ABSTRACT BOOK

16th EMGM Congress

European Meningococcal and Haemophilus Disease Society

29 May to 1 June 2023 I Dubrovnik, Croatia

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CONTENTS

MAY 29, 2023

Clinical Aspects Posters, 09:30 - 10:50

Moderators: Anna Skoczyńska; Paula Kriz

OC 19 - First study on the Invasive Meningococcal Disease (IMD) outcomes in Greece (2010-2020)

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Background

Invasive meningococcal disease (IMD) is a major cause of meningitis and/or septicemia, has a severe acute and long-term burden and sequelae among survivors. Comprehensive consideration of these factors (e.g., underreported sequelae, multiple sequelae, burden beyond the patient) is important when assessing IMD burden and potential interventions to reduce it with vaccination programs.

Aims: Scarce evidence and underreporting of sequelae worldwide is challenging, although useful for potential interventions to reduce IMD, this is the first attempt aiming to analyze data on the outcomes in Greece during 2010-202 .

Materials and methods

Medical records from children 0-15 years of age from 5 major paediatric hospitals in Greece suffered from IMD were retrospectively collected and analyzed.

Results

During the study period (2010-2020) among 266 patients with signs and symptoms of meningitis or/and septicemia, Neisseria meningitidis (NM) was confirmed in 123 according to the Greek National Meningitis Reference Laboratory records. Among those, the medical records of 63 (51.2%) children were retrieved. The children's age ranged from 22 days to 15 years old (median=36 months). Diagnosis was meningitis (46%;29/63), meningitis and septicemia (38%; 23/63) and septicemia (16%;10/63). The Hospital time admission for 62 eligible children (one transferred and lost to follow up) was 1-44 days (median=9 days), 23 (37%) patients were admitted in the ICU for 1-11 days (median=3 days); 11.3% (7/62) required intubation.

On discharge, 6.45% (4/62) of the patients suffered gangrenous skin and soft tissue complications. Among those, pelvic ulcers, gangrenous lesion in the left wrist were observed for one each while 2 patients suffered from ulcer lesions in the lower limbs and were subjected to amputation. With regards to neurological conditions, 6.45% (4/62) suffered as mild

walking imbalance (1/4), strabismus, dorsal imbalance, head, speech and movement difficulties (discharged with antiepileptic treatment) (1/4)) walking imbalance and abducens nerve palsy (1/4), suffered seizures and discharged on antiepileptic medication (1/4). Further, among the 11 patients underwent audiograms, one (1,6%) showed abnormal audiogram attributed to middle ear effusion. Three fatal cases were reported.

Conclusion

During the study period, 14.5% (9/62) of the IMD patients suffered complications while the case fatality rate was 4.8%. This comes to an agreement to 10-20% complication rate along with 8% case fatality rate reported in the few published studies. As this is the first attempt in Greece, in order to eliminate missing data and to better understand the burden of IMD electronic files are imperative.

OC 59 - Invasive Meningococcal disease: consequences, disability, sequelae

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Background

Invasive Meningococcal disease (IMD) is a severe infection that can cause serious sequelae. Recent publications provide valuable estimates of the frequency of the sequelae, their impact on quality of life and their financial cost.

Aim/Methods

This review aims to consolidate this current knowledge on outcomes and potential long-term consequences of IMD. A literature review on Neisseria meningitidis, IMD, sequelae, quality of life and cost in survivors of all ages and their caregivers, including family, was conducted.

Results

The risk of having at least one sequela for IMD survivors is estimated between 19% and 43% [1-4]. Long-term sequelae in survivors include somatic, neurological, and psychological consequences, such as hearing loss, amputations, skin scarring and neurodevelopmental deficits [1-5]. Somatic and neurological sequelae are likely to be reported because they are often rapidly apparent compared to psychological or behavioural sequelae, which may take longer to develop [3,5]. The category of sequelae also varies according to patient age. Beyond the impact on patients, the consequences of an IMD also affect their families, with lower quality of life scores and risk of high psychological distress at hospital discharge [6]. Sequelae also represent a significant financial cost to the health care system and to families. For instance, in France, the cost of hospitalisation is estimated between 14,469€ and 15,151€ for patients with sequelae compared to 5365€ and 9393€ for patients without sequelae [2,7].

