Microbiology

February 5 - March 30, 2018

UCM Course SCI2040

University College Maastricht

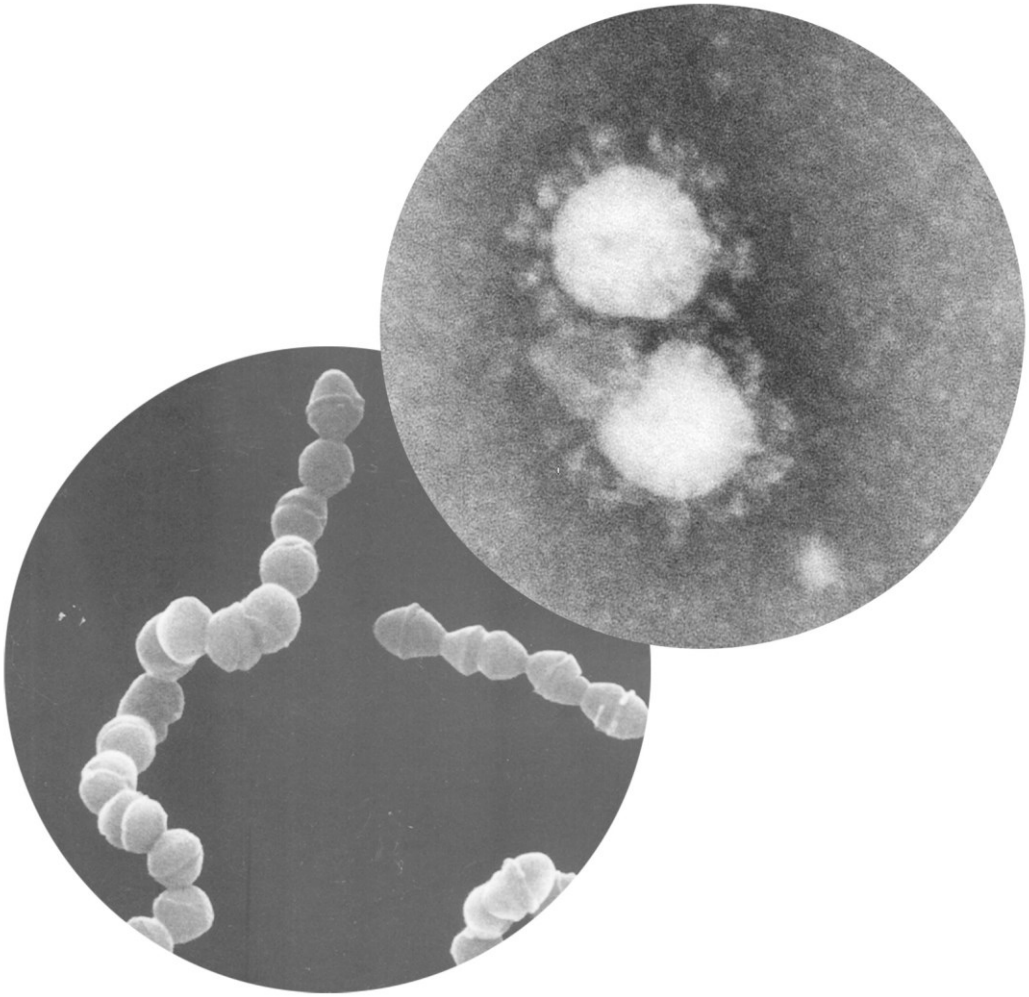

Table of Contents

1. General information

Microbiology is a rapidly growing and changing subject. New micro-organisms, especially viruses, are constantly identified and our knowledge of the pathogenic potential of micro-organisms is being expanded.

1.1 Introduction

New and important infections have been discovered during the last twenty years, for example MERS, AIDS, SARS and Avian flu. In addition, new possibilities to treat and to prevent infections are now available. Microorganisms are also widely utilized in industry and scientific research.

