Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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level and this predictable relationship may be exploited for vaccine design and evaluation. These approaches can be enhanced by also incorporating phylogenetic analysis. Specifically the relationship between HLA alleles and HIV polymorphism in chronically infected patients may be used to predict protective responses to a preventative vaccine in a population with similar HLA diversity exposed to a similar range of HIV diversity. Importantly, the innate advantage provided by intense human HLA diversity can then be exploited to ameliorate problems posed by HIV diversity. Analyses of real and theoretical candidate vaccines suggest that polyvalent and more specifically “polyalleric” vaccines will most effectively exploit known regional HLA diversity to cover HIV diversity.

**K5 Nucleic acid amplification tests for detection of respiratory viruses**

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**Background and Aim:** We aimed to introduce respiratory virus nucleic acid amplification tests (NATs) into routine diagnostics and assess the impact on laboratory work-flow and costs.

**Methods:** Polymerase chain reaction (PCR) and nucleic acid sequence based amplification (NASBA) were utilised for identification of influenza (IFV) A and B, parainfluenza (PIV) 1–4, respiratory syncytial virus (RSV), adenovirus (ADV) and human metapneumovirus (hMPV). Nucleic acid extraction was automated (bioMerieux). In a two phase process, NATs were first used to replace DFA and culture for lower respiratory specimens and then to replace culture for DFA negative nasopharyngeal samples. The impact of these changes was assessed over a period of one year with more than 10,000 specimens analysed.

**Results:** NATs identified a significant proportion of mixed infections and picked up IFV, PIV and RSV positives missed by DFA. NATs identified hMPV and ADV as a probable cause of respiratory symptoms in a wider range of patients than previously appreciated. hMPV was also found to be associated with outbreaks of respiratory infection in the elderly. The feasibility of direct amplification, typing and sequence analysis of influenza A from clinical specimens (without prior culture) was confirmed.

**Discussion and Conclusions:** NATs for respiratory viruses can be incorporated into a routine diagnostic laboratory. Direct analysis of respiratory specimens (without prior culture) is feasible and real-time provision of influenza A subtyping, strain drift and antiviral resistance data will have a positive impact on outbreak management and pandemic preparedness.

**K6 The Gardner lecture: New respiratory viruses: from viral RNA to symptomatic patients**

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Respiratory viruses are a major cause of morbidity and mortality worldwide. These viruses can be classified in one of five viral families including DNA viruses (Adenoviridae) and most commonly RNA viruses (Orthomyxoviridae, Paramyxoviridae, Picornaviridae and Coronaviridae). Five new viral agents associated with respiratory symptoms have been discovered since 2001: The human metapneumovirus (hMPV) belonging to the pneumovirinae subfamily in the Paramyxoviridae family, the SARS-coronavirus as well as two other members of the Coronaviridae family i.e. coronavirus-NL and -HKU1 and finally parechovirus type 3 which belongs to the Picornaviridae family. Most of these new respiratory viruses with the exception of SARS-coronavirus are probably old pathogens whose fastidious growth in conventional culture precluded earlier detection.

This presentation will primarily review the virological, epidemiological and clinical features of emerging respiratory viruses such as hMPV, the new coronaviruses and parechovirus type 3. Also, in the case of hMPV infections, the potential therapeutic and prophylactic modalities will be discussed. Human metapneumovirus infects virtually all children by the age of 5–10 years and is associated with upper respiratory tract infections (URTI), bronchiolitis and pneumonia like those caused by human respiratory syncytial virus. Viral inhibition has been reported with ribavirin and intravenous immunoglobulins and live-attenuated vaccines generated by the reverse genetics technology are currently under development and evaluation. The SARS-coronavirus was responsible for about 800 cases of severe acute respiratory syndromes worldwide in 2003 with a 10% fatality rate. Coronavirus-NL has been associated mainly with upper and lower respiratory tract infections as well as with Kawasaki’s disease in some studies. Coronavirus HKU1 seems to be a rare cause of URTI and pneumonia in studies from Hong Kong, Europe and North America. It has also been recently detected in stool samples of symptomatic children. Finally, parechovirus type 3 has been detected in a variety of clinical samples of neonates presenting with sepsis-like syndromes with or without respiratory symptoms.

The development of sensitive molecular methods has allowed the detection of these emerging viral pathogens in many parts of the world. Careful prospective studies are now needed to fully describe the clinical burden associated with these new respiratory viral agents. Furthermore, the development of new therapeutic modalities as well as effective and safe vaccines constitutes another important research priority.