Conclusion

The results of the review show that a solid knowledge base on sequelae is now available. These data should be systematically used by policy makers when considering IMD-specific intervention measures, especially when new meningococcal vaccines become available. It should generate additional opportunities to improve the quality of life of patients and their family after IMD, saving health resources for other needs.

OC 61 - Clinical diagnoses and outcomes of patients with meningococcal disease in Taiwan

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Introduction & Aims

Invasive meningococcal disease (IMD) was a category III notifiable disease in Taiwan. The incidence of IMD was low in Taiwan (It was estimated 4 to 5 cases each year). It was underestimated because of only the culture proved cases were enrolled. We collected the meningococcal cases treated in a medical center to verify the need of re-establishing the criteria of IMD in Taiwan.

Materials and Methods

Cases of laboratory confirmed meningococcal diseases (MD) were defined either by culture, gram stain, meningococcal antigen test or PCR.

Results

A total of 11 MD cases were collected during 2001 to 2022. Three cases were younger than 1 year-old (2 bacteremia, and one septic shock and expired); 3 cases were age 6~7 year-old (One meningitis and 2 contact colonization); one teenage boy got fulminant purpura and needed multiple skin debridement and graft; 2 young adults presented with meningitis and one young adult had pansinusitis (AIDS patient); and one elder women got meningitis the same time with her young adult friend. There were 9 meningococcal culture proved, one was cerebral spinal fluid (CSF) gram stain positive and the other one was CSF meningococcal antigen positive. There were 7 serotype B and 2 serotype Y and 1 serotype X.

Conclusion

There were 11 documented MD cases during the past 2 decades. We believed that it was under-estimated because most of IMD patients were sent to this tertiary hospital after initiating broad spectrum antimicrobial agents. The inadequate microbiological investigating method in clinical practice and the inclusion criteria of IMD in Taiwan, also contributed the lower than expected incidence in Taiwan.

OC 13 - Adherence to vaccination guidelines of splenectomised patients in Norway

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Background

The spleen is a large lymphoid organ that is responsible for the regulation of immune responses and blood filtration. Absence of the spleen (asplenia) can be congenital or acquired when the spleen is removed surgically. People without a spleen are at increased susceptibility to severe invasive infections caused by the encapsulated bacteria, Streptococcus pneumoniae, Neisseria meningitidis and Haemophilus influenzae type b (Hib). To protect splenectomised people against these bacterial infections, vaccinations are recommended. This study aimed to evaluate the vaccination coverage (VC) of splenectomised patients in Norway following the advised vaccination protocol from the Norwegian Institute of Public Health (https://www.fhi.no/nettpub/vaksinasjonsveilederen-for-helsepersonell/vaksinasjon-ved-sykdom/vaksinasjon-og-manglende-miltfunksjon/).

Methods

We performed a registry-based retrospective study, calculating VC and infection rate of invasive infections in splenectomised patients registered in Norway from 2008 to 2020. Patient data (age, sex, and date for splenectomy) were obtained from the Norwegian Patient Registry (NPR) together with the Nomesco Classification of Surgical Procedures codes. Vaccination status of the splenectomised patients was provided by the National Immunization Registry and records of bacterial infection were extracted from the Norwegian Surveillance System for Communicable Diseases.

Results

From the total population of Norway (5,379 million in 2020), 3,155 patients had undergone complete splenectomy. Of these asplenic patients, 914 (29.0%) had received at least one dose of pneumococcal conjugate vaccine, 1324 (42.0%) at least one dose of pneumococcal polysaccharide vaccine and 589 (18.7%) had received both. Only 4.2% of the patients had received two doses of a meningococcal ACWY conjugate vaccine, while 8.0% of 1467 patients splenectomised after 2014 had received at least two doses of serogroup B meningococcal vaccine. An average of 18.7% of the patient group had received Hib-vaccine. Nearly all splenectomised children under the age of 10 were vaccinated with Hib- and pneumococcal conjugate vaccine as these vaccines are included in the childhood immunisation program. For all vaccines, vaccination coverage decreased with age. Twenty-eight invasive bacterial infections were registered in 25 asplenic patients. There was one case of meningococcal meningitis (serogroup Y), one case of H. influenzae (serotype unknown) and 23 patients with pneumococcal infections (one patient twice and one patient three times). Vaccination according to national recommendations could possibly have prevented 11 (39%) infections in the patient group in the study period.