During the 7-week-period that will be spent on studying microbiology, we would like to introduce you in the fields of both medical and applied microbiology. We will give you basic information about microbiology, especially bacteriology and virology. The basic mechanisms of disease are discussed using some examples of infections that can occur in humans. The diagnosis, prevention and therapy of these diseases will also be topics for discussion. Resistance to therapy, immunity to infections and immunisation (vaccinations) will be discussed in the context of infection.

In addition, insights will be provided in the field of outbreak management and infection control, molecular pathogenesis, antimicrobial resistance and virulence factors. We will then focus on the role of micro-organisms in the environmentent and (industrial) applications of micro-organisms.

1.2 Course objectives

Objectives

- To obtain basic knowledge of microbiology, i.e. of bacteriology, virology and environmental and applied microbiology.
- To study the characteristics of a selection of micro-organisms in relation to the diseases they cause, more specific pathogenesis, immunity, epidemiology, diagnosis and therapy.
- To study environmental microbiology by looking at the role micro-organisms play in our environment and how micro-organisms can be used to our advantage, fx in industrial settings.
- To gain insight in the spread of micro-organisms and how outbreaks of micro-organism happen and can be controlled.

1.3 Instructional format

The field of microbiology is constantly evolving and this course will introduce you to most aspects, including cutting edge knowledge from the field. For this, experts are invited for plenary sessions to discuss a wide range of topics, including Bacteriology, Virology, Epidemiology & Outbreaks, Antimicrobial resistance and Applied and environmental microbiology. In addition, there will be expert meetings, case studies and two practical (laboratory) sessions.

Expert meetings

For each of the two expert meetings, a list of questions is provided in this manual. All participants individually answer each of these questions and dedicate one or two Powerpoint slides to each answer. Please state your name and the question number on each of your Powerpoint slides. All presentations have to be sent by email to your tutor, at the latest by 4 PM the day prior to the expert meeting.

The tutor will compile one combined presentation and will bring this to the expert meeting where a computer and a beamer will be provided. During this meeting, the tutor will invite each student to answer one or two questions. This will be done randomly, so you will have to address all questions, even if you don't present the majority of them.

Case Report

Case briefings are provided in this manual for all case reports that will be discussed during this course. All participants will discuss the case together during the case briefing using the Problem-Based Learning method. The resulting learning goals will each be addressed individually. During the case report meeting, the learning goals will be discussed group-wise.

Practical session

The first two tutorials consist of practical sessions. **Presence at these sessions is obligatory**. Here, we will look at transient and resident flora present on your own body. We will look at bacteria under the microscope and we will analyse the transmission of microorganisms.

1.4 Study materials

There are many microbiology-related books available at the University Library at the UNS50 location. For the topics that will be discussed in the tutorial meetings two study books are particularly useful

- Murray. *Medical Microbiology*. (7th ed.)
  ISBN-13: 978-0323086929 ISBN-10: 0323086926
- Tortora *Microbiology: An Introduction* (12th Edition)
  ISBN-13: 978-0321929150 ISBN-10: 0321929152

In addition, recent scientific literature will be used (see the case studies for some suggestions) and students are expected to look online for other relevant literature.

1.5 Course schedule (subject to change, this is to give an overview only)

Course Schedule Microbiology

Week 1.
Lecture: Introduction (**L. van Alphen**) & **Lecture Bacteriology** (**S. Erkens**)
Tutor group:
Monday, Feb 5 Practical course commensal flora and antimicrobial resistance I.
Thursday, Feb 8 Practical course commensal flora and antimicrobial resistance II.
+ Case briefing Good, bad and ugly bugs
Week 2.
No Class (Carnaval)

Week 3
Lecture: Epidemiology, Outbreaks & Infection control (L. van Alphen)
Tutor group:
Monday, Feb 19 Expert meeting Bacteriology
Thursday, Feb 22 TG: Case report Good, bad and ugly, Case briefing Outbreak