**K7 Emergence of clear pathways for treatment of HIV/hepatitis co-infection**

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Chronic liver disease has emerged as an important cause of morbidity and mortality for patients with HIV infection. Most liver disease is due to viral hepatitis B and C. For patients with blood-borne risk factors, HIV/HCV co-infection predominates. For those with sexually transmitted infection, HIV/HBV co-infection is more often observed. During the past 5 to 10 years significant advances have been observed for the antiviral treatment of patients with chronic viral hepatitis. For HIV co-infected patients, the greatest impact has been observed for the management of HIV/HBV infection. Nucleoside analogues have transformed the management of chronic HBV infection in the HIV-negative population. Indeed, the beneficial effect of lamivudine for treatment of chronic HBV infection was first observed in the co-infected patient. However, HBV resistance to lamivudine emerges at a rate of about 20% per annum, so few patients derive benefit for more than 5 years. Thus, until recently, many HBV-infected HAART-treated patients had developed HBV lamivudine resistance. Treatment options for the HBV under this circumstance include addition of HBV-specific therapy (such as low dose adeovir, entecavir, or interferon) or manipulation of the HAART treatment to include tenofovir. It is clear that tenofovir, with lamivudine or emtricitabine, provides potent and sustained suppression of HBV replication. The majority of patients achieve serum HBV DNA negativity during treatment. For treatment-naive co-infected patients, initiation of treatment will be determined by the need for HIV and/or HBV suppression. Frequently, suppression of both viruses is necessary and HAART including tenofevir and either lamivudine or emtricitabine is necessary. For the patient that needs HBV without HIV suppression, HBV-specific drugs such as entecavir, low-dose adeovir and interferon can be used. An alternative approach is to commence HAART at an earlier stage of the HIV infection. For the patient that needs HIV but not HBV suppression, suppression of the HBV will be beneficial. The treatment of HCV infection in the HIV-positive patient poses a greater challenge. In the context of HIV infection, HCV treatment requires the combination of pegylated interferon and ribavirin, given for a period of 48 weeks independent of HCV genotype. Side-effects of HCV treatment are significant, and appear more troublesome for the co-infected than for the HCV mono-infected patient. Cure can be achieved for a significant number of treated patients, though response is inferior to that observed for HCV mono-infected patients. Drug interactions with HAART should be avoided if possible. Thus, treatment of HCV before initiation of HAART should be considered when CD4 count and HIV titre permit. Serious interactions with ribavirin have been most often observed with DDI and AZT. Therefore, HAART should be chosen to avoid those drugs for HCV co-infected patients. HCV-specific protease and polymerase inhibitors are at an advanced stage of clinical development and may be available in the not-too-distant future. The HCV protease inhibitors...
may be "boosted" by inhibitors of cytochrome p450 3A4, a potentially beneficial interaction.

**K8** Surveillance, laboratory diagnosis and research of communicable diseases in EU

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The European Centre for Disease Control and Prevention (ECDC), recently established in Stockholm, Sweden, is continuing the work of the network of state epidemiologists of the member states (MS) and the "network committee" under the Commission, building a surveillance system to support common public health policies and actions related to communicable diseases within the European Union. Since public health is primarily the responsibility of individual member states, the main focus is to provide coordination and collaboration but it will also pool together scientific expertise and provide a mechanism for rapid common actions in emerging health threats.

Since ECDC does not have and will not have laboratory capacity of its own, it has to work in close collaboration with the resources available in MS. "Designated Surveillance Networks" (DSN) have been an important tool in harmonising the data collection, laboratory diagnostic methodology and recommendations for actions for certain important diseases such as enteric bacterial and viral infections, imported viral haemorrhagic fevers, legionellosis, tuberculosis, HIV, influenza etc. Participants in the DSN's are usually national reference laboratories which are supposed to influence practices in their own countries and provide harmonisation in diagnostic microbiological laboratories, which is important for the quality of information that ECDC can collect.

The DSNs cannot cover all issues of detection and surveillance that may emerge in Europe. At the same time there is a wide range of high level academic and public health expertise which do not work and cannot work inside the formal DSNs. Linking this pool into close collaboration is an important tool for the future of ECDC. The centre not only needs to know that key resources are available in case of urgency, it also needs an ongoing dialogue with the expertise that is driving the scientific research and development of paradigms.

A strategy is being developed in ECDC to make this process possible. It has to take into account the availability of scientific and diagnostic resources and propose practical arrangements including expected inputs from ECDC and outputs from the participating laboratories.

Challenges include data sharing, development of diagnostic and scientific capacities and resources throughout the EU, links with public health actions, collaboration with other supranational structures such as WHO, etc. The strategy should also enhance regional collaboration to stimulate development of clinical microbiology throughout the EU.

