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Under the auspices of the Belgian Association of Public Health
# Programme

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SCIENTIFIC COMMITTEE

Boudewijn Catry  
Head of unit Healthcare-associated infections and antimicrobial resistance,  
Scientific Institute Public Health, Brussels  
boudewijn.catry@wiv-isp.be

Hector Rodríguez-Villalobos  
Microbiologist  
Cliniques universitaires Saint-Luc  
hector.rodriguez@uclouvain.be

Wim Flipse  
Infectious Disease control Antwerp  
Zorg en Gezonheid  
wim.flipse@zorg-en-gezonheid.be

Carole Schirvel  
Head of Infectious disease surveillance unit  
Fédération Wallonie Bruxelles  
carole.schirvel@cfwb.be

Greet Ieven  
Head of unit Clinical Microbiology, Antwerp-University Hospital  
Professor Microbiology, University of Antwerp  
greet.ieven@uza.be

Mireille Thomas  
Health promotion  
Ministerium der Deutschsprachigen Gemeinschaft  
mireille.thomas@dgov.be

Tinne Lernout  
Chair of SsID scientific committee  
Scientific Institute Public Health, Brussels  
tinne.lernout@wiv-isp.be

Jean-Marie Trémérie  
Health inspector Commission Communautaire  
Commune - Gemeenschappelijke Gemeenschapscommissie, Brussels  
jmtremerie@ccc.irisnet.be

Annick Linden  
Health and pathologies of wildlife  
University of Liège  
a.linden@ulg.ac.be

Viviane Van Casteren  
Head of unit Healthcare services research  
Scientific Institute Public Health, Brussels  
viviane.vancasteren@wiv-isp.be

Pierrette Melin  
Head of unit Clinical Microbiology, CHU de Liège  
Professor Microbiology, Université de Liège.  
pierrette.melin@chu.ulg.ac.be

Steven Van Gucht  
Head of unit Viral diseases  
Scientific Institute Public Health, Brussels  
steven.vangucht@wiv-isp.be

Marcella Mori  
Head of Unit Coordination Veterinary Diagnosis Epidemiology and Risk Analysis  
CODA-CERVA, Brussel  
m.mori@coda-cerva.be

Yves Van Laethem  
Head of the Clinical Dept. Infectious Diseases  
CHU St-Pierre  
yves_vanlaethem@stpierre-bru.be

Elizaveta Padalko  
Head of Clinical Virology,  
University Hospital Ghent  
elizaveta.padalko@uzgent.be

Herman Van Oyen  
Operational director, Scientific Institute Public Health, Brussels  
Professor of epidemiology, University Ghent  
herman.vanoyen@wiv-isp.be

Denis Piéard  
Head unit Microbiology and hospital hygiene  
UZ Brussels  
denis.pierard@uzebrussel.be

Jan Verhaegen  
Clinical microbiologist  
University Hospital Gasthuisberg  
jan.verhaegen@uzleuven.be

Catherine Potvliege  
Microbiologist, Head of Laboratory  
CHU Tivoli  
catherine.potvliege@chu-tivoli.be

Kris Vernelen  
Quality of Medical Laboratories  
Scientific Institute of Public Health, Brussels  
kris.vernelen@wiv-isp.be

Sophie Quoillin  
Head of unit Epidemiology Infectious Diseases  
Scientific Institute Public Health, Brussels  
sophie.quoillin@wiv-isp.be
Multi Drug Resistant Organisms On The Move. What’s Next?

BD leads a global effort, helping convene a group of antimicrobial resistance experts

The emergence and rapid global spread of highly resistant bacteria, especially those resistant to last-line antibiotics, is a significant threat to patients, healthcare systems and the economy.

Poor patient outcomes, higher morbidity and mortality, and higher costs and length of hospital stay are associated with infections caused by highly resistant bacteria.\(^{[1]}\)
ABSTRACTS OF PRESENTATIONS
BIOGRAPHY

In 1984, I finished my studies in zoology at the University of Namur in the field of cytogenetics. Afterwards, I carried out genetic studies in Lausanne and Oxford (UK) where I obtained my D.Phil. in early 1992. Several post-doc positions followed at the Laboratoire de Biochimie (ULg), the Centre d’Ingénierie des Protéines (ULg), the Laboratorium voor Moleculaire Biotechnologie (UIA) and the Laboratorium voor Anatomopathologie (UIA), ranging from molecular to cellular biology and genetics. Since 2004, I work as scientific expert at the Superior Health Council preparing advisory reports in transfusion science. I completed in 2007 a Master in Transfusion Medicine (ULg-UCL-ULB) and started teaching courses on the organisation of blood transfusion systems and on emerging infectious diseases and blood transfusion.

KEEPING BLOOD TRANSFUSIONS SAFE: THE CHALLENGE OF EMERGING INFECTIOUS DISEASES

In modern medical practice, transfusion of blood products sourced from donors and prepared for administration to recipients remains a very common procedure. Nowadays, civilian blood transfusion commonly uses only components of the blood (such as red blood cells, plasma or platelets) and a number of proteins purified from pooled plasma that are made available as stabilised solutions (e.g. albumins, coagulation factors). The safety of blood intended to be transfused can be compromised by the presence of transfusion-transmissible pathogens (mainly viruses, some bacteria, parasites, prions). To keep blood transfusions safe a number of safeguards have been combined into a comprehensive strategy encompassing for instance the organised recruitment of low risk donors and infectious disease marker testing (syphilis, HIV, HCV, HBV). Newly emerging pathogens, or pathogens of new concern, may defeat the donor questionnaires and blood tests. Plasma is an acellular blood component and amenable to virus inactivation and/or elimination methods based on heat, solvent-detergent, methylene blue/light, nanofiltration. Platelets are vulnerable to bacterial proliferation because they are kept at room temperature for up to a week. Several methods for universal bacterial detection (nucleic acid testing, culture, immunoassay, flow cytometry) and pathogen reduction (photochemical, illumination) have been deployed. Red blood cells have not been safely and efficiently treated by novel pathogen reduction methods likely caused by harm to intracellular content and/or surface proteins or lipids essential for integrity, oxygen delivery and rheological proper-
ties. The ideal method would target pathogen nucleic acids without harming the blood cells or generating toxic chemical agents. The greatest strength of pathogen reduction over donor questioning and testing is its precautionary benefit albeit not all pathogens might be reduced sufficiently (e.g. bacterial spores, prions, overwhelming viral loads, coated viruses). Infectious disease marker testing shifts more and more to multiplex nucleic acid testing as well as to nanoparticle and gene chip based detection assays (sensitivity, specificity and throughput). Strategies to contain expenses are pursued more intensively, for instance CMV negative components limited to neonates and immunocompromised patients, seasonal West-Nile virus screening in endemic regions. In stark contrast, mostly untested whole blood is transfused in developing countries. Finally, research on synthetic analogues or in vitro expansion of respective stem cells continues.
Dr. Marie-Laurence Lambert
Scientific Institute of Public Health
marie-laurence.lambert@wiv-isp.be

BIOGRAPHY

Marie-Laurence Lambert graduated as a medical doctor from ULB in 1986. She obtained a master in public health from the Harvard School of Public Health (1993) and a PhD in public health from Ghent University (2007). She has worked several years with Doctors without Borders, then at the Institute for Tropical Medicine in Antwerp. Since 2007, she works in the unit “healthcare associated infections and antimicrobial resistance” at the Scientific Institute for Public Health. She is in charge of C. difficile surveillance, and of the project “quality indicators for infection controls in hospitals”. She is also main supervisor for Belgium for the European Programme for Intervention Epidemiology (EPIET).

CASE-TO-CASE TRANSMISSION OF C DIFFICILE INFECTIONS IN BELGIAN HOSPITALS

*Clostridium difficile* infections (CDI) are a leading cause of health-care acquired infections. Our objective was to estimate what proportion of hospital-associated (HA) CDI results from case-to-case transmission within the same hospital.

Material/methods: Hospitals participating to the study agreed to record all their symptomatic CDI according to the Belgian CDI surveillance protocol from January 1st 2015 to January 31th 2016, perform culture for all episodes, and send isolates for typing to the National Reference Laboratory (NRC). We defined (1) HA-CDI as CDI with onset of symptoms 2 days or more after admission in the reporting hospital, (2) a secondary case as an HA-CDI due to a ribotype previously isolated in the same hospital (either from a HA or non HA CDI) less than one month earlier.

Results: During the study period 27 hospitals registered 1,240 culture-positive CDI cases (median per hospital: 41), 58% were HA-CDI. Cultures from 1,121 episodes (completion: 90%) were received by the NRC; cytopathogenic *C. difficile* was recovered from 1042 cultures and 147 different ribotypes were isolated, 70 only once. After exclusion of recurrent HA-CDI episodes, and episodes occurring during the first month of the study (run-in) we found that 148 /517 HA-CDI (29%) were possible secondary cases. This proportion varied from 0 to 52 % (median: 21%) between hospitals. The more discriminatory MLVA typing is ongoing to ascertain
the similarity of strains within clusters, but the proportion of true secondary episodes can only be lower than what has been identified using ribotyping.

Conclusions: The majority of HA-CDI in Belgium cannot be attributed to case-to-case transmission within the hospital, although variation between hospitals is high and sporadic outbreaks do occur. Prudent use of antimicrobials rather than preventing case-to-case transmission is required to improve control of endemic CDI in hospitals. However the number of different C. difficile strains circulating in Belgium points to a large variety of sources of transmission, and the role of colonized patients and of the environment in the epidemiology of C. difficile needs to be better understood.
Dr. Youri Glupczynski  
Head of Microbiology Laboratory, Director of the National Reference Centre for monitoring Antimicrobial Resistance in Gram-negative bacteria  
gerald.glupczynski@uclouvain.be

**BIOGRAPHY**

Graduated as MD (1980) and PhD (1983 at the Université Libre of Bruxelles (ULB)  
Head of the Clinical microbiology department and of the clinical biology laboratory at CHU UCL Namur (Mont-Godinne) since 1998. Expert at the Belgian Superior Health Council (infection control) since 2006. Ordinary professor of bacteriology and of hospital hygiene at the Université catholique de Louvain (UCL) since 2010. Head of the National Reference Center of antimicrobial resistance in gram-negative bacteria since 2010.  
Current research topic and area of interest:

- Molecular epidemiology of antimicrobial resistance in gram-negative bacteria.
- Evaluation and integration of innovative diagnostic tools in clinical practice.