Week 4
Lecture Virulence and Antimicrobial resistance (J. Penders)
Tutor group:
Monday, Feb 26 TG: Case report Outbreak, case briefing ESBL
Thursday, Mar 1 TG: Minisymposium (L. van Alphen, S. Erkens)

Week 5
Lecture + Expert meeting Virology and Immune response (G. Oudhuis)
Tutor group:
Monday, Mar 5 TG: Case report ESBL, case briefing HIV
Thursday, Mar 8 TG: Case report HIV, case briefing Pandemic Flu

Week 6
Lecture **Applied & Environmental Microbiology** (**L. van Alphen**)
Tutor group:
Monday, Mar 12 TG: Case report Pandemic Flu, case briefing Salmonella in space
Thursday, Mar 15 TG: Case report Salmonella in space, Case briefing Tb

Week 7
No Lecture
Monday, Mar 19 TG: Case report Tb, case briefing Biofilm and Biosensors
Thursday, Mar 22 TG: Case report Biofilm and biosensors

Week 8
Monday, Mar 27 No class
Thursday, Mar 30 Written Exam

1.6 Course evaluation

The students will be assessed in three areas; the distribution of the final mark is shown in brackets.

1. A final exam (60%)

In the final week, the course will be evaluated by a written exam which consists of open questions.

2. A Powerpoint presentation on a selected topic in Microbiology (30%)

A scientific meeting/mini-symposium will be held in week 5. Students will team up in pairs of two and choose their favorite contemporary microbiological subject. A list of subjects is provided in this manual. Alternative subjects are also allowed, provided that these subjects are endorsed by the course coordinator. During the symposium, the students will present a 15-minute presentation in which they will show the results of their literature study on the chosen microbiology topic, followed by 5 minutes of discussion. The literature study should include a research question (aim) and should show **recent breakthroughs/recent finding**s on the topic. At least half of the presentation should be dedicated to recent literature on the subject. Please put (short) references **on each slide** (example: penders et al (2014))

The assessment of the presentation will be based on the following criteria:

- The quality of the content of the presentation (Are you able to explain the context and relevance of your research question and does your presentation show in-depth analysis of the literature studied)
- The use of recent scientific literature
- The quality of the presentation (Presentation layout and presentation skill).
- The handling of questions/discussion (Are you able to answer questions and discuss the problem?)
- The coherence of the presentation: the team should present one coherent presentation, which shows equal distribution of tasks and knowledge.

The presentations will be scored by at least two staff members and/or tutors of the department of Medical Microbiology.

3. Active participation in the expert meetings and tutorial groups. (10%)

This includes active participation in practicals, case briefings, case reports and expert meetings. It also includes handing in expert meeting questions complete and on time.

1.7 Participation requirements

In total, 12 meetings are scheduled. The **practical sessions and minisymposium** (3 meetings) are **mandatory** and should be attended. The participation requirement for the other tutor groups and expert meetings is 80%. You are allowed to miss two meetings without further consequences. However, it is required that you yourself notify the tutor of your absence **BEFORE** the start of the tutorial group. If you miss more meetings, you will have to apply for an additional assignment. Request forms are available at the Office of Student Affairs and should be completed and handed in ten working days after finishing this course. Be aware that in order to qualify for an additional assignment you have to have valid reasons to have missed a session (see student handbook).

Attendance of lectures is not mandatory, but is highly recommended, as not all material discussed in the lectures will come back in the cases studies and expert meetings. We will keep track of attendance and this might inform the decision whether a resit is allowed after a failed exam.

Please note that you are not allowed to miss any of the practical course meetings or the minisymposium meeting.

Be on time for class. If you are 5 minutes late or more, you are still allowed to be present, but you will not get your attendance.

