of this chapter the PhD student will be able to:

1., understand the basic principles of vaccination and how vaccine responses are elicited
2., name the most important types of vaccines

3., develop an understanding about the immune memory development

Chapter: Preclinical models of infectious diseases (Knapp)

Preclinical models are a helpful tool to study the in vivo behaviour and biology of pathogenic microbes. Species-specific differences between humans and commonly used animals as such as rodents meet some limitations and require certain adaptations to best possibly mimic relevant diseases in vivo. In this chapter we will provide insights into the set-up of animal models of infectious diseases, explain the usefulness and information than can be gained, as well as the limitations of this approach.

After completion of this chapter the PhD student will be able to:

1., understand the basic principles of preclinical modelling of infectious diseases
2., appreciate the vast information that can be obtained from preclinical models
3., comprehend the pitfalls and limitations of this approach

Chapter: Post-infection disorders (Untersmayr-Elsenhuber)

After infections, a not yet well-defined number of patients are experiencing long-term consequences and continuous symptoms, which have been present before the infection. Viral, bacterial but also parasitic infections are known to trigger disease aftermath. The observed disorders range from post-viral fatigue, which is self-limiting and well-recognized for several virus infections to chronic disorders or even cancer development. In many cases immunological changes are known to trigger long-term symptoms, but in other cases direct involvement of target organs might lead to disease onset. Furthermore, post-infection disorders might also be associated with pathogen-host cooperation and immune escape as it is known eg. for cancer development.

After completion of this chapter the PhD student will be able to:

1) Understand the connection of specific mechanisms associated with post-infection disorders-
2) Define the current evidence of occurrence of post-infection disorders.
3) Acknowledge research gaps associated with symptom development.

3.1.2. Journal Clubs

(2 semester hours/ semester, 1st-6th semester)

Journal Clubs will be held weekly by the supervisors of this PhD programme. These will allow students to critically read and discuss relevant current literature from the field, within a group and under supervision.

3.1.3. Thesis seminars

(2 semester hours/ semester, 3rd-6th semester)

Thesis seminars will be held weekly and will allow the students to present and discuss their own work within the group, guided by the respective supervisors. During these seminars, also methodological problems can be discussed and students will be supported in solving issues of project planning, data interpretation or publication.