**COLISTIN-RESISTANCE IN ENTEROBACTERIACEAE: A MAJOR POTENTIAL THREAT ENDANGERING THE LAST ANTIBIOTIC TREATMENT LINE AND OPENING THE WAY TOWARDS PAN-DRUG RESISTANCE**

The fight against multidrug-resistant (MDR) bacteria is a major public health challenge. This challenge is well illustrated by the dissemination of carbapenemase-producing *Enterobacteriaceae* (CPE) that usually remains susceptible only to colistin. Colistin is widely used in veterinary medicine for the treatment of Gram-negative bacilli related infections in livestock. At the opposite, this molecule has longtime been ruled out of treatment protocols due to its nephrotoxicity. Nowadays, colistin is prescribed again in human medicine as a last resort antimicrobial therapy for the treatment of severe infections caused by extremely drug-resistant bacteria, such as CPE. Unfortunately, in countries where CPE prevalence is high (for example Greece or Italy), the resistance to colistin has rapidly increased following its reintroduction in clinical usage. In most cases, this resistance results of modifications in various chromosomally-encoded genes leading to modifications of the lipopolysaccharide (LPS) structure with changes in the global charge (decrease in the negative net charge), consequently impairing the fixation of the colistin to the bacterial cell membrane. Recently, plasmid-mediated resistance to colistin, due to mcr-1 (including at least two mcr-1 mutant variants) and mcr-2 genes, has been described in *Enterobacteriaceae* (mostly in *Escherichia coli* and in *Salmonella enterica* serovar...
Typhimurium, but also albeit less frequently in other species such as Klebsiella pneumoniae). Following the princeps report in China in 2015, MCR-producing isolates have been reported worldwide on all continents and in many countries in Europe including Belgium. The majority of these MCR-positive isolates are E. coli that have been recovered from animals or animal food products and also from human samples. Currently reports of plasmid-mediated colistin resistance seems to remain rare in humans but a more thorough systematic evaluation of the incidence and prevalence of colistin resistance and of plasmid-mediated colistin resistance is absolutely required in different settings (e.g., in antibiotic susceptible isolates and not only in the setting of multi-drug resistant organisms like ESBL or CPE). The emergence and spread of plasmid-mediated resistance to colistin is worrisome since it compromises the last remaining resources against pan-drug resistant organisms.

This threatening perspective is stressed by the fact that the pipeline and the prospect of new antimicrobial molecules are quite limited. Testing for colistin resistance in medical microbiology laboratory and optimizing its clinical usage in human medicine is becoming nowadays increasingly important.

In parallel with the recent release on the market of new diagnostic tests (including rapid tests) for detecting colistin resistance, practical methodological and interpretative guidelines are being developed by EUCAST and will be briefly reviewed. This threatening perspective is stressed by the fact that the pipeline and the prospect of new antimicrobial molecules are quite limited. Testing for colistin resistance in medical microbiology laboratory and optimizing its clinical usage in human medicine is becoming nowadays increasingly important.

In parallel with the recent release on the market of new diagnostic tests (including rapid tests) for detecting colistin resistance, practical methodological and interpretative guidelines are being developed by EUCAST and will be briefly reviewed.
BIOGRAPHY

Bénédicte Delaere is specialized in infectious diseases (1994), head of the infectious diseases dpt since 2010 (University hospital CHU UCL Namur, Université Catholique de Louvain). Specific interests include antibiotic stewardship, osteoarticular infections management, infections and zoonotic diseases. She is involved in the redaction of the Belgian guidelines for Borreliosis.

FRANCISELLA TULARENSIS, A RARE PATHOGEN IN BELGIUM?

Since 2012, 7 cases of tularemia have been reported to ISP by a tertiary hospital (south Belgium area). Previously, only 3 cases were described since 1960.
All but one of the patients presented the ulceroglandular form of the disease, with a wound at the site of inoculation and inflammatory/painful adenitis with mild to moderate systemic symptoms. Bacterial inoculation was related to insect bites in 2 cases, contact with contaminated environment in 2 cases and direct contact with animals in 2 cases (1 unknown).
The diagnosis delay ranged from one week to two months. A favourable outcome was obtained for all patients, 2 out of 7 requiring 2 consecutive antimicrobial courses.
Tularemia is a vector-borne zoonotic disease caused by Francisella tularensis, a Gram negative bacteria with a broad host range including invertebrates, mammals and birds. Rodents and lagomorphs are suspected as main reservoirs.
There are 4 subspecies of F. tularensis, but human infections are mainly due to F. Tularensis tularensis (Type A, more virulent) and F. Tularensis holarctica (or type B, less virulent). Only F. T. holarctica has been reported in Europe.
If the disease is endemic in some northern european countries (i.e. Scandinavia), outbreaks and clusters were recently reported in France, Switzerland, Germany, etc. Wild animals and arthropods appear to be important sources of infection.
Transmission might occur by 3 major routes: direct transmission from the animal reservoir (handling an infected animal, ingestion of undercooked meat, animal bites), arthropods bites (mainly ticks and mosquitoes) and contact with contaminated environment (water, soil).
The main clinical presentations in Europe are ulceroglandular or glandular forms, but the oropharyngeal form is frequent in some areas (i.e. Turkey, mainly in children). Pneumonic and typhoidal forms are rare in Europe, but more frequently des-
cribed in US and related to the virulent subspecies *F. T. tularensis*. Some infections can remain subclinical with spontaneous recovery. A 2-10% seroprevalence is reported in specific groups (hunters, foresters, ...). Tetracyclines or fluoroquinolones (in severe cases, aminoglycosides) are the mainstay of therapy for the forms related to *F. T. holarctica*. Diagnosis is mainly based on

REFERENCES

BIOGRAPHY

Prof Heidi Theeten, MD, is a staff member of the Centre for Evaluation of Vaccination, UA, since 2001. She conducted clinical trials with candidate vaccines against different diseases (hepatitis A and B, adult diphtheria-tetanus-pertussis booster, human papilloma virus, meningococcal C), as well as seroprevalence studies on vaccine-preventable diseases on a national level (in cooperation with the IPh) and vaccination coverage studies in Flanders. She defended a PhD on assessment of vaccination programs through serological surveys and vaccination coverage studies in 2011. Afterward, as a post-doctoral researcher, she has continued supervising vaccination coverage and seroprevalence studies, she has been funded by the Flemish Research Fund for a 3-year fellowship to look at cytomegalovirus infection and its association with immunosenescence, and currently she coordinates a new project to monitor pneumococcal carriage in infants in Belgium. Next to her research activities she teaches and coordinates education on Youth Health Care and works in a well-baby clinic.

VACCINATIONS: DO WE HAVE TO FEAR ANY SHIFTS?

Vaccines are amongst the most effective methods to prevent infectious disease morbidity and mortality, especially when used in universal programs. However, using them at large scale might impact on their field effectiveness in different ways.

A major fear is a shift in microbial ecology: vaccination pressure could possibly promote mutants or variants to replace the pathogens the vaccines are directed against. Shifts in strain composition can also occur naturally, independent from vaccine pressure, as seen for influenza. With respect to the vaccines that are currently recommended for universal use in Belgium, surveillance should primarily focus on rotavirus and *S Pneumoniae* for which vaccines are not covering all circulating strains and thus carry a risk of replacement by non-vaccine-strains. Pneumococcal carriage studies in other countries in children vaccinated with conjugate pneumococcal vaccines as well as invasive pneumococcal disease surveillance suggest replacement, not only by non-aggressive pneumococcal serotypes. In contrast, a serogroup switch in *N meningitidis* in countries with long-term use of meningococcal C vaccine has not been reported yet. Immune escape by mutants has been postulated for mumps and pertussis, but is currently not considered to substantially hamper vaccine effectiveness.
Additionally, other shifts related to vaccination deserve attention and surveillance. Former childhood diseases such as mumps and measles are shifting to adolescent and adulthood disease, in many of our surrounding countries and in Belgium, as a consequence of historical suboptimal vaccination coverage in the first place. A similar age shift for varicella has to be avoided at any price. Last but not least, effective vaccination programs can cause a shift in the public perception of the vaccines’ risk-benefit ratio and public acceptance of vaccine programs can shift in very short term as a consequence of perceived risk. Therefore public confidence in vaccination is another area that needs to be monitored and sustained, a baseline measurement was included in the 2016 vaccination coverage survey in Flanders.

REFERENCES

BIOGRAPHY

Robb Butler is Programme Manager for Vaccines and Immunization at the WHO European Regional Office, in Copenhagen, Denmark. The Programme provides policy guidance and technical assistance to 53 countries to maximize equitable access to vaccines of assured quality, including new immunization products and technologies. Prior to joining WHO in 2009, Robb served as an advocacy and communications adviser on communicable disease prevention, humanitarian assistance and social protection projects and programmes, for major donors, agencies and NGOs: designing communication strategies and advocacy campaigns, evaluating social mobilization and demand generation projects, and coordinating social marketing initiatives in over 20 countries of Asia and Africa. Since joining WHO, Robb has served as a Group Lead on vaccine communications and advocated for the strengthening of people-centred public health – leading on introducing and scaling-up WHO’s use of behavioural insights and behavior change communications to promote vaccination and tailor service delivery.