1. 8 Educational team

The following staff members from the Faculty of Health Sciences and Medicine are responsible for this course:

- Lieke van Alphen, (course coordinator), PhD, Molecular Microbiologist. Department of Medical Microbiology, MUMC, Maastricht.
  Email: lieke.van.alphen@mumc.nl, Tel: 043-3875095
- Sandra Erkens, MD, PhD, Specialist in Medical Microbiology en Infection Prevention, Department of Medical Microbiology, MUMC, Maastricht.
  Email: s.erkens@mumc.nl,

2. Case Briefings

2.1 Case Briefing: Good, bad & ugly bugs

Miss Adams visits her general practitioner (GP) with complaints of persistent diarrhea. Two weeks earlier, she had visited the GP for a bacterial skin infection for which she was prescribed oral penicillin. The skin infection completely cleared, but ever since she started with penicillin she suffers from diarrhea.

The GP explains that the complaints could be caused by the antibiotic treatment for her skin infection, so called antibiotic associated diarrhea. Miss Adams is puzzled and says: “I thought that antibiotics kill bacteria?” The GP confirms this and explains that antibiotics do not differentiate between good and bad bacteria.

The GP advises Miss Adams to eat a lot of yogurt with added probiotics, in order to balance her commensal intestinal microflora, as this might resolve her complaints.

Additional Literature:

- Goldin BR and Gorbach SL. Clinical indications for probiotics: an overview. (2008)Clin Infect Dis. Feb 1;46 Suppl 2:S96-100;

2.2 Case Briefing: Foodborne outbreak alarms Germany

2011: Germany is alarmed at the scale of a food poisoning outbreak. Cases have occurred in multiple regions of Germany, but the source of the outbreak remains unknown. Investigation into the source have started and focus on small clusters within the large outbreak.

Public Health officials have interviewed cases and identied one cluster of 46cases to be linked to a particular restaurant ('restaurant x'). These cases all displayed symptoms of gastroenteritis (bloody) diarrhea and two cases displayed symptoms of hemolytic-uremic syndrom (HUS).

Below is depicted a graph of the number of cases per day of onset of cluster 'restaurant X'. (Fig 1). In combination with the the information of Table 1, the outbreak investigation team tried to deduce the pathogen causing the outbreak, while stool samples were collected from cases and send to the lab for identification of the pathogen.

Figure 1: cases of gastro-entritis per day of onset, linked with restaurant X

Table 1: Average incubation time per gasto enteritis causing pathogen

Pathogen	Average incubation time (days)	95% CI (days)
Norovirus*	1.2	1.1-1.2
Astrovirus*	4.5	3.9-5.2
Sapovirus*	1.7	1.5-1.8
Rotavirus*	2.0	1.4-2.4
Campylobacter	3.5	1.5-10.0
E. coli (STEC)	3.5	1.0-11.0
Salmonella	1.0	0.5-3.5

*Lee et al. BMC Infectious Diseases 2013, 13:446

2.3 Case Briefing: ESBL

On Friday, September 24, 2010, the Dutch media reported a fatal case caused by infection with an extended spectrum betalactamase- (ESBL) producing enterobacterial strain. Scientists hypothesized that this was caused by eating contaminated poultry meat.

A few months earlier, microbiologists already warned that 94% of all chicken meat in Dutch supermarkets was contaminated with ESBL-producing bacteria. These bacteria are resistant against 3rd-generation cephalosporins. The former ministers of agriculture and public health were advised to release new guidelines to halt the progress of ESBL-producing bacteria.

Currently, through the conservative use of antibiotics by Dutch public health workers, the incidence of infections by ESBL-carrying enterobacteriaceae is relatively low. However, world-wide, a broad range of different ESBL-producing strains have caused a true ESBL pandemic, which seems to shadow that of methicillin-resistant staphylococcus aureus (MRSA). ESBL, in contrast to MRSA, seems to spread frequently through horizontal gene transfer. Such a mode of dissemination makes it even harder for health care workers to counter ESBL outbreaks in hospitals and nursing homes.