Conclusion

Although recording of vaccination might have been somewhat suboptimal in the time period, our study showed that efforts are required to increase the vaccination coverage of splenectomised individuals in Norway.

Surveillance and Strain characterisation 1, 11:15 - 12:55

Moderators: David Litt; Martin Maiden

OC 3 - Persistent increase in invasive Haemophilus influenzae serotype a (Hia) disease: prospective national surveillance, 2008/09 to 2021/22, England

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Background

Invasive H. influenzae serotype a disease is rare, with most cases reported among indigenous populations in North America. In England, national surveillance was enhanced following an increase in laboratory-confirmed invasive Hia disease since 2016/2017.

Aim/Methods

Hospital laboratories in England routinely submit invasive H. influenzae isolates to the UK Health Security Agency for confirmation and serotyping. General practitioners and clinicians were contacted to complete a clinical questionnaire for all confirmed Hia cases since 2008/2009. Multilocus sequence typing (MLST) and whole genome SNP and kmer-based analysis of bacterial isolates was performed following Illumina whole genome sequencing (WGS).

Results

There were 0-2 annual Hia cases (accounting for <2% of serotyped H. influenzae isolates) until 2015/16, after which cases increased, with a small decline during pandemic restrictions in 2020/21, to 19 cases affecting all age groups across England in 2021/22 (incidence, 0.03/100,000), when Hia accounted for 3.9% (19/484) of all serotyped H. influenzae isolates and 19.0% (19/100) of capsulated cases. Most of the recent increase in cases occurred among ≥65-year-olds, who typically presented with bacteraemic pneumonia, while infants aged <1 year had the highest incidence (0.33/100,000) and were more likely to present with meningitis. Overall case fatality rate was 7.7% (4/52). WGS found that closely related MLST sequence types (ST) 1511 (40%), ST23 (24%) and ST56 (and 14%) accounted for most cases, with no evidence of capsule switching from Hib strains. Duplication of the capsule operon, which has been associated with more

severe disease, was present in these STs. Genomic kmer analysis grouped most strains into a single PopPUNK clone. There was no association between Hia ST and clinical outcomes.

Conclusion

The persistent increase in invasive Hia cases across England and across all age-groups suggests widespread transmission, consistent with reports from other European countries, and will require close monitoring.

OC 14 - An Evaluation of Genotypic Diversity in Contemporary Invasive MenB Isolates

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Background

Neisseria meningitidis is an important cause of invasive meningococcal disease (IMD) and mortality worldwide. The distribution of the most prevalent disease-causing serogroups (A, B, C, W, and Y) can vary by geography and over time. Factor H binding protein (fHbp), a key meningococcal virulence factor, is an antigen included in both vaccines currently licensed to prevent meningococcal serogroup B (MenB) disease. The fHbp family of proteins includes >1000 sequence variants that can be grouped into 2 subfamilies, designated A and B. To maximize the breadth of functional immune response, Pfizer's MenB vaccine, Trumenba®, contains 2 lipidated fHbp antigens, one from each subfamily.

Aims

To compare the genotype of IMD-causing MenB strains from a contemporary period (2007-2021) to a strain collection from 2000-2006, with a focus on clonal complex and MenB vaccine antigen profiles.

Materials and Methods

The genome sequence of 13,799 IMD-causing, globally sourced strains posted on PubMLST on 25 March 2022 was accessed (serogroups A, B, C, W, X, Y). The genotype of the contemporary MenB subset of this collection of strains from 2007-2021 (n=5659) has been compared with MenB strains from a Pfizer prevalence-based collection of strains from the United States and 6 European countries from 2000-2006 (n=1814) that were used to support Trumenba licensure.

Results

All IMD-causing MenB strains in the contemporary PubMLST collection carried full-length genes capable of expressing functional fHbp and porin A (PorA), and nearly all carried Neisseria heparin-binding antigen (NHBA), whereas ~80% were "null" at the Neisseria adhesin A (NadA) locus. MenB genotypes were largely comparable regarding the representation of the most prevalent MLST/clonal complexes, fHbp subfamily distribution, and fHbp and PorA variant types between the two collections. Minor differences included a subset of fHbp variants in the global 2007-2021 collection that were not represented in the Pfizer 2000-2006 collection. NHBA and NadA data were unavailable for the 2000-2006 collection.