VACCINE HESITANCY

After providing a short update on the status of immunization coverage and vaccine-preventable disease incidence, the presentation will consider the impact that vaccine hesitancy is making on disease outbreaks and resurgence in the European Region. The speaker will define hesitancy and its dimensions with examples of how vaccine hesitancy is manifested in decisions to vaccinate. The presentation will cover the behavioural determinants influencing vaccination and the role of healthcare workers in counteracting and managing hesitant parents/caregivers. The presentation will end by prompting the audience to discuss the real impact of the anti-vaccine lobby and hesitancy on under-performing immunization programmes - with the spotlight of the discussion upon Belgium.
real impact of the anti-vaccine lobby and hesitancy on under-performing immunization programmes - with the spotlight of the discussion upon Belgium.

REFERENCES


BIOGRAPHY

Since 2015 Anne Botteaux is associate professor of bacteriology and PI of the Molecular Bacteriology Lab at the Free University of Brussels (ULB). After completing her PhD in Biomedical Sciences at the ULB, she spent 10 years working on deciphering the regulation and the activation mechanism of the bacterial Type 3 secretion system. Her actual research interests include understanding the virulence mechanisms of Group A Streptococcus, vaccination and new diagnostic tests development.

STREPTOCOCCUS PYOGENES: A GLOBAL PATHOGEN THAT NEEDS A GLOBAL VACCINE

Streptococcus (GAS) causes >500,000 deaths per year. Two vaccine candidates are currently progressing towards clinical trials and all target the surface M protein. The M protein, encoded by the emm gene, has a variable amino acid sequence, resulting in antigenic diversity and it is the substrate for the emm-typing and emm-cluster schemes defining 223 different emm-types and 48 different emm-clusters respectively. Marked epidemiological differences have been demonstrated, especially between high-income countries and resource-poor regions. A lower number of emm-types are found in high-income settings, with 5 predominant emm-types accounting for >50% of circulating isolates. In marked contrast, in low-income settings there are a large number (up to 80) of different emm-types with none predominant. Recent discoveries offer an exciting new approach to developing global vaccines. Animal and in vitro studies suggest that cross-protection can be induced against different emm-types. The emm-cluster system serves as a framework to investigate this cross-protection phenomenon and has identified coverage gaps in the formulation of the current vaccine candidates.
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**Parasites**
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Dr. Pieter-Jan Ceyssens
Scientific Institute of Public Health, Brussels
pieter-jan.ceyssens@wiv-isp.be

BIOGRAPHY

In 2009, Pieter-Jan Ceyssens graduated from the KU Leuven (Bioscience Engineering, Lavigne lab) with a dissertation on arly bacteriophage infection mechanisms in Pseudomonas aeruginosa. After 4 years as postdoctoral fellow at the universities of Vienna, Leuven and Pittsburg, he joined Synthetic Genomics (San Diego) in 2013. In 2014, he returned to Belgium to head the unit ‘Antibiotics and Resistance’ embedded in the National Reference Centres for Salmonella, Shigella, Listeria, Neisseria and Mycobacteria at Belgian’s Scientific Institute of Public Health.

CLINICAL IMPACT OF NEW LAB TECHNOLOGIES

In my part of the presentation, I will focus on the impact that novel technologies, and more specifically whole-genome sequencing (WGS), exert in the various Reference Centres embedded in the Division of Bacterial Diseases (WIV-ISP). Thanks to advances in WGS and associated bioinformatics, we are currently witnessing a true paradigm shift in the ever slowly changing field of bacteriology, which has been guided by culture and biochemistry for decades. This shift translates to both an organisational shift in lab structure, as to the deeper level of analyses in the various studied bacteria. However, and apart from its far-stretching possibilities, I will also point at significant drawbacks still associated with wide implementation of the technique. These are found mainly in the time for analysis, the cost-effectiveness and the legal obligation of reference centres to keep performing certain tests.
Dr. Brecht Devleesschauwer  
Scientific Institute of Public Health, Brussels  
brecht.devleesschauwer@wiv-isp.be

**BIOGRAPHY**

Dr Brecht Devleesschauwer is a senior epidemiologist within the Health Indicators Units of the Scientific Institute of Public Health. He conducts policy-driven research on composite measures of population health and health inequalities, and is coordinator of the Belgian national burden of disease study. Brecht holds a joint PhD degree in public health and veterinary sciences and MSc degrees in biostatistics and veterinary medicine.

**THE DISEASE BURDEN OF INFECTIOUS DISEASES IN BELGIUM**

Although the health impact of infectious diseases in high-income countries has been surpassed by that of non-communicable diseases, infectious diseases continue to pose a major burden to healthcare systems, while new and re-emerging infectious diseases warrant continuous awareness. This multitude of challenges, coupled with increasing budgetary restrictions, calls for comparable information on the population health impact of these diseases, forming a crucial evidence base for rationally allocating health resources and prioritizing future health research.

The multitude of health outcomes associated with infectious diseases makes it particularly challenging to quantify and compare their population health impact. Indeed, health outcomes may range from self-resolving acute illness, over severe acute and long-term health outcomes, to death. Infectious diseases furthermore vary widely in incidence and mortality, but also in their extent of being reported.

In recent years, a methodological framework has emerged to address these challenges and generate estimates of the true burden of infectious disease. This framework builds on statistical tools for unraveling the true disease epidemiology, and on summary measures of population health, most notably the Disability-Adjusted Life Year (DALY), for quantifying the true disease burden. DALYs correspond to the number of healthy life years lost due to illness and death, and take account of both disease occurrence and severity. Furthermore, through the elaboration of disease models, they allow capturing the often complex courses of disease, which may be characterized by various health states (e.g. acute or chronic phases, short-term or long-term sequelae), that each may occur at different severity levels.

In Belgium, information on the burden of infectious diseases, expressed as DALYs, is available through a limited number of disease-specific studies. To address the need for a more comprehensive approach, the Scientific Institute of Public Health
(WIV-ISP) has initiated a project that will allow assessing the true burden of community- and hospital-acquired infectious diseases in Belgium on a regular basis. In this presentation, we will present the methodological framework for quantifying the true burden of infectious disease; summarize available information on the burden of infectious diseases in Belgium; and present preliminary results of the WIV-ISP burden of infectious disease project.
BIOGRAPHY

Carole Schirvel is a medical doctor, trained on tropical medicine in Antwerp and on public health in Brussels (ULB). After several years on the field of humanitarian aid and development cooperation and, she has been working for nearly 6 years for the french community and Wallonia (AViQ), as coordinator of the infectious disease surveillance cell.

Wim Flipse is a medical doctor and worked 9 years in public health in Africa. He got a Master Degree in Epidemiology at the London School of Hygiene and Tropical Medicine. Afterwards he was employed in different Municipality Health Services in the Netherlands mainly in the subject of infectious diseases. Since 2010 he is an infectious disease control physician for the Flemish Agency for Health and Care now stationed in Antwerp.

FOLLOW-UP OF MANDATORY REPORTED DISEASES IN BELGIUM

The reporting of cases of infectious disease is an important aspect in the planning and evaluation of disease prevention and control programs in public health. The reporting system concerns a wide range of diseases: zoonotic, vector borne, food- and waterborne, vaccine preventable,… Rapid reporting is an opportunity to limit the spread of disease and the concomitant secondary cases. Mandatory notification sets up in a framework of legal matter, specific of each community in Belgium. Data collected through the system of notification should provide the basis for planning and implementing specific programs. Actually, the mandatory notification that target between 40 and 50 diseases (depending on communities) is unfortunately not exhaustive. The report of infectious case has to be done by a large variety of healthcare professionals: family doctors, school doctor, laboratories, hospital clinicians, occupational health,… This presentation will present you the follow up done by health authorities after the notification of infectious disease.
**BIOGRAPHY**

Nathalie Shodu has been working for 9 months as an inspector for the infectious disease surveillance cell for the Wallonia region (AViQ). She joined the team with Doctor Schirvel and Sylvie Leenen. She studied as a nurse at ISEI and then took her Master in Public Health at the Catholic University of Louvain.

**UPDATE ON THE MEASLES OUTBREAK IN WALLONIA, BELGIUM, DECEMBER 2016 TO APRIL 2017**

This presentation describes the measles outbreak that affected Wallonia, in Belgium from 20 December 2016 to April 2017. Up to 16/04/2017, the Infectious Disease Surveillance Cell recorded 288 measles cases. Of these cases, 163 have been confirmed by the National Reference Center for measles, mumps and rubella. Four of the five provinces in Wallonia have been affected by this epidemic. Among the 288 cases reported, 111 (38%) were hospitalized and 37 cases were detected among hospital workers (nurses, doctors, lab technicians, etc.). No deaths were reported during this epidemic, but some patients presented severe complications.

We have encountered various difficulties in the management of this epidemic:

- Insufficient human resources;
- Difficulties to identify clearly the diagnosis of measles due to an atypical clinical presentation in some cases;
- The question of post-exposure vaccination etc.
- A high workload due to contact tracing, etc.

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ABSTRACTS OF POSTERS
Background

The Belgian National Reference Centre (NRC) for Bordetella pertussis is responsible for the epidemiologic surveillance of pertussis and pertussis-like disease caused by *B. pertussis*, *B. parapertussis*, and *B. holmesii*. The NRC is composed of the WiV-ISp which performs serodiagnosis of pertussis and the UZ Brussel, which performs diagnosis by qPCR and culture on respiratory samples. The diagnostic assay for pertussis developed by the UZ Brussel is based on qPCR detection of four target genes: IS481, IS1001, *recA*, and IS1002, the combination of which allows for the differentiation between the different *Bordetella* spp.

In 2016, only 3944 qPCR tests for the diagnosis of pertussis were performed by the UZ Brussel, for 3835 different patients. This is less than in previous years (4096 tests in 2015 and 4733 in 2014). Despite this, 2016 showed a rise in the amount of cases diagnosed as positive for *B. pertussis* by qPCR: 439 (11.1%) compared to 392 (9.6%) in 2015.