Fourth-generation cephalosporins, carbapenems, are currently the last resort for treatment of most infections with ESBL-producing bacteria. Unfortunately, new evolutionary cousins of ESBL-producing bacteria are already lurking. In November 2010, the first infection with a bacterial strain producing the so-called New Dehli Metallobetalactamase 1 (NDM-1) was reported. According to the media, this strain is resistant against all know antibiotics.

2.4 Case Briefing: HIV

A 43- year old man visits the out-patient clinic for sexually transmitted diseases. A week before, he was seen with complaints of urethritis and secretion from the urethra. Screening for several sexually transmitted diseases was performed. In this second consultation he was told that he suffered from an infection with *Neisseria gonorrhoea.* For this, he gets an antibiotic prescription. The doctor also told him he is sero-positive for HIV. Therefore he is sent to the specialized out-patient clinic for HIV patients.

At his first visit to this out-patient HIV clinic he reports that he has lost some weighth over the last few weeks and he suffers from joint pain. He also mentions has recurrent cold sores on his upper lip and he has noticed white spots in his mouth.

The infectious diseases specialist tells him that he suffers from herpes reactivation and it is most likely that he has a Candida infection in his mouth. In general, in immune-competent patients this yeast gives no disease, but HIV infects the CD4 positive cells. " The population of CD4 cells is destroyed and therefore the immune response is less effective" the specialist explains. "First we are going to determine the number of CD4 cells in your blood and depending on the number it may be necessary to start with anti-retroviral therapy."

2.5 Case Briefing: Pandemic Flu

It is Monday morning, November 2009. Students are entering the lecture hall at het Faculty of Economics. Klaas is looking for his friend Jos in the crowd of students entering the lecture hall. Klaas asks Janet, who just took the seat next to him: “Have you seen Jos”? “No, he will not come today.” Says Janet. “He called me yesterday evening and said that he was unable to attend the lectures today, as he suffered from Mexican flu; he stayed in bed all day with high fever.”

“Oh no” said Klaas. “Did he only have a fever? Is it just a common cold? We planned to go to a movie tonight” Janet answers: “Why don’t we visit Klaas this evening instead of going to the movie?” “That’s a good idea” answers Klaas, “But we might be at risk of being infected by this flu. This new flu virus seems to be quite infectious; 8 children at school of my nephew were infected. “It doesn’t matter” says Janet, “we will see. By the way, I have had flu last winter. A few days in bed and I recovered rather quick. Flu is only dangerous for the elderly.”

“Last time I had flu was about 5 years ago, I had to stay in bed for a week.” said Klaas. “I will call him and say we would like to visit him, but I will disinfect my hands with disinfecting soap. If I get ill I will ask my physician to give me oseltamivir. This Mexican flu will probably not be as severe as the avian flu.”

Two days after visiting his friend, Klaas is entering the lecture hall again. He wanted to switch off his mobile and sees a message from Janet: “Klaas, I am ill, the flu! I won’t come. J.” Klaas thinks, “Janet already had the flu last year and now she is ill. How is that possible?”

2.6 Case Briefing: *Salmonella* in Space

Salmonella grown in space shows altered gene expression and is deadlier in mice

Space flight increases *Salmonella* virulence in mammals, PNAS reported online in 2007. *Salmonella typhimurium* grown on a space shuttle mission showed altered gene expression and was more lethal to mice than control *Salmonella* grown on the ground. This work is "the first study to examine the effect of space flight on the virulence of a pathogen and the first to obtain the entire gene expression response of a bacterium to space flight," senior author Cheryl Nickerson of Arizona State University (ASU) in Tempe told The Scientist in an email.
In addition to its relevance for infectious disease risks in astronauts, the study also sheds light on bacterial behavior on Earth, especially growth in biofilms and the cell-cell communication necessary to develop biofilms, as well as the regulation of virulence in the intestine, according to Max Mergeay of the Belgian Nuclear Research Center in Brussels, who was not involved in the work.