Conclusions

The similar genotypes, distribution, and diversity of fHbp variant types detected among the contemporary strains further support the breadth of coverage provided by Trumenba against the diversity of MenB strains by targeting both subfamilies of FHbp.

Funded by Pfizer Inc

OC 30 - Rare serotype c Haemophilus influenzae invasive isolate: characterization of the first case, in Portugal

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Background

Haemophilus influenzae serotype c has rarely been described worldwide, with few available genomes on the PubMLST website1. In the era of a conjugate Hib vaccine, invasive non b-serotypes may be of clinical concern.

Aim/Methods

In the course of laboratory-based surveillance of invasive H. influenzae disease, we identified a serotype c isolate for the first time in Portugal. Our aim is to characterize this isolate and describe the clinical case.

A 56-year-old male, born in São Tomé and Príncipe, unvaccinated for Hib, followed at the Infectious Diseases outpatient clinic for HIV-1 infection with concomitant disseminated Kaposi sarcoma (KS) with lung involvement under doxorrubicin treatment presented to the Emergency Department after three days of fever, productive cough and pleurytic pain. Blood cultures were obtained and empiric therapy with ceftriaxone and azithromycin was started.

Gram staining revealed Gram-negative coccobacilli in blood cultures that were identified with MALDI-TOF (Bruker) and serotyped by conventional PCR, as previously described2.

Antibiotic susceptibility testing was determined according to EUCAST guidelines3. Whole-genome sequencing (WGS) (MiSeq, Illumina) was performed for further characterization and typing of the isolate. After genome assembly (INNUca pipeline4), a core-SNP-based phylogenetic analysis was conducted using parsnps5, including all Hic genomes available at PubMLST1.

Results

Sepsis was assumed of probable respiratory focus with elevated inflammatory markers and thoracic CT scan showing diffuse opacities compatible with the previously known lung involvement from KS.

H. influenzae was identified in the blood cultures. The isolate was characterized as Hic and was susceptible to ampicillin, cefotaxime and azithromycin.

WGS confirmed serotyping results and showed that the isolate belongs to the clonal complex ST-7. Integration of the novel genome with other Hic genomes retrieved from PubMLST (n=12) revealed that it was genetically distinct, being the closest related isolate one collected in France, in 2020, presenting >100 SNPs differences.

Clinically, the patient showed continuous improvement and antibiotic therapy was de-escalated to ampicillin, having underwent a total of 25 days of effective antibiotic therapy before being discharged.

Conclusion

The importance of continuous surveillance of invasive H. influenzae disease is highlighted by this example of a close collaboration between hospitals, its clinicians and pathologists, and reference laboratories that allowed the characterization of a rare serotype, which may reflect the emergence of non-b strains causing invasive disease.

OC 43 - The expansion of a group B invasive meningococcal ST-485 (ST-41/44 clonal complex) strain in England: 2010-2022

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Introduction

Serogroup B has been the predominant disease-causing meningococcal serogroup in England and across Europe since the turn of the century. Throughout this period, the ST-41/44 clonal complex (cc) been one of the major hypervirulent group B lineages and strains of this cc were used in the development of the protein-based MenB vaccines licenced today.

Aims

Here we describe the changes in sequence type distribution among group B strains in recent years in England with a focus on the expansion of ST-485 (cc41/44). We also describe a 2022 community IMD outbreak caused by an ST-485 strain in England, as well as the subsequent public health response.

Materials and Methods

Draft genomes for isolates were submitted to the PubMLST Neisseria database. Subtyping of PCR-only strains was performed using PCR and Sanger sequencing directly from clinical specimens.

The local UKHSA Health Protection Team coordinated the public health response to the described outbreak with support from national UKHSA colleagues and local representatives.

Results

Between 2010 and 2022, the proportion of cc41/44 strains belonging to ST-485 has increased substantially. In 2022, ST-485 was the predominant ST among all invasive group B isolates in England. Over 90% of ST-485 strains had the subtype P1.12-1,16,37-1.

Strain coverage of 4CMenB and MenB-fHbp vaccines remains high among ST-485 strains due to Factor H-Binding Protein (fHbp) peptide 4 predominance, with good cross-reactivity to both vaccines. Additionally, Neisserial Heparin Binding Antigen (NHBA) peptide 2, the exact variant in 4CMenB, was the most common among these strains.