The number of *B. pertussis* cases peaked strongly in August and September, while being the lowest during the winter months both at the beginning and end of the year. This seasonal pattern is typical for pertussis infection, even though it was less pronounced in 2015.

Similar to other years, recovery of *B. pertussis* strains in culture, which is attempted after detection by qPCR, was little less than 30%. There is a strong correlation between this recovery and the Cp value for IS481 by qPCR. For Cp values below 20, there was a recovery rate of 74%. For Cp values above 30, this rate drops to no more than 10%. As NRC, it is important to maximize the number of strains we culture and collect, as this allows for additional typing and epidemiologic surveillance.

In total, 118 *B. pertussis* strains were recovered. Macrolide sensitivity was determined using disk diffusion susceptibility testing. All strains were found to be sensitive to erythromycin. Susceptibility testing to sulfamethoxazole/trimethoprim is currently being performed, as is further molecular typing of the 118 collected strains.
In addition to *B. pertussis*, 48 cases of *B. parapertussis* and 5 cases of *B. holmesii* were detected. Out of these, 9 *B. parapertussis* and 2 *B. holmesii* strains were recovered in culture. There were three cases of co-infection: two where both *B. pertussis* and *B. parapertussis* were found, and one where both *B. pertussis* and *B. holmesii* were found.

Serological diagnosis for pertussis is based on the detection of high levels of anti-pertussis toxin IgG antibodies (ELISA). In 2016, 5457 tests were performed, resulting in 937 cases diagnosed as positive for recent *B. pertussis* infection. Compared to 2015 and similar to qPCR-based diagnosis, serodiagnosis revealed a rise in the number of positive cases. Overall, in 2016 an increase of the total number of confirmed cases for *B. pertussis* (1293 compared to 1185 in 2015) was seen in Belgium.
WHAT MOTIVATES HEALTHCARE WORKERS IN GETTING VACCINATED AGAINST SEASONAL INFLUENZA?

Lise Boey¹, Charlotte Bral¹, Mathieu Roelants², Antoon De Schryver³, Lode Godderis², Karel Hoppenbrouwers¹, Corinne Vandermeulen¹

1. Leuven University Vaccinology Center, Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, Belgium
2. Environment and Health, Department of Public Health and Primary Care, KU Leuven, Belgium
3. Department of Epidemiology and Social Medicine, University of Antwerp, Belgium
4. IDEWE Occupational Health Services, Heverlee-Leuven, Belgium

Background
Healthcare workers (HCWs) can play an important role in the transmission of influenza during nosocomial outbreaks, which causes increased morbidity and mortality in patients and residents of nursing homes. Therefore, the Belgian Superior Health council recommends influenza vaccination for all HCWs. The Flemish target of 80% influenza vaccination coverage in HCWs has not yet been attained. With this study, we aimed to gain insight in the motivation of HCWs for influenza vaccination.

Methods
Potential influencing socio-demographic and professional factors, and attitude towards influenza and influenza vaccination was surveyed in 5141 HCWs in hospital and nursing homes. Additionally, influenza campaign coordinators of 13 hospitals and 14 nursing homes were interviewed to gain insight in the key factors of success/failure of influenza vaccination campaigns.

Results
Up to 90% of HCWs think it is important not to infect their patients. However, only 50% considers influenza vaccination as a duty. Factors that positively influence vaccination coverage are: (i) good practical organization, such as vaccination at a suitable moment, vaccination without the need of subscription, the use of a mobile cart program and vaccination on the ward, and (ii) encouragement by a supervisor, whereas the (i) existence of misconceptions about influenza and its vaccine and (ii) underestimation of the risk of contracting influenza by patients or HCWs has a negative impact on vaccination coverage.

Conclusion
The pentaplex immunoassay is validated and used for testing a new serumbank of more than 3000 samples.
FIRST EVALUATION OF THE XPERT® XPRESS FLU/RSV FOR THE DETECTION OF INFLUENZA VIRUS

Anneleen Daems¹, Tom Spiritus², Danielle Van der beek²

¹. Thomas More Kempen
². AZ AZ Herentals

Background
Seasonal epidemics of influenza are responsible for significant morbidity and mortality worldwide.
Real-time RT-PCR assays for influenza are widely used. Rapid and sensitive detection has a significant advantage as it can optimize management by limiting administration of unnecessary antimicrobials and enhancing decision making on infection control practices.

Methods
In this study, we evaluated the performance of the new Xpert® Xpress Flu/RSV (Cepheid, Sunnyvale), a next generation automated, multiplex RT-PCR assay for the qualitative detection and differentiation of influenza A, influenza B and RSV. The performance of the Xpert Xpress Flu/RSV assay for the detection of influenza was compared to the Alere Binax now Flu A&B and Alere i Flu A&B assays.
Fifty fresh consecutive samples were collected from ambulant and hospitalized patients from February 4th to February 13th 2017. They consisted of 41 nasopharyngeal swabs and 9 nasopharyngeal aspirates.
Testing and interpretation of results were done according to the assay package inserts.
Discrepant results were resolved by in house real-time PCR performed at the national reference lab (WIV-ISP) for influenza and other respiratory viruses.

Results
Of the 50 samples tested, 26 were positive for influenza A by Xpert Xpress Flu/RSV, 18 were positive for influenza A by Alere i and only 6 were positive for influenza A by Binax Now. The eight samples that were negative by Alere i and positive by Xpert were sent to the national reference lab WIV-ISP for analysis by in house real-time PCR. The reference lab confirmed 5 positive influenza A cases but argued that the other 3 discrepant samples were most likely positive containing an amount of virus below the detection limit of the in house PCR.

Conclusion
Xpert Xpress Flu/RSV demonstrated better sensitivity (100%) versus the Binax now Flu A&B (23%) and Alere i Flu A&B assays (69%). The accuracy and reliability associated with the 30 mins turnaround time makes the Xpert Xpress Flu/RSV suitable for point-of-care and routine diagnosis of influenza viral infections.
ANNUAL REPORT 2016
The number of STEC infections identified at the NRC STEC/VTec in 2016 remained stable in comparison to the years before: 106 different STEC strains were isolated from 105 Belgian patients. In the fecal sample of one patient two nearly identical STEC O157:H7 were found; one strain carried the stx subtypes stx1a and stx2c while the second one only possessed the stx1a subtype.

Eighty seven strains were ‘typical’ enterohemorrhagic E. coli (EHEC) isolates; defined as STEC positive for the additional virulence genes eaeA (intimin) and hlyA (enterohemolysin). Nineteen isolates were atypical STEC; lacking one or both of these virulence determinants. None of the STEC strains was found positive for the Enteroaggregative (EaggEC) virulence genes aaiC and/or aggR.

As seen in previous years, the majority (63/106; 59.4%) of the STEC isolates belonged to serogroup O157 (serotype O157:H7 or O157:H-), all of them were typical EHEC (eaeA+, hlyA+). Four of the ‘top 5’ non-O157 serogroups were represented: 12 O26 strains, 2 O103 strains, 6 O145 isolates and 1 STEC O111. Nine isolates could not be typed with our in-house serotyping techniques. The remaining 13 strains belonged to 9 different O-serovars: O63, O78, O79, O80 (n=2), O91 (n=3), O128, O153, O156 and O174 (n=2).

More than half the isolates were stx2 positive (55/106, 51.9%), 17.9% (19/106) were stx1 positive and 30.2% were stx1 and stx2 positive (32/106). They belonged to various stx subtypes: stx1a (n=13), stx1c (n=6), stx1a+stx2a (n=9), stx1a+stx2a+stx2c (n=1), stx1a+stx2b (n=3), stx1a+stx2c (n=17), stx1a+stx2d (n=1), stx1a+stx2? (n=1) (stx2 gene lost in the lab), stx2a (n=33), stx2a+stx2c (n=8), stx2b+stx2d (n=1), stx2c (n=7), stx2d (n=1), and stx2f (n=5).

A STEC strain could be isolated from the fecal samples of 17 patients suffering from the haemolytic uremic syndrome (HUS): 9 STEC O157:H7/H-, 3 STEC O26:Hunk, 1 O111:H-, 2 O145:Hunk, 1 O80:H-, and 1 O174:Hunk. Additionally, STEC infection could be confirmed in 9 HUS patients by detection of antibodies against STEC O lipopolysaccharide in their serum samples (2 times O26 and 7 times O157).

In 2016 most of the STEC infections were sporadic, but six small clusters of infection with EHEC O157:H7/H- in families and day-care centers were detected in different parts of the country.

RISK ASSESSMENT FOR THE DEVELOPMENT OF THE HAEMOLYTIC UREMIC SYNDROME
Since 2009 it is mandatory in Belgium to report STEC infections to the local health inspection authorities. They investigate each notified case separately and decide whether it is necessary to install measures to prevent further spread of the infec-
tion or to perform further outbreak screening and investigation. To facilitate this decision making, information regarding the risk factors for the development of HUS can be helpful. Previous studies identified the presence of the STEC virulence genes stx2 in general, stx2a specifically, and eaeA, as well as low age of the patient as risk determinants for HUS development. Since the large-scale STEC O104:H4 outbreak in 2011, the rare combination of EaggEC virulence genes and stx2 is also considered as high risk (Scheutz et al. 2014, Brandal et al. 2015).

In order to provide insight in the risk determinants for HUS development in Belgium we performed statistical multivariate analyses (using the SPSS software) on a dataset containing STEC strains isolated at the NRC between 2011 and 2016. In total 411 STEC isolates from patients with known clinical manifestations were included; 75 (18.3%) of which were associated with HUS. Different logistic regression models were implemented including following variables: patient’s age, STEC O-serogroup, stx, stx subtype, eaeA, ehxA, sorbitol fermentation, and β-glucuronidase production.

In concordance with previous findings stx2, the stx2 subtype stx2a more specifically, and the virulence gene eaeA each contained a significant higher risk for HUS development. The presence of stx1 and the patient’s age groups 19-45 years and 46-64 years each had a significant reduced risk for HUS development. Further analyses are still ongoing, but based on the results of this risk assessment we will adapt our screening algorithm and our results report to be as informative as possible to healthcare workers.

