**A. REZIDENCY SUBJECTS LABORATORY MEDICINE - VIROLOGY MODULE (3 MONTHS)**

**Lecture topics**

**General virology - 24 hours**

1. Viruses generalities. Viral taxonomy. Viral structure. Virus-prions differences. Transmissible spongiform encephalopaties. 3 hours
2. Viral replication. Viral genetics. Functioning of the viral parasite cell. 4 hours
3. Viral infection pathogenesis. Viral persistence. 2 hours
4. Immunity in viroses. Natural immunity effectors. Interferons. Acquired immunity effectors. 4 hours
5. Viral vaccines. 4 hours
6. Main viral syndromes. Epidemiology concept for viroses. Bacterial-viral and viral-viral co-infections. Viral evolution. Zoonoses. 4 hours
7. Antiviral therapy. Antiviral resistance. 3 hours

**Special virology - 58 hours**

1. Picornaviridae. Classification. Structure, replication, pathogenesis, clinical syndromes, diagnosis principles, epidemiology notions. Anti-polio vaccines. 4 hours
2. Viral gastroenteritis. Viral agents involved in VGE. Structure, replication, pathogenesis, clinical syndromes, diagnosis principles, epidemiology notions, prevention methods. 2 hours
3. Arboviruses. Classification. Structure, replication, pathogenesis, clinical syndromes, diagnosis principles, epidemiology elements, prevention methods, treatment. 4 hours
4. Rhabdoviridae. Structure, sensibility to physical and chemical agents, habitat, replication, pathogenesis, clinical syndromes, diagnosis principles, epidemiology elements, anti-rabies vaccination. 2 hours
5. Ortomyxoviridae. Structure, replication, pathogenesis, clinical syndromes, diagnosis principles, epidemiology elements. Aviary flu. Anti-flu vaccines. Drugs that are active on flu viruses. 4 hours
6. Paramyxoviridae. Classification. Structure, replication, pathogenesis, clinical syndromes, diagnosis principles, epidemiology elements, prophylaxis methods- the MMR vaccine. 4 hours
7. Retroviridae. Classification. Structure, replication, pathogenesis, clinical syndromes, diagnosis principles, epidemiology elements. 2 hours
8. HIV-AIDS. Structure, replication, pathogenesis, clinical syndromes, diagnosis principles, epidemiology elements. HIV infection vesus AIDS, making the difference by clinical arguments and laboratory results. Antiretroviral therapy. 6 hours
9. Parvoviridae. Classification. Structure, replication, pathogenenis, clinical syndromes, diagnosis principles, epidemiology elements. 2 hours
10. Fecal-oral transmitted hepatitic viruses. Definitions. Classification. Structure, replication, pathogenesis, clinical syndromes, diagnosis principles, epidemiology elements. Prophylaxis and treatment methods. 2 hours
11. Parenteral transmitted hepatitic viruses. Definitions. Classification. Structure, replication, pathogenesis, clinical syndromes, diagnosis principles, epidemiology elements. Prophylaxis and treatment methods. 6 hours
12. Adenoviridae. Classification. Structure, replication, pathogenesis, clinical syndromes, diagnosis principles, epidemiology elements. 2 hours
13. Herpesviridae. Classification. Structure, replication, pathogenesis, clinical syndromes, diagnosis principles, epidemiology elements. Drugs active on herpes viruses. 4 hours
14. Papovaviridae. Structure, replication, pathogenesis, clinical syndromes, diagnosis principles, epidemiology elements. Human papiloma viruses involved in cervical carcinoma. 4 hours
15. Poxviridae. Classification. Structure, replication, pathogenesis, clinical syndromes, diagnosis principles, epidemiology elements, vaccination. 2 hours
16. Cancer and viruses. Oncogenes and anti-oncogenes. Viral transformed cells.DNAand RNA viruses involved in carcinogenesis. 4 hours
17. Emerging viruses. Filoviruses. Arboviruses. New coronaviruses SARS/MERS. 2 hours
18. Diagnosis and prevention of viral infections with bioterrorism potential. 2 hours