In April/May 2022, three group B cases in young adults with no epidemiological links were confirmed in a small town in England. An epidemiological link to a fourth case in a neighbouring town was subsequently reported. All four strains had subtype P1.12-1,16,37-1. Isolates obtained for two cases belonged to ST-485 and were genetically almost identical with only a single core gene difference. In response, two doses of 4CMenB was offered to all young adults living within the local area. Approximately 46% and 35% of the target population received one and two vaccine doses, respectively. No additional cases were identified.

Conclusion

These data illustrate the dynamic and changing nature of group B meningococcal epidemiology. ST-485 strains have expanded in England in recent years and have caused community outbreaks. Monitoring of these strains is ongoing.

OC 34 - Interlaboratory quality study among laboratories members of the EMGM

Eva Hong, Muhamed-Kheir Taha

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Eva Hong and Muhamed-Kheir Taha Institut Pasteur, Paris, France.

On behalf of the EMGM participant laboratories

Introduction

This study aims at assessing the performance of the diagnosis and typing of the major pathogens (mainly Neisseria meningitidis and Haemophilus influenzae) involved in invasive bacterial infections.

Materials and Methods

An interlaboratory study was organized by the EMGM through the distribution of two culture sets: the 'Haemophilus Set" and the "Neisseria Set" with each including 4 cultured isolates, H1 to H4 and N1 to N4, and a non-Culture Set including 5 lyophilized samples, labeled NC1 to NC5 were distributed to 19 laboratories members of the EMGM network. Participant laboratories were solicited to characterize each isolate by species and group identification, as well as minimum inhibitory concentrations (MICs) of several antibiotics. For the non-culture set, the participant laboratories are solicited to characterize each sample by species and group identification.

Results

For Nm culture set, there were 15 participant laboratories. The strains MenY, MenW and MenC were correctly identified by all participants. Neisseria bergeri was correctly identified by 60% of the participant laboratories and by 93% of the participants when the identification as non-N. meningitidis or Neisseria sp. was included as acceptable.

For Hi culture set, there were 14 participant laboratories. Samples were correctly identified (mean 89%, range 50-100%). All laboratories identified the correct antibiotic susceptibility profile for all 4 isolates of the set.

For NC set, there were 16 participant laboratories. Samples containing MenB and MenW were correctly identified (NC1 and NC2 scores of 88 % each). The sample NC3 that was positive for a non-groupable Nm was identified by 56% of the participants. This score may be due to the use of ctrA as the target gene for the species identification PCR. Hi was correctly identified in both samples NC4 and NC5. The detection of Haemophilus species reached 81% and 94% in those 2 samples respectively. However, the serotypes were correctly identified by only 31% and 38% of the participants, respectively.

Conclusion

Culture and non-culture identification of atypical N. meningitidis and other Neisseria as well as non-culture serotyping of H. influenzae may need to be strengthened. It is important to continue and to support the organization of such quality studies among reference laboratories in Europe and to secure funding for this activity.

Surveillance and Strain characterisation 2, 14:00 - 15:40

Moderators: Paola Stefanelli; Suzana Bukovski

OC 22 - Laboratory surveillance of invasive meningococcal disease in Germany before, during and after the COVID-19 pandemic (2019-2022)

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Background

In Germany, invasive meningococcal disease (IMD) must be notified to the Robert Koch-Institute. Meningococcal isolates and culture-negative specimen are submitted for laboratory surveillance to the German national reference laboratory for Meningococci and Haemophilus influenzae (NRZMHi) on a voluntary basis.

The emergence of SARS-CoV-2 in spring 2020 led to containment measures which resulted in a decrease of invasive diseases caused by respiratory-associated bacteria.

Aim

To report the epidemiology of IMD in Germany 2019-2022.

Materials and Methods:

We analysed data of the reference laboratory according to age, serogroup, antimicrobial susceptibility, finetype and whole genome sequencing.

Results

In 2019, the epidemiology of IMD was representative for the previous years. Of 228 cases submitted to the NRZMHi 17% (n=39) occurred in adults aged 20-29 years, 13% (n=30) in 1– 4-year-olds and 11% (n=24) in 50–59-year-olds. MenB (59%) was the predominant serogroup, followed by MenC (11%), MenW (8%) and MenY (19%).