References
COMBINATION OF LINE IMMUNOASSAYS MIKROGEN RECOMLINE CMV IGG AND RECOMLINE CMV IGG AVIDITY HELPS TO DATE THE ONSET OF CMV PRIMARY INFECTION

ML Delforge, J Eykmans, D Steensels, I Montesinos

Department of Microbiology, Hôpital Erasme, Université Libre de Bruxelles
National Reference Center for Congenital Infections

Objectives
1. To assess the ability of the line immunoassays Mikrogen RecomLine CMV IgG and RecomLine CMV IgG Avidity to date the onset of CMV primary infection comparing to VIDAS CMV IgG Avidity.
2. To evaluate the added value of the combination of RecomLine CMV IgG and RecomLine CMV IgG avidity compared to VIDAS CMV IgG Avidity.

Study design
1. For the first objective, a panel of 69 sequential sera collected from 36 women with precisely determined onset of CMV primary infection was tested with VIDAS CMV IgG Avidity, Mikrogen RecomLine CMV IgG and RecomLine CMV IgG. 36 sera were drawn within 12 weeks of infection and 33 were obtained more than 12 weeks after infection.
2. A second panel of 73 sera collected from pregnant women presenting with positive CMV IgM and a borderline CMV IgG avidity with VIDAS was analysed.

Results
1. Among the 36 sera ≤ 12 weeks of infection, VIDAS CMV IgG Avidity showed a reliable low avidity result in 25 cases, a borderline not contributory result in 10 cases and a false positive high avidity in 1 case. The combination of RecomLine CMV IgG and RecomLine CMV IgG avidity showed 32 reliable results with the following interpretation: n=6 <6-8 weeks, n=1 between 6-8 and 14 weeks, n=23 <14 weeks and n=2 negative IgG (in 2 very recent infections), and 4 non-contributory positive IgG results. Among the 33 sera >12 weeks of infection, VIDAS gave 22 reliable high avidity results and 11 borderline non-contributory results. The combination of RecomLine CMV IgG and RecomLine CMV IgG avidity gave 23 reliable results (n=21 >12weeks, n=1 >24 weeks, n=1 between 6-8 and 14 weeks), 3 infection <14 weeks and 5 non-contributory positive IgG. For 2 sera (same patient), the RecomLine CMV IgG gave >24 weeks at 18 and 22 weeks of infection.
2. Among the 73 sera with a borderline avidity with VIDAS, the combination of line immunoassays yielded following results: 6 infections <6-8 weeks, 6 infections >6-8 weeks without additional statement, 10 infections between 6-8 and 14 weeks, 10 infections >12 weeks, 1 infection >24 weeks, 26 infections <14 weeks, 1 negative IgG and 13 cases of non-contributory positive IgG.

Conclusions
The combination of Mikrogen RecomLine CMV IgG and RecomLine CMV IgG avidity showed a good reliability to date CMV infection and less non-contributory results than VIDAS CMV IgG Avidity. Among a panel of non-contributory results with VIDAS CMV IgG Avidity, this combination helped to date the onset of infection in 82% of cases.
BURDEN OF MEDICALLY ATTENDED ACUTE GASTROENTERITIS IN ENGLAND: A COHORT STUDY IN CPRD

Germano Ferreira, Ben Lopman, Clarence Tam, John Harris, Tom Cattaert, Kaatje Bollaerts, Margarita Riera, Thomas Vestaeten

Background
Medically attended acute gastroenteritis (MAAGE) is due to multiple causes including viruses, bacteria and parasites. The objective was to assess the episode rates of MAAGE to inform the cause-specific MAAGE burden of disease.

Material/methods
Patients registered in general practices contributing to CPRD (Clinical Practice Research Datalink) from January 2006 to December 2014 and eligible for Hospital Episode Statistics (HES) Inpatient linkage data were included. Cases were defined based on MAAGE related READ and ICD-10 codes. Episodes were defined as events separated by a minimum 14-day disease-free period. Episode rates with 95% CIs were calculated by calendar year and month, age group (<1, 1-4, 5-9, 10-17, 18-64, 65-74, 75-84 and 85+ years old), gender, region, healthcare setting (GP care only or requiring hospitalization) and aetiology.

Results
A total of 5,124,812 subjects (50.9% female) were included in the study with a median follow-up time in CPRD of 7.6 years. 273,774 cases were identified with at least one MAAGE episode, representing an overall episode rate of 12.95 per 1000 person-years (95%CI: 12.90-12.99). The highest burden was observed in <1 years old, 1-4 years old, and 85+ years old, with episode rates of 95.57 (94.38-96.76), 39.26 (38.89-39.62) and 36.02 (35.56-36.49) respectively. Episode rates were stable year-on-year with marked winter seasonality. Episode rates requiring GP care only vs. requiring hospitalization were 7.43 (7.40-7.47) and 5.52 (5.49-5.55) respectively. The episode rate with aetiology unspecified was 11.81 (11.77-11.86).

Conclusions
Burden of MAAGE is high in the CPRD population with the highest episode rates in children and elderly. In order to assess cause-specific burden of MAAGE further statistical modelling development is required to attribute the high proportion of cause-unspecified MAAGE.
ANTI-BIOTIC SUSCEPTIBILITY OF BURKHOLDERIA CEPACIA COMPLEX IN CLINICAL ISOLATES OF CYSTIC FIBROSIS PATIENTS

Herpol M1, Echahidi F1, Peeters C2, Wybo I1, Vandamme P2, Piérard D1

1. Department of Microbiology and Infection Control, Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (VUB), Brussels, Belgium
2. Department of Biochemistry and Microbiology, Faculty of Sciences, Ghent University, Ghent, Belgium

Background

Burkholderia cepacia complex (BCC) infections in CF patients cause severe morbidity and mortality. Especially in more advanced lung disease or after lung transplantation these bacteria can cause acute “cepacia syndrome”, frequently followed by death. Treatment of BCC infections requires extensive and aggressive antibiotic therapy but is hampered by intrinsic resistance and chronically selective pressure. The aim of this study was to determine the in vitro susceptibility of BCC.

Material/method

We tested 95 unduplicated isolates of CF patients from 2012 to 2016 against 13 antibiotics. Species identification was performed by recA gene sequence analysis. MIC’s were determined by microdilution in a self-designed microtiter plate (Sensititre®). As no EUCAST species-specific breakpoints were available, non-species related breakpoints were used. Breakpoints for aminoglycosides, colistin and trimethoprim-sulfamethoxazole were based on those from EUCAST for non-fermenters, respectively of Pseudomonas spp. and Stenotrophomonas maltophilia. For temocillin, breakpoints described by Fuchs et al. were used.

Results

The most prevalent species was B. multivorans (53%), followed by B. vietnamiensis (17%). The other species count for less than 10%: B. cenocepacia (9%), B. stabilis (9%), B. contaminans (5%), B. cepacia (3%) and B. lata (3%). Table 1 shows MIC50, MIC90 and the antibiotic susceptibility. As expected, all strains were resistant to colistin and most showed high MIC’s to amikacin and tobramycin. Of all tested antibiotics, trimethoprim-sulfamethoxazole (SXT) had highest in vitro activity: more than three quarters of the strains were susceptible. For temocillin, ceftazidime, piperacillin-tazobactam and meropenem, at least half of the strains were susceptible. No significant difference between species was observed except for B. stabilis, which was more resistant; only trimethoprim-sulfamethoxazole, temocillin, ceftazidime and cefepime showed in vitro activity. There was also a difference noted for B. vietnamiensis where only 50% of the tested strains were susceptible to trimethoprim-sulfamethoxazole. Nine percent of the tested strains were resistant or intermediate susceptible to all antibiotics, whereas thirteen percent were only susceptible to trimethoprim-sulfamethoxazole.
Conclusions

EUCAST does not recommend susceptibility testing for BCC. The MIC distribution for relevant antibiotics is wide and encompasses the non-species related pharmacodynamic breakpoints. Clinical studies are still needed, but the results of the current study may help clinicians with the antibiotic treatment of their patients, taking into account previous clinical responses and their own experience.

Table 1

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>MIC50 (mg/L)</th>
<th>MIC90 (mg/L)</th>
<th>Susceptibility (%)</th>
<th>Breakpoint (mg/L):s</th>
</tr>
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<tbody>
<tr>
<td>Trimethoprim-sulfamethoxazole (SXT)</td>
<td>≤0,5</td>
<td>8</td>
<td>83</td>
<td>4</td>
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<tr>
<td>Temocillin</td>
<td>16</td>
<td>64</td>
<td>67</td>
<td>16</td>
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<td>Cefazidime</td>
<td>4</td>
<td>≥32</td>
<td>61</td>
<td>4</td>
</tr>
<tr>
<td>Peperacillin-Tazobactam</td>
<td>4</td>
<td>&gt;64</td>
<td>56</td>
<td>4</td>
</tr>
<tr>
<td>Meropenem</td>
<td>4</td>
<td>16</td>
<td>50</td>
<td>2</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>8</td>
<td>&gt;64</td>
<td>45</td>
<td>4</td>
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<tr>
<td>Aztreonam</td>
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<td>&gt;32</td>
<td>44</td>
<td>4</td>
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<tr>
<td>Cefepime</td>
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<td>&gt;64</td>
<td>3</td>
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<td>Tobramycin</td>
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<td>&gt;16</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>2</td>
<td>16</td>
<td>1</td>
<td>0,25</td>
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<tr>
<td>Tigecycline</td>
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<td>16</td>
<td>1</td>
<td>0,25</td>
</tr>
<tr>
<td>Collatin</td>
<td>&gt;32</td>
<td>&gt;32</td>
<td>0</td>
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</table>
Background
Hospital acquired viral respiratory infections are common and constitute a serious risk among patients with underlying disease and those of extreme age. Respiratory syncytial virus (RSV) and influenza virus are frequently transmitted in hospital settings. In order to further strengthen the prevention of nosocomial transmission, we reviewed all influenza and RSV orders in OLV Hospital from 1 December 2016 to 31 March 2017. Viral detection was performed on invasive samples as well as on sputa and nasopharyngeal swabs, using an in house multiplex RT-PCR. We defined nosocomial transmission of influenza and RSV if a first positive sample occurred later than respectively 4 days and 8 days since hospitalization, according to the upper range limit of the incubation periods.