**Practical activities (12 weeks)**

1. **General principles of viral diagnosis.** Sampling, transport, processing pathological products. Strains storage. Labelling and recording. Organising a viral strain collection. Professional safety in the laboratory. Decontamination and sterilization techniques. Maintenance and control of the equipment in the laboratory. Quality control. Standardization and accreditation. Knowledge needed for a correct data management. 2 days
2. **Cell cultures.** Classification criteria. Equipment and maintaining the cell culture laboratory. Maintenance of the lab equipment. Sources to obtaining cell cultures. Preparing and controlling culture media. Primary cell cultures and cell lines obtaining methods. Cultivating variants: roller, adherent cultures and suspension cultures. Other uses for cell cultures (cytotoxicity, bacterial, mycoplasma, Chlamydia isolation etc). Practical uses in viral diagnosis; viral vaccines production; monoclonal antibodies production. 1 week
3. **Viral isolation on cell cultures.** Cytopathic effects. Titration of viral infectivity on cell cultures (DIC50 PFU). 1 week
4. **Serological diagnosis in viroses.** (I). Classical serology techniques. Processing samples for viral serological diagnosis. Hemagglutination reaction and hem agglutination inhibition reaction. Hemadsorbent and hemagglutinin positive viruses. Serological neutralization. Principles. Technique. Interpreting. 2 days
5. **Serological diagnosis in viroses** (II). Immuno-enzymatic techniques. Indirect, competitive and capturing ELISA. Western Blot. RIBA. Dot Blot. Principles. Technique. Interpreting. 3 days
6. **Highlighting the viral genome.** Functioning and maintaining the equipment. Preparing the reagent. Collecting samples. Isolating/purifying RNA/DNA. Hybrid genome assembly. PCR and RT-PCR. Real time PCR. Electrophoresis. Amplicon highlighting. Colour highlighting techniques for proteins and nuclear acids. 1 week
7. **Rapid diagnosis in respiratory viroses.** Possible etiologic agents: influenza viruses, parainfluenza viruses, respiratory syncytial virus, adenoviruses. Diagnosis algorithm in case of epidemics/pandemics. Isolating the etiologic agent. Highlighting the virus in the pathological product. Isolating in cell cultures. Direct/indirect immunofluorescence reaction. Immuno-enzymatic kits for detecting viral antigens. Molecular diagnosis by highlighting the viral genome. Serology. 3 days
8. **Laboratory diagnosis of non-bacterial diarrhoea.** Possible etiologic agents: rotaviruses, calciviruses. Collecting the samples. Immunoenzymatic reactions. Latex agglutination reactions. Molecular diagnosis by highlighting the viral genome. 2 days
9. **Laboratory diagnosis of cutaneous and ocular viral infections.** Possible etiologic agents: herpes viruses, adenoviruses, measles virus, rubella virus. Isolating the viral agent. Shell vial method. Isolating the virus in the pathologic sample. Immunofluorescence. Serology. Highlighting the viral genome. 3 days
10. **Neuroviroses laboratory diagnosis.** Possible etiologic agents: enteroviruses ( Polio, Coxsackie, ECHO); mumps virus, measles virus, herpes viruses, rabies, arboviruses. Viral isolation methods. Isolating the virus in the pathologic sample. Viral identification - viral neutralization reaction. Serology. Highlighting the nucleic acids. 1 week
11. **Laboratory diagnosis in sexually transmitted viral diseases.** Possible etiologic agents: herpes viruses, papiloma viruses. Isolating the virus on cell cultures, detecting viral antigens by immunofluorescence/EIA. Serological diagnosis. PCR for DNA of human papiloma viruses and genotyping to identifying the strains with high cancer risk. Diagnosis in Chlamydia and Mycoplasma determined STDs. 1 week
12. **Laboratory diagnosis in congenital and perinatal viral infections.** Possible etiologic agents: Rubella virus, Herpes Simplex 2 virus, Cytomegalovirus, Epstein Barr virus. Detection of viral antigens by immunofluorescence. Serological diagnosis. Detection of viral genome (PCR). Diagnosis of viral infection that benefit from vaccination (measles, rubella etc). 1 week
13. **Laboratory diagnosis in acute viral hepatitis.** Serological diagnosis. Viral genome detection - qualitative techniques. 2 days
14. **Laboratory diagnosis in chronic viral hepatitis.** Serological diagnosis. Viral genome detection - quantitative techniques. Genotyping. Prediction markers of infection evolution. 1 week
15. **Laboratory diagnosis in HIV infection and other parenteral transmitted viral infections.** Professional risk and iatrogenic infections. Viral agents isolation. Serology - screening ELISA. Positivity criteria. Confirmation diagnosis in HIV infection. Western Blot. Principles. Technique. Interpreting. Immunofluorescence. 1 week
16. **Prediction markers of HIV infection evolution.** p24 antigenemy. Viral load determining techniques. Genotyping. Antiviral resistance detection. 1 week