Previous work on *Salmonella* grown in a space-flight simulator on Earth showed that these bacteria become more virulent and resistant to environmental stresses in a space-like environment. To see if these results held up in true outer space, researchers led by James Wilson of ASU sent cultures of *Salmonella typhimurium* aboard the Space Shuttle Atlantis in September 2006. Astronauts cultured the bacteria for one to three days. After the shuttle returned to Earth, the researchers found that mice infected with a sample of the *Salmonella* grown in space were more likely to die and died more quickly than mice infected with Earth-grown bacteria -- the same result that the researchers had found with space-flight simulators.

Source: www.the-scientist.com

Additional literature:

- J. W. Wilson *et al*. Space flight alters bacterial gene expression and virulence and reveals a role for global regulator Hfq. (2007) PNAS, 104 (41) 16299-16304; doi:10.1073/pnas.0707155104
- Fàbrega A and Vila J. Salmonella enterica serovar Typhimurium skills to succeed in the host: virulence and regulation. (2013) Clin Microbiol Rev. Apr;26(2):308-41.

2.7 Case Briefing: Tuberculosis

The seventeenth global report on tuberculosis (TB) was published by WHO in a series that started in 1997. It provides a comprehensive and up-to-date assessment of the TB epidemic and progress in implementing and financing TB prevention, care and control at global, regional and country levels using data reported by 204 countries and territories that account for over 99% of the world's TB cases.

Key facts for the executive summary are:

- Progress towards global targets for reductions in TB cases and deaths continues.
- However, the global burden of TB remains enormous.
- Access to TB care has expanded substantially
- Progress in responding to multidrug-resistant TB (MDR-TB) remains slow.
- There has been further progress in implementing collaborative TB/HIV activities
- Innovations in diagnostics are being implemented.
- The development of new drugs and new vaccines is also progressing.
- There are critical funding gaps for TB care and control.
- There are also critical funding gaps for research and development.

Additional literature

World Health Organization (WHO) Global Tuberculosis report 2013. Geneva WHO, 23 oct 2013. Available from:

https://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf

2.8 Case Briefing: 'Biosensors'

Faculty members from Botany and Plant Pathology, Biological and Ecological Engineering and Environmental Engineering of the university of Oregon have combined efforts to develop a biosensor that could increase the efficiency of wastewater treatment plants. In this program they will make use of new genomic approaches to study bacteria that remove nitrogen from wastewater.

"The problem that we approached has to do with wastewater treatment where one of the goals is to remove of nitrogen. One of the many steps in the treatment process is the conversion of nitrogen (in the form of ammonia) into nitrate. This process is carried out by ammonia oxidizing bacteria. The challenge in wastewater treatment is, that while these bacteria are a critical component of the treatment process, they are also very sensitive. They are easily damaged by a number of things present in the waste stream, such as chlorinated aliphatic compounds, metals and other contaminants".

The goal is to be able to run wastewater treatment plants efficiently. There are many compounds that can inhibit the performance of ammonia oxidizing bacteria so, at the moment, treatment plants have to run at a low capacity so that they can ensure that all nitrogen is removed. But if they had a warning system to identify problems, such as increasing concentrations of contaminants , maybe they could run the plants at a higher capacity. To solve this the researchers propose to use bacterial biosensors as early warning system. Biosensors would be ideal in this system and they have also proven their use in other settings. For example: Quantification of adherent bacteria or bacteria in a on certain materials is difficult. Biosensors have been developed that allow counting of bacteria both in planktonic,aggregated, adherent and biofilm lifestyles.