Results
Over a period of 4 months, 1965 clinical samples were analyzed from 1717 different patients. Fifteen % of all samples were found positive for influenza A, 0.5% for influenza B and 12 % for RSV. Co-infection of RSV and influenza was observed in 0.5% of the cases. More detailed information about the distribution in function of time can be found in figure 1.
Influenza
Regarding the 290 patients who tested positive for influenza, 71% was 60 years or older and three quarters were hospitalized. In-hospital mortality rate was 12% with an average age of 81.7 years. Nosocomial transmission was suspected in 20% of the hospitalized patients with influenza. The median time between the first day of hospitalization and a positive test result for influenza in this group was 12 days. Seven patients (between 57 and 94 years old) died following nosocomial infection with influenza, which equals a 19% nosocomial mortality rate.

RSV
For 228 patients a positive test result for RSV was found. As expected, 59% were children under the age of 5 (90% ≤ 2 years) and 25% were patients of 70 years and older. 62% of the RSV positive cases were hospitalized. Only 6% of the hospitalized patients with RSV had an RSV infection due to nosocomial transmission (n=8), none of them were children. Eleven patients died eventually, all older than 47 years old, 2 of them following a hospital acquired RSV infection.

Discussion and conclusion
Despite the efforts of infection control, nosocomial transmission with a significant mortality is still common, especially for influenza. A possible explanation for this high number of hospital-acquired influenza is the extensive testing for respiratory viruses in our hospital. Also delayed testing after admission can cause an overestimation, due to a prolonged positive test result with PCR. In addition, it forms a permanent risk for nosocomial transmission. This urges for early screening of admitted patients when respiratory infection is suspected. On the other hand, nosocomial transmission of RSV is probably underestimated due to the longer incubation period of RSV and the rather short duration of hospitalization in the pediatric department. Nosocomial RSV transmission was only observed in older patients with a longer hospital stay. Furthermore, it must be noted that the highest prevalence of RSV-infection was observed in November 2016, one month before the reviewed period. This may have had an influence on the results. These results emphasize the need for permanent attention and further expansion of preventive measures to reduce hospital-acquired respiratory infections and the corresponding mortality.

Table 1 | Results in hospitalized patients

<table>
<thead>
<tr>
<th></th>
<th>Influenza</th>
<th></th>
<th>RSV</th>
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<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
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<tr>
<td>Respiratory infection</td>
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<tr>
<td>Community-acquired</td>
<td>175</td>
<td>81%</td>
<td>128</td>
<td>94%</td>
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<tr>
<td>Hospital-acquired</td>
<td>42</td>
<td>19%</td>
<td>8</td>
<td>6%</td>
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<tr>
<td>Mortality of hospitalized patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>12%</td>
<td>11</td>
<td>8%</td>
</tr>
<tr>
<td>After hospital-acquired infection</td>
<td>8</td>
<td>19%</td>
<td>2</td>
<td>25%</td>
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IMPLEMENTATION OF COPAN FECALSWAB™ AND COPAN SELENITE ON WASP™ FOR THE AUTOMATED PROCESSING OF STOOL SPECIMENS

Ann Lemmens, Truus Goegebuer, Luc Hendrickx

AZ Sint Maarten Hospital, Microbiology lab, Mechelen

Background
Automated processing of stool specimens is difficult due to different sample consistency, volume availability and variety of primary containers. Appropriate specimen collection and transportation systems can standardize the stool sample processing, enhancing the diagnostic process. Copan FecalSwab™ (FS), a tube with 2ml Cary-Blair medium and a flocked swab, can be used for culturing most relevant enteric pathogens from both rectal swabs and stool samples. Copan Selenite broth, available in a 2ml tube, can be used for selective enrichment of Salmonella spp. The scope of this study was to validate the implementation process of FS and Selenite on WASP™ for the clinical microbiology laboratory in order to convert stool processing from the manual streaking process to an automated procedure.

Material/methods
Spiked negative stools and clinical stools were used for this study (n=97). Aliquots (3 grams) of the negative stools were spiked with 300 µl of diluted Y. enterocolitica serovar 3 biotype 4, S. typhimurium (ATCC 25241), S. flexneri (clinical strain) and Campylobacter jejuni (ATCC 33560) to obtain final bacterial concentrations/stool of 10⁸ CFU/g, 10⁷ CFU/g, 10⁶ CFU/g. All clinical stool samples (n=61) and spiked stools in triplicate (n=36) were transferred in FecalSwab medium tubes using the flocked swab. All samples were manually plated onto the first quadrant of McConkey, XLD, CIN, Campylosel agar plates using a swab and streaked with a 10 µl loop, while the FecalSwab stools were loaded on WASP and processed using a 10 µL loop and a 4 quadrants streaking pattern. All clinical stool samples and the negative ones spiked with S. typhimurium (n=73), were also inoculated in selenite broth, from FS and from the sample directly, and then plated on SS-agar after overnight incubation.

Results
For the spiked samples we found 100% concordance for S. flexneri and C. jejuni. Discrepant results were found in the stools spiked with the lowest concentration of S. typhimurium and Y. enterocolitica, negative when manually plated but positive from FS and selenite broth.
We found 100% concordance in the clinical samples with S. typhimurium and Y. enterocolitica, three Campylobacter coli were not isolated from FS.
Culture via FS yielded the isolation of two extra Aeromonas species possibly because streaking by WASP resulted in more isolated colonies to perform successive analysis.

Conclusions
FS and Selenite are facilitating WASP automation stool processing and are reliable devices for diagnosis of gastric infections. Automatic processing of FS and Selenite allows standardization and time reduction of sample processing. Streaking by WASP resulted in more isolated colonies to perform successive analysis.
PREVALENCE AND DISTRIBUTION OF HCV GENOTYPES IN BELGIUM FROM 2008 TO 2015

Bouacida Lobna¹ and Hutse Veronik²,²², Suin Vanessa²,²², Boudewijns Michaël³, Cartuyvels Reinoud⁴, Debaisieux Laurent⁵, De Laere Emmanuel⁶, Hallin Marie⁷, Hougardy Nicolas⁸, Lagrou Katrien⁹, Oris Els¹⁰, Padalko Elizaveta¹¹, Reynders Marijke¹², Roussel Gatien¹³, Senterre Jean-Marc¹⁴, Stalpaert Michel¹⁵, Ursi Dominique¹⁶, Vael Carl¹⁷, Vaira Dolores¹⁸, Van Acker Jos¹⁹, Verstrepen Walter²⁰, Van Gucht Steven²,²², Kabamba Benoit²¹,²², Muyldermans Gaetan²³.

1. WIV-ISP, LMM, Brussels
2. WIV-ISP, Viral diseases, Brussels
3. AZ Groeninge, Kortrijk
4. Jessa Ziekenhuis, Hasselt
5. CUB-Hopital Erasme, ULB, Brussels
6. AZ Delta Laboratorium, Roeselare
7. LHUB-ULB, Site Porte De Hal, Brussels
9. UZ-KULeuven, Leuven
10. Ziekenhuis Oost-Limburg Labo Klinische Biologie, Genk
11. UZ Gent, Gent
12. AZ Sint Jan Laboratorium, Brugge
13. Clinique St. Pierre, Ottignies
14. Ch Regional De La Citadelle Laboratoire, Liège
15. AML, Antwerp
16. Universitair Ziekenhuis Antwerpen Laboratorium, Edegem
17. AZ Klina Laboratorium, Brasschaat
18. CHU de Liège, Liège
19. AZ Sint Lukas, Gent
20. ZNA Klinisch Laboratorium Campus Middelheim, Antwerp
21. Cliniques Universitaires Saint-Luc, Brussels
22. National reference center, Belgium
23. WIV-ISP, Epidemiology of infectious diseases, Brussels

Background
The knowledge of circulating HCV genotypes and subtypes in a country is crucial to guide antiviral therapy and to understand local epidemiology. Studies investigating circulating HCV genotypes have been conducted in Belgium. However they are outdated or lack a nationwide representativity, because they were not conducted in the general population.

Methods
In order to determine the prevalence of different circulating HCV genotypes in Belgium we conducted a multicentre study with all the 19 Belgian laboratories performing reimbursed HCV genotyping assays. Available genotype and subtype data were collected for the period from 2008 till 2015. Furthermore, a limited number of other variables were collected: some demographic characteristics
from the patients and laboratory technique used for the determination of the HCV genotype.

Results
For the study period, 11,211 unique records collected by the participating laboratories were used for further investigation. HCV genotype 1 was the most prevalent (53.7%) genotype in Belgium. Genotype 3 was the next most prevalent (21.9%). Further, genotype 4, 2, and 5 are responsible for respectively 16.0%, 6.2%, and 1.9% of HCV infections. Genotype 6 comprises the remaining <1%. Throughout the years, a stable distribution was observed for most genotypes. Only for genotype 5 a decrease in function of the year of analysis was observed, with respectively 3.5% for 2008, 2.2% for 2009 and 1.5% for the remaining years. The overall M:F ratio was 1.59 and was mainly driven by the high M:F ratio of 3.03 for patients infected with genotype 3. Patients infected with genotype 3 are also younger (mean age 41.7 years) than patients infected with other genotypes (mean age above 50 years for all genotypes). The patients for whom a genotyping assay were performed in 2008 were significantly younger than those from 2015. Geographical distribution demonstrates that HCV patients live not only in the big Belgian cities.