During the last two decades a change has taken place in providing microbiology laboratory services diverting, in many cases, clinical diagnostic work from public health needs and actions. Turning the course is necessary to build a proper European response to threats due to communicable diseases. Harmonisation of methodology, application of EQA using common criteria, particularly at the basic laboratory level, and reliable flow of information are among the challenges for the decade to come.

**K9** Adaptive immunotherapy for viral infections

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An increased understanding of the mechanisms by which T cells recognize virus- and tumor-specific antigens has stimulated much interest in the use of specific T cells as adaptive immunotherapy for viral and malignant diseases.

Unselected populations of lymphocytes from the peripheral blood of the seropositive donor usually contain herpes virus-specific T cells and therefore can be used to control herpes virus infections. However, the utility of such therapy is limited by potentially fatal complications that arise from alloreactive T cells also present in the donor lymphocyte infusion. The transfer of syngeneic (i.e., involving genetically identical donors and recipients), polyclonal CD8+ T cells from immune mice to immunosuppressed mice provided protection from a viral challenge. In humans polyclonal populations of lymphocytes obtained from the peripheral blood of the donor have been used successfully to treat the Epstein–Barr virus (EBV) lymphoproliferative syndrome that can develop after allogeneic bone marrow transplantation. However, the transfer of these unselected lymphocytes also caused graft-versus-host disease (GVHD). Enrichment of the lymphocytes in cytotoxic T cells specific for EBV by in vitro culture before transfer appears to reduce the risk of GVHD. Antigen-specific T cells can be generated by repetitive stimulation with antigen-presenting cells presenting peptide antigens. Most often CMV-infected fibroblasts have been used very effectively as antigen-presenting cells for stimulating CMV-specific CD8+ CTLs. But there has been concern abut the potential for viral reinfetion concurrent with adoptive cellular therapy.

Thus, antigen-presenting cells pulsed with either CMV protein or immunogeneic CMV peptides are increasingly used to try to generate and to expand CMV-specific T cells. Depending on the APC used (monocytes vs dendritic cells) and the mode of antigen presentation (protein vs peptide pulsing) different CMV-specific T cell populations of varying frequency can be generated. New technologies allow to isolate virus-specific T cells via cytokine secretion upon specific stimuli (e.g. IFN-gamma), or via TCR-MHC/peptide binding. To circumvent these limitations, a clinical-scale protocol was developed to generate CMV-specific T cells by using autologous cellular and serum components derived from a single 500 mL blood draw. CMV-specific T cells were stimulated simultaneously with CMV-specific major histocompatibility complex class I (MHC I)-restricted peptides and CMV antigen. Activated T cells were isolated with the interferon-gamma (IFN-gamma) secretion assay and expanded for 10 days. In 8 randomly selected, CMV-seropositive donors, CD4+ and CD8+ CMV-specific T cells were generated. CMV-infected fibroblasts were enzymatically lysed by the generated T cells, and CMV-specific CD4+ and CD8+ T cells expanded if they were stimulated with natural processed antigen. On the other hand, CD4+ and CD8+ T cell-mediated alloreactivity of generated CMV-specific T cell lines were reduced compared with that of the starting population.

Adoptive transfer of activated CMV-specific CD8+ and CD4+ T cells isolated with the IFN-gamma-secretion assay and expanded for 10 days in vitro has been started in a clinical protocol in patients with CMV-infection not responding to antiviral chemotherapy. First results of this study will be presented. A further strategy is to boost immune reconstitution post transplant using peptide-pulsed dendritic cells generated from peripheral blood mononuclear cells obtained from the patient.

**K10** Measles and rubella in Europe – reaching for elimination

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The WHO Regional Committee for Europe approved a resolution at its 55th session in September 2005 entitled Strengthening national immunization systems through measles and rubella elimination and prevention of congenital rubella infections, which provides the policy level framework and national commitment to achieve the elimination targets by 2010.

Considerable progress was achieved between 2002 and 2005 among the 52 countries within the European Region toward improving control of measles and rubella, as measured by the number of countries having routine 2-dose measles vaccination programmes (52/52, 100%); the number of countries using rubella vaccines (48/52, 92%); the number of countries undertaking national or subnational supplementary immunization activities to address measles and rubella susceptible populations (>10); and the number of countries reporting an incidence of measles of <1 per million population (26/52, 54%). In 2004, 14 (27%) countries reported a rubella incidence of <1 per million population. While WHO has previously only received monthly reports of measles cases from countries, monthly reporting for rubella was initiated in 2006. A measles/rubella laboratory network was established in 2002, consisting of 47 national laboratories, three regional reference laboratories and one of the global specialized laboratories.

Large measles outbreaks in 2005 and 2006 have occurred in a number of countries in the European Region with known susceptible