Source: http://sbi.oregonstate.edu/news/200712.htm

Additional literature:

Dai et al Technology and Applications of Microbial Biosensor *Open Journal of Applied Biosensor*, 2013, 2, 83-93

Chapter 24 de Gusti et al. from "Biosensors - Emerging Materials and Applications", book edited by Pier Andrea Serra, ISBN 978-953-307-328-6, Published: July 18, 2011

3. Expert meetings

3.1 Expert meeting Bacteriology

1. What are the most important differences between prokarya and eukarya?
2. How are bacteria classified?
3. What is the difference between bacterial species, strains, isolates and colonies?
4. Describe the lay-out of a bacterial cell.
5. Describe the replication cycle of bacteria and their DNA.
6. What is LPS and why is it important?
7. How do bacteria control gene expression?
8. What are bacterial virulence factors and how are they important?
9. How are mutations classified?
10. Which classes of antibiotics exist? How do they work?
11. Which antibiotics are bactericidal and which are bacteriostatic?
12. What are the most important mechanisms for resistance against antibiotics?
13. How does antibiotic resistance spread from one bacterial cell to the other?
14. How can bacteria be detected and identified in diagnostic analysis?
15. How can the antibiotic resistance of bacterial isolates be measured?

3.2 Expert meeting Virology

1. What are the basic steps in viral disease?
2. In what way can viruses be classified?
3. Describe the virus structure.
4. Which features determine the specificity of a virus for a certain host and/or certain type of cell?
5. Which viruses are resistant to extreme conditions? Which viruses are not? What consequences does this have for possibilities for transmission?
6. In what way can transmission of viral infection can occur? Describe some examples of routes of transmission.
7. What is the difference between horizontal and vertical transmission?
8. How can viruses be detected in infected persons? In other words what different tests are available for diagnosing a viral infection?
9. How does the body defend itself against viral infection?
10. What groups of antiviral agents do exist? What effect do they have on the viruses; in other words how do they work?
11. What is the difference between a lytic and non-lytic infection? What is an abortive infection?
12. Describe the structure of picornaviruses.
13. What is the replication mechanism of picornaviruses in the host cell, from entry to release?
14. What are the cell tropisms for the various picornaviruses?
15. Describe the structure of herpes viruses.
16. Explain the replication cycle of herpes simplex virus.
17. What are the target cells for the different herpesviruses?
18. Which diseases are caused by the different herpesviruses?

4. Mini Symposium

4.1 The assignment

At the first case briefing meeting, please for a tema with another student from your tutor group. Choose three topics from the list below (or make up a similar topic by yourself, discuss with course coordinator regarding suitability), and hand out this list in order of preference to the course coordinator (l.van.alphen@mumc.nl).

Within a few days, a final list of topics per team will be presented. Within the weeks, prepare for a 15-minute lecture (using Powerpoint slides if necessary) for the final symposium. This lecture should consist for **at least half** of **recent** breakthroughs/ **recent literature** on the topic. Please note that the lectures will be graded and account for 30% of your final course rating.

4.2 List of topics

1. How did we get rid of SARS so fast?
2. Detective work: proving the source of an outbreak by molecular typing
3. The dangers of biofilms
4. Creating new species in the lab
5. Mind-altering bugs: Microorganisms affecting our behavior
6. A vaccine against cervical cancer. Are we doing it right?
7. Mad cows- mad humans? Prion diseases
8. The role of the human microbiome in health & disease
9. Efficacy of pre- and probiotics
10. Risks of travelling to tropic areas
11. Tick bites and Lyme's disease
12. Social interactions in microbial communities
13. Extremophiles, bacteria under exterme conditions
14. Bacteria's natural predators: Bacteriophages
15. Hemorrhagic fever viruses
16. Eradication of poliomyelitis: a partial failure?
17. Making them work: using bacteria in industrial processes
18. Bacteriophages as new therapy against antimicrobial resistance?
19. Bioremediation: making bacteria work for us
20. Changing weather, changing infections? Role of climate change
21. Ebola: outbreak management, what could have been done better?
22. Crime Scene Investigation: Could we use micro-organisms?
23. A Microscopic Arms Race: The Battle Against Antibiotic Resistance
24. Gut bacteria and weight, what is the link?
25. Waterpollution: the role of micro-organisms