Conclusions
This national monitoring study allowed a clear and objective view of the circulating HCV genotypes in Belgium and will help health authorities in the establishment of cost effectiveness determinations before implementation of new treatment strategies. This baseline characterization of the circulating genotypes is indispensable for a continuous surveillance, especially for the investigation of the impact of migration from endemic regions.
EPIDEMIOLOGY OF ENTEROCOCCI ISOLATED FROM AN INFECTION IN BELGIUM

K. Loens, M. Leven, E. Yusuf and H. Goossens

Background

*E. faecalis* and *E. faecium* are common gastrointestinal commensal organisms acquiring resistance through the transfer of plasmids and transposons and recombination or mutation events. Infection with vancomycin-resistant enterococci (VRE) is a growing problem. The Belgian National Reference Centre (NRC) for enterococci received since 2012 an increasing number of enterococcal strains (mainly VRE) from all over Belgium. The aim of this study is to report the epidemiology of enterococci isolated from infections/invasive sites in Belgium on strains received from hospital laboratories between 01/01/2011 and 31/10/2016.

Methods

Species identification was confirmed by conventional diagnostics, by MaldiTOF Mass Spectrometry and by sod/ddl/16S rDNA-PCR and sequencing. Antibiotic susceptibility was determined by using disk diffusion and E-test and interpretation according to CLSI (up to 2012) and EUCAST from (from 2012 onwards). The following antibiotics were tested: ampicillin, vancomycin, teicoplanin, linezolid) and tigecycline. PCR targeting vanA and vanB genes was applied to confirm VRE.

Results

The number of enterococcal strains isolated from infections was steadily increased during the study period: n=59, 102, 152, 192, 275 and 207 in 2011, 2012, 2013, 2014, 2015 and 2016, respectively. The VRE% ranged between 40.8 and 75.5 of which vanA increased from 45.5% to 91.4% in the same period. The number of isolates increased from 20 to 79, from 13 to 94, from 5 to 34 and from 3 to 10 for resp. isolates from blood (B), urine (U), wound infections and peritoneal fluids. Table 1 shows the proportions of VSE and VRE per species for blood and urine isolates.

Conclusions

In the last 6 years, the NRC received an ever increasing number enterococci isolated from an infection. The highest increase was found to be caused by vanA positive *E. faecium* isolated from urine. Yet, since Belgian laboratories for clinical microbiology are not legally bound to submit their VRE strains to the NRC one should be cautious about the interpretation.
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</tr>
<tr>
<td>U. E. faecalis VSE</td>
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<td>0</td>
<td>22</td>
<td>20</td>
<td>3</td>
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</tr>
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Background
The Belgian National Reference Centre for toxigenic Corynebacteria confirms the identification of Corynebacterium diphtheriae, Corynebacterium ulcerans and Corynebacterium pseudotuberculosis, and determines their toxigenicity. In 2016, fifteen cases of Corynebacterium infections were confirmed, thirteen of which in human patients (the other two were cases of C. ulcerans in canine skin lesions). Five cases of toxigenic C. ulcerans were found in human patients. Three were found in foot ulcers, one in the throat of an immunocompromised 67-year-old patient presenting with respiratory diphtheria, and one in the throat of an asymptomatic carrier.

Six C. diphtheriae strains were found, only one of which was toxigenic. The strain in question was isolated from the throat of a three-year-old, unvaccinated patient from Chechen origin with severe respiratory diphtheria. Diphtheria antitoxin (DAT) was not available in Belgium at the time of diagnosis, but was supplied from RIVM and administered to the patient seven days after disease onset. Even so, the patient developed cardiac complications and died the next day. This case highlights the great importance of acquiring and maintaining a national stock of DAT, and of upholding a good vaccination policy.

Besides C. ulcerans and C. diphtheriae, two cases of C. pseudotuberculosis were found in 2016. No others had previously been confirmed by the NRC. Both strains were non-toxigenic.

The NRC collects additional data on all confirmed cases. From this we could find that the probable country of infection was usually Belgium (seven out of thirteen cases, the other six were unknown). Vaccination status was, unfortunately, usually unknown.

The NRC also collects and preserves all strains, and performs further typing. Susceptibility testing was performed for penicillin, erythromycin, clindamycin and rifampicin. Multi-locus sequence typing (MLST) was performed as well and all types were submitted to the PubMLST database (https://pubmlst.org/).

In total, six toxigenic Corynebacterium strains isolated in human patients were confirmed in 2016, twice as much as in 2015. Before that, the NRC had only found three toxigenic C. ulcerans strains in total (in humans), one in 2013, one in 2012, and one in 2010. It seems therefore that toxigenic Corynebacteria are on the rise in Belgium, however, it is difficult to say whether this effect is due to an actual rise in number of infections, or whether it is just diagnosed more frequently due to improved techniques and higher awareness.
MOLECULAR EPIDEMIOLOGY OF LEGIONELLA PNEUMOPHILA IN BELGIUM FROM 2011 TO 2016


a. Department of Microbiology, National Reference Centre for Legionella pneumophila, Hôpital Erasme, Université Libre de Bruxelles, Route de Lennik 808, 1070 Brussels, Belgium.
b. Vrije Universiteit Brussel (VUB), Universitair Ziekenhuis Brussel (UZ Brussel), Department of Microbiology and infection control, National Reference Centre for Legionella pneumophila, Laarbeeklaan 101, 1090 Brussels, Belgium.

Background

*Legionella pneumophila* (*L. pneumophila*) is the etiological agent of legionnaires’ disease (severe pneumonia) and Pontiac fever. This microorganism can be found in natural aquatic environment as well as in artificial water systems. Infection occurs mainly through inhalation of contaminated aerosols. To discriminate between *L. pneumophila* strains, Sequence Based Typing (SBT) has been widely used as typing method. In this study, we have investigated by SBT clinical and environmental isolates of *L. pneumophila* collected between 2011 and 2016 in the Belgian National Reference Centre.

Material/methods

*L. pneumophila* isolates of respiratory samples (n=112) and related environmental samples (n=8) recovered in Belgium between 2011 and 2016 were genotyped using the internationally standardised SBT protocol of the European Working Group for Legionella Infections (EWGLI). The eBURST algorithm v3 was applied using a less stringent definition [sequence types (STs) were included in the same group if they share at least five of seven SBT loci].

Results

Clinical isolates of *L. pneumophila* serogroupe 1 (Sg1) (n=107, 95.5%) could be classified into 39 STs (Simpson’s index of diversity: 0.908). The most frequent STs were ST1 (24.3%) and ST47 (19.6%). The other serogroups (n=5, 4.5%) were represented by 5 distinct STs. Among all serogroups, five STs, ST1214, ST1220, ST1387, ST1735, ST2213, were newly characterised. The eBURST analysis showed that *L. pneumophila* Sg1 isolates from Belgium were distributed into six clonal complexes (CCs) and five singletons. The main lineages were CC1 (n=45, 44.1%) and CC932 (n=27, 26.5%). The SBT-typing of clinical and environmental samples confirmed the infection source for five cases and excluded one case. However, two cases were linked to the less discriminatory ST1 and remained inconclusive.

Conclusions

This study shows that currently ST1 and ST47, belonging respectively to CC1 and CC932, are the most frequent STs in Belgium, confirming previous epidemiological observations for the period 2000-2010 [Vekens et al. *Euro Surveill.* 2012,
and in agreement with the epidemiology in northwest Europe. The SBT analysis of recent *L. pneumophila* isolates has updated the Belgian database and has been useful to confirm the link between clinical and environmental samples.
SURVEILLANCE OF INFLUENZA IN BELGIUM DURING THE WINTER SEASON 2016-2017

Isabelle Thomas¹, Cyril Barbezange¹, Nathalie Bossuyt², Viviane Van Casteren², Steven Van Gucht¹ and the Belgian Network of sentinel GPs

¹. Scientific Institute of Public Health, Operational Directorate of Communicable and Infectious Diseases, Viral Diseases, Brussels, Belgium
². Scientific Institute of Public Health, Operational Directorate of Public Health and Surveillance, Brussels, Belgium

Background

Each year, during the winter season, an influenza epidemic occurs. The severity of the epidemics varies depending on the type and subtype of the circulating influenza virus and the degree of vulnerability of the population to the virus. Influenza surveillance is therefore a process that must be repeated every year. We present here the results of the season 2016-2017.

Material and methods

In Belgium, the influenza surveillance is performed by the National Influenza Centre and the Unit of Epidemiology of Infectious Diseases of the Scientific Institute of Public Health in Brussels. A network of sentinel general practitioners (SGPs) has been involved since 2007 in the clinical and virological influenza surveillance. The main purposes of the surveillance are the early detection of an influenza epidemic, the study of the intensity and duration of the epidemic, the identification and characterization of circulating viruses and the participation to the selection of next-season influenza vaccine strains by WHO. In addition, the development of capability to detect new emerging viruses, the estimation of vaccine effectiveness and the monitoring of the antiviral susceptibility are also important tasks.