**Compulsory activities grading:**

1. Preparing and maintaining culture media - 10 activities
2. Maintaining cell cultures in 10 consecutive passagings - 10 activities
3. Determining cell viability - 10 activities
4. Isolating cytopathogenic viruses on cell cultures - 20 activities
5. Recognising cytopathic effects on coloured smears - 20 activities
6. Titration of infectivity on cell cultures - 5 activities
7. Processing samples for virology diagnosis - 10 samples
8. Hemagglutination reaction and hemagglutination inhibation reaction - 20 reactions
9. Serological neutralization - 10 reactions
10. Viral antigen detection by immunofluorescence - 30 samples
11. ELISA immunoenzymatic techniques for detection of markers in hepatitic viruses infections (HVA, HVB, HVC, HVD) - 50 reactions
12. RIBA/Western Blot techniques for confirming HVC infection - 20 reactions
13. ELISA immunoenzymatic techniques for triage diagnosis of HIV infection - 30 reactions
14. Western Blot technique for confirming HIV infection - 20 reactions
15. Isolation/purify viral RNA/DNA from different pathologic samples - 20 reactions
16. Qualitative PCR and RT-PCR for amplifying viral nucleic acids - 20 reactions
17. Quantitative PCR and RT-PCR for determining viral loads in infections with HVB, HVC and HIV - 20 reactions
18. Detection of amplicons after electrophoresis - 20 reactions
19. Hybrid genome assembly (Southern/Northern) - 20 reactions
20. Genotyping HPV - 20 reactions

**REZIDENCY SUBJECTS INFECTIOUS DISEASES**

**Virology conference lessons themes**

1. Virology diagnosis algorithm. Virology diagnosis methods (using the data in the clinic). Molecular epidemiology elements
2. Particular aspects in:
   1. Poliomyelitis and laboratory diagnosis of neuroviroses
   2. The flu and the laboratory diagnosis of viral respiratory infections
   3. Hepatitis virus infection and the laboratory diagnosis of chronic viral hepatitis
   4. HIV infection and viral monitoring of the infection and the resistance to antiretroviral drugs.
   5. Herpes viruses infection and the laboratory diagnosis of latent viral infection
   6. Laboratory diagnosis in eruptive viral diseases
   7. Laboratory diagnosis in viral sexual transmitted diseases
   8. Laboratory diagnosis in maternal-fetal transmissible diseases and potentially teratogenic viral infections

**Practical activities grading for laboratory medicine module**

1. Collecting pathological samples (viral transport media and conditions) and processing of the samples (blood, pharyngeal culture, CRL, different secretions - ocular, vezicular) - 20 each
2. Inoculation of pathological samples on cell cultures. Highlighting the cytopathic effect - 10
3. Identifying the viral antigenes - interpreting. 50
4. Serological diagnosis in viral diseases: determining antigenes and antibodies, interpreting - 20
5. Molecular techniques in infectious diseases diagnosis. Interpreting - 20.