The following two years, 2020 and 2021, were dominated by the COVID-19 pandemic. The number of submissions to the NRZMHi reduced to 103 in 2020 and to 58 in 2021. Most cases occurred in infants (2020: 15% (n=16), 2021: (21%, n=12) and 1–4-year-olds (2020: 17% (n=18), 2021: (19%, n=11)). No major changes were observed among the serogroups: MenB (55%), MenC (8%), MenW (12%) and MenY (20%) in 2020, whereas MenY (3%) decreased significantly in 2021.

Not before May 2022, the numbers of IMD cases increased slowly. Finally, 125 cases were processed at the NRZMHi, of which mostly infants (20%, n=25) and 1–4-year-olds (11%, n=14) were affected, but also adolescents aged 15–19 years (15%, n=19). MenB (62%) was still at a high level and the proportion of MenY cases (22%) reached a level as before 2021. Both the proportion of MenC (5%) and MenW (6%) cases decreased.

B:P1.22,14:F5-5 cases were prevalent in all four years. In contrast, no W:P1.5,2:F1-1 cases

occurred in 2022 and no Y:P1.5-1,2-2:F5-8 cases in 2021. Based on WGS, eight genetic clusters were detected in 2019, two in 2020 and none in 2021.

No major changes in antimicrobial susceptibility were detected.

Conclusions

Whereas the epidemiology of IMD in 2019 was comparable to previous years, Germany experienced an unimaginable decline of IMD cases, not only in 2020 and 2021 but also in 2022 when most COVID-19 containment measures already had ended. Long term effects of the pandemic on IMD remain to be observed in the near future.

OC 37 - Reduction and re-emergence of invasive Haemophilus influenzae disease during the COVID-19 pandemic in Finland

Maija Toropainen, Anni Vainio, Tuija Leino

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Aims

Incidence of invasive bacterial disease has decreased worldwide during the COVID-19 pandemic (1,2). We investigated changes in invasive Haemophilus influenzae disease (IHD) in Finland in 2017-2022.

Materials and methods

Notification of IHD is mandatory in Finland and all clinical microbiology laboratories report isolations of H. influenzae or detection of bacterial specific nucleic acid from blood or cerebrospinal fluid into National Infectious Diseases Register (NIDR), a population-based electronic surveillance system maintained by the Finnish Institute for Health and Welfare (THL). H. influenzae isolates are requested to be sent to the THL's specialist microbiology laboratory, where their species is confirmed, serotype determined and, if needed, isolates are further characterized using whole genome sequencing (Illumina) and sequence analysis tools. In the present study, we analysed IHD surveillance data collected at THL from January 2017 to December 2022. Vaccination coverage of at least one dose of DTaP-IPV-Hib has remained high (98%) during pandemic, the coverage of three doses being 90%.

Results

During 2017-2019, a total of 239 laboratory-confirmed IHD cases were notified to NIDR. The annual incidence varied from 1.3 per 100,000 population (73 cases) in 2017 to 1.6 (89 cases) in 2018. The median age of patients was 68 years (range 0–99 years), and 56% were 65 years or older. Most cases (80%) were caused by non-typeable H. influenzae (NTHi), followed by Hif (12%), Hib (5%) and Hie (3%). After the introduction of COVID-19 restrictions in mid-March 2020, IHD incidence decreased markedly and remained low until June 2022. Decrease was observed in all age groups and all serotypes. Incidence rates decreased by 47% (IR 0.8, 42 cases) in 2020 and 87% (IR 0.2, 15 cases) in 2021 compared to the average incidence in the three previous pre-pandemic years 2017-2019. IHD cases increased from July 2022 onwards, and by the end of the year the annual incidence rate had returned to pre-pandemic levels (IR 1.4, 78 cases). In 2022, the median age on patients was 72 years (range 2-97), and 62% were 65 years or older. 90% of serotyped cases were caused by NTHi and the rest by Hif (7%) and Hie (3%).

Conclusion

COVID-19 control measures markedly reduced IHD incidence in Finland in 2020 and 2021. After lifting of non-pharmaceutical measures in spring 2022, the incidence of IHD quickly returned to pre-pandemic levels. No major changes in the age or serotype distribution of cases have been observed since the re-emergence of IHD.