Results

The Influenza activity started quite early during the 2016-2017 winter season (in week 2-2017) and lasted for 7 weeks. The epidemic was of medium intensity. The peak was observed in week 5-2017, with an incidence of 745 consultations for influenza-like syndromes per 100,000 inhabitants. After week 6-2016, the number of influenza-like syndromes fell and dropped below the threshold in week 9-2017. The severity of the epidemic was moderate. In the first 7 weeks of 2017 (02/01/2017 – a significant excess mortality in the Belgian population aged 65 years and older was observed, most notably in the age group 85 years and older. However, the preliminary results of the sentinel surveillance of severe acute respiratory infections show that although the number of hospitalizations due to a severe acute respiratory infection was high, the fraction of hospitalized flu patients that had severe complications or died during the hospitalization was comparable to mildest of the previous seasons. It is likely that the excess mortality in January 2017 was not only...
driven by the flu epidemic but also by other factors (e.g. cold weather and air pollution peaks) in that period.
From week 40-2016 to week 12-2017, 634 respiratory samples were sent by the sentinel GPs network and analysed at the National Influenza Centre. Among these samples, 332 (52.4%) were positive for influenza with 331 (52.3%) positive for influenza A and 1 (0.2%) positive for influenza B. Among the influenza A samples that were subtyped, 97% (322/331) were A(H3N2), 0.9% (3/331) were A(H1N1)pdm2009 and 6 samples (1.8%) could not be subtyped due to their low viral load. Only one influenza B virus was detected in the sentinel surveillance of IILI and belonged to the Yamagata lineage. Sequencing of a subset of the different viruses has shown that the strains belonged to groups that were close to the corresponding vaccine strains. Few A(H1N1) pdm2009 were sequenced and belonged to group 6B.1, represented by the reference strain A/Michigan/45/2015. These viruses are antigenically homologous and similar to the vaccine strain A/California/7/2009. The majority of the A(H3N2) strains belonged to the newly emerging subclade 3C.2a1, represented by the reference strain A/Bolzano/7/2016 which is antigenically close to the vaccine strain A/Hong Kong/4801/2014. Independently of this surveillance, three influenza B viruses from the Yamagata lineage which were genetically characterized belonged to clade 3 represented by the vaccine strain B/Phuket/3073/2013 present in the quadrivalent vaccine. Only one influenza B viruses from the Victoria lineage was detected during this season and belonged to clade 1A, the B/Brisbane/60/2008 clade which is present in the trivalent vaccine.

**Conclusion**
The 2016-2017 influenza epidemics was characterized by an early start, short duration, moderate intensity and severity and the predominance of A(H3N2). As observed in other countries, a new subclade has emerged: the 3C.2a1 but which still remains antigenically similar to the vaccine strain A/California/7/2017.
Background
Knowing that cervical cancer is the third most common cancer in women worldwide and following WHO recommendations that each country should have a HPV reference laboratory, Belgium set-up the National Reference Centre for Human Papillomavirus (NRC HPV) in 2016. The NRC HPV consists of a consortium between WIV-ISP (Brussels), AML (Antwerp) and the University Hospital Ghent (UZ Gent). The NRC HPV aims to organize a structured surveillance system for HPV, including a follow up of HPV genotypes in vaccinated versus non-vaccinated cohorts (women < 30 years old), confirmation testing on all histologically confirmed cervical cancer cases, on specific HPV-related cancer cases (head-and-neck tumours, anal dysplasia and cancer) and on 10% of the CIN3 cases. When HPV negative cancers are found (after negative confirmation exploiting three different HPV assays), samples are subjected to next-generation whole genome sequencing. With the introduction of the HPV test, self-sampling became a valid option to reach out towards formerly non-attenders. Identification of the optimal methods for processing such self-samplers are currently not readily validated or available. Therefore, this consortium will has developed standard operating procedures for processing of self-sampling devices on different (commercial) test systems. The procedures will be published shortly.

In 2016, 1200 samples were analysed for the follow up of HPV genotypes in vaccinated versus non-vaccinated women < 30 years old. Statistical analysis is ongoing. Different devices of self-samplers (Evalyn and Qvintip) have been tested and the standard operating procedures for processing have been evaluated. The concordance of different HPV assays in self-samplers has also been measured. In 2017-2018, a HPV ring test will be initiated and evaluated for Belgian clinical laboratories.
Background

Rabies is an invariable fatal infectious disease caused by the rabies virus. Annually, millions of people are exposed to the virus, mainly in developing countries, and 59000 die because of the disease. Most mammals are susceptible to the virus, but most infections occur after close contact (bite, scratch, lick) with an infected carnivore (mainly dog) or bat. Belgium has been free from the classical rabies virus (a species within the Genus *Lyssavirus*) since 2001. Our surveillance system aims to guarantee the rabies-free status of Belgium.

The National Reference Center/Laboratory (NRC/NRL) performs serology testing for humans and animals to evaluate vaccine-induced immunity. Most of the human samples are submitted to evaluate the immune response after a preventive vaccination for example for people at risk (travelers to endemic regions, veterinarians, soldiers…). Serology testing on animal samples are performed in the frame of the European regulations concerning the international movement of pets (dogs, cats and ferrets).

A small portion of the human samples are submitted to confirm the immune response after post-exposure treatment upon contact with a potentially rabid animal in a rabies-endemic region (travelers, health care workers, …). We tested a total of 5857 sera for rabies antibodies in 2016.

Besides serology testing, the NRC/NRL is also responsible for the diagnosis of rabies in clinically suspected humans or animals (both wild and domestic animals). In 2016, a total of 443 samples were submitted to our laboratory for diagnosis. One bat from Bertrix tested positive for the presence of European bat Lyssavirus-1 (EBLV-1), a virus belonging to the same genus as the classical rabies virus. This virus can cause the same disease as the classic rabies virus.

The continuous surveillance of wild and domestic animals is performed in collaboration with the Federal Agency for the Safety of the Food Chain (FAVV-AFSCA). This activity permits to guarantee the rabies-free status of Belgium, since the main threat of re-introduction of the virus is associated with the illegal importation of animals from rabies endemic countries, mainly in Africa and Asia.
SURVEILLANCE OF HEPATITIS E VIRUS INFECTION IN BELGIUM: EPIDEMIOLOGICAL TRENDS DURING THE 2010-2016 PERIOD

Vanessa Suin1, Magali Wautier1, Veronik Hutse1, Marjorie Jacques1, Mona Abady1, Sophie Lamoral1, Vera Verburgh1, Sofieke Klamer2, Bernard Brochier1, Isabelle Thomas1, Steven Van Gucht1.

1. Scientific Institute of Public Health, Operational Directorate of Communicable and Infectious Diseases, Viral Diseases, Brussels, Belgium

Background

Hepatitis E virus (HEV) is a non-enveloped, positive-stranded RNA virus with a small genome of 7200 bases. HEV is one of the most important causes of acute hepatitis in adults in developing countries. Contrary to the dogma, however, the virus is not restricted to developing countries, and sporadic cases are increasingly recognized in Europe, as awareness of the potential for infection spreads and tests for the virus are performed. HEV infection causes an acute self-limited or fulminate hepatitis that does not evolve into chronicity, except in organ transplant recipients or immune depressive patients. In developing countries, the mortality rate is low (1-3%), but in pregnant women the mortality can be high as 25%.

There are more and more indications that HEV might also be an emerging food-borne infection in Western countries. From its discovery in 1983, documented HEV transmission was linked almost exclusively to contaminated water; that association changed abruptly with the discovery of HEV infection following ingestion of raw or insufficiently cooked deer, wild boar, pork meat or shellfish. Moreover, HEV transmission by blood transfusion has also been described. The seroprevalence in blood donors from non-endemic countries ranges from 2 to 73 %. HEV RNA has also been detected in healthy populations from many European and non-European countries. More recent evidence suggest that HEV could be a viral zoonosis with the pig as an animal reservoir. In the USA, a higher prevalence has been seen in persons working with swine.

The epidemiology of HEV in Belgium is far from understood, and the zoonotic aspects, in particular, require further study. In 2010, a National Reference Centre (NRC) for Hepatitis Viruses B, C, D and E was officially recognized at the Scientific Institute of Public Health. Each year, the NRC receives an increasing number of clinical samples for laboratory diagnosis of HEV. From 2010 to 2016, we have received 313, 477, 592, 695, 1072, 1453 and 1941 suspected samples of which 25, 34, 29, 31, 36, 65 and 86 were laboratory-confirmed (IgM+ and/or RNA+). Genotypes 3c and 3f were most dominated in the Belgian population between 2010 and 2016.
**RECENT TRENDS IN ARBOVIROSES DIAGNOSED IN BELGIUM**

Yolien Van der Beken¹, Dorien Van den Bossche¹, Lieselotte Cnops¹, Marjan Van Esbroeck¹

¹. Institute of Tropical Medicine Antwerp

**Introduction**

Arboviruses like dengue (DENV), chikungunya (CHIKV) and Zika virus (ZIKV) have caused significant public health problems, due to their expanding distribution. In the scope of its function as National Reference Center (NRC) the Institute of Tropical Medicine offers a panel of diagnostic tests for these viruses.

**Aim**

The aim of this study is to look into the number of tests performed, the number of infections imported in Belgium and trends that have been set due to specific outbreaks during the past few years.

**Results**

In the beginning of the symptomatic phase viral RNA can be detected by real-time RT-PCR. A rapid diagnostic test (RDT) detecting DENV antigen is a helpful tool in this phase. Detection of IgM and IgG antibodies by ELISA or Indirect Immunofluorescence assay (IFA) is useful as from 5-7 days after symptoms appear. Virus neutralization tests are available in case confirmation is needed.

The emergence of arboviruses worldwide has resulted in an increase of tests performed. A fivefold increase in PCR analyses and an increase with 60% of serological analyses for DENV has been observed over the past 5 years.

Due to the ZIKV epidemic that started at the end of 2015, a total of 2452 ZIKV serological screening tests and 720 RT-PCR’s was executed in 2016. The same increasing trend was observed for CHIKV diagnostics in 2014 after the virus was introduced in the Americas.

A total of 117 DENV infections was diagnosed in 2016. This is in line with previous years. Remarkably, the number of ZIKV infections diagnosed in 2016 (n=130) exceeded that of DENV infections. This might be explained by the high number of tests performed, a consequence of the concern for the ZIKV congenital syndrome and the possible neurological complications of a ZIKV infection. The CHIKV outbreak in 2014 in the Caribbean islands was reflected by a 10 time increase in the number of diagnoses compared to 2013. Tick borne and Japanese encephalitis infections are rarely diagnosed.

**Conclusion**

The incidence of imported arboviral infections in Belgium fluctuates substantially and reflects outbreaks in (sub)tropical areas. The emergence of arboviral infections leads to the development of new diagnostic tests with a better performance in attendance of anti-viral drugs and vaccines to be developed.
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