OC 33 - Rapid rebound of invasive meningococcal disease in France at the end of 2022

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Introduction

Invasive meningococcal disease (IMD) cases declined upon the implementation of non--pharmaceutical measures to control the COVID-19 pandemic (1). A rebound of these cases was feared upon easing these measures (2).

Aims

We aimed to analyze the evolution of IMD cases before and since the COVID-19 pandemic

Materials and Methods

We conducted a retrospective cohort study using the French national Reference Centre database for meningococci between 2018-2022. We scored serogroups, sex, age groups and clonal complexes of the corresponding isolates.

Results

Our data clearly showed the decline of IMD cases for all serogroups and all age groups until 2021. This decline was mainly due to the decrease in IMD cases provoked by the hyperinvasive ST-11 clonal complex. However, since the fall of 2021, an increase in IMD cases was observed that accelerated in the second half of 2022. This rebound concerned all age groups, particularly 16-24 years of age and serogroup Y. Serogroup W cases were mainly due to the expansion of ST-9316

isolates that were first detected in France in 2013 (3). The rebound at the end of 2022 matched with an early and important peak of flu-like syndromes.

Conclusion

IMD epidemiology remains unpredictable. Surveillance of IMD requires to be enhanced using powerful molecular tools. Additionally, vaccination strategies need to be updated to acknowledge the recent epidemiological changes.

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OC 50 - Group B Clonal lineages associated with IMD in Spain before and after the COVID-19 pandemic period.

Raquel Abad[1], Marina Montes[1], Cristina García-Amil[1], Elena Martín[1], Carmen Navarro[1], Julio Vázquez[1]

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Background

The COVID-19 pandemic resulted, in 2020 and most of 2021, in the adoption of containment measures, including the mandatory use of masks. These measures had the result of reducing the circulation of the coronavirus, but also the transmission of other airborne microorganisms was affected, with generalized falls in the incidence rates of the diseases associated with them. In Spain, the incidence rate for IMD has been the lowest in the last 75 years. The aim of this study was to compare serogroup B clonal lineages associated with IMD before and after the pandemic period to check if there have been changes and which lineages have been affected.

Methods

For the pre-pandemic period we used data from 410 group B invasive meningococcal strains isolated in 2015 to 2018 period, while for post-pademic period we included 73 B strains isolated from patients and received in the National Reference Laboratory in 2021 and 2022. All the strains were analysed by WGS.

Results

In the pre-pandemic period, strains belonging to the ST213cc were predominant, reaching 35% in 2018, followed by those isolates from ST269cc (10% in 2018). Looking at the 2021-2022 period, the most prevalent clonal lineage was the ST213cc clonal lineage (38%), with those belonging to the ST162cc (8,2 %) in the second place. Those strains from the ST269cc only represented 4% in post-pandemic time.

Looking at the fHbp subfamilies distribution, before the pandemic time 65.9% of the serogroup B invasive strains harboured subfamily A, while this proportion slightly fell to 59% in the post-pandemic period.

Conclusions

No significant changes were detected in the clonal lineages of the serogroup B strains associated with IMD in Spain comparing the pre- and post-pandemic periods. There have also been no relevant changes in the distribution of the subfamilies of the fHbp antigen used in vaccine formulations.

The main change observed is a greater proportion of serogroup B strains and a significant decrease in the rest of the serogroups, mainly in 2021 and somewhat less in 2022, perhaps reflecting how those serogroups less frequent in nasopharinx were affected by the containment measures.

Finally, a comparison using gMATS to predict the potential coverage with the 4CMenB vaccine (recently included in the Spanish National Immunization Calendar), show a high proportion of isolates with unpredictable coverage in both study periods.

OC 64 - Re-emergence of invasive meningococcal disease after cessation of COVID-19 control measures in England

Helen Campbell, Stephen A. Clark, Sonia Ribeiro, Xilian Bai, Aiswarya Lekshmi, Jay Lucidarme, Ray Borrow, Shamez Ladhani

Introduction

Invasive meningococcal disease (IMD) incidence in England fell from 0.95 per 100,000 population in 2018-19 to 0.74 per 100,000 in 2019-20 after the first COVID-19 national lockdown began in March 2020 (1). IMD incidence was 75% lower (IRR 0.25, 95% CI 0.18–0.35) during April–August 2020 than during April–August 2019, with most cases caused by group B meningococci (MenB).

Aims

To review the epidemiology of IMD in England before and after COVID-19 containment measures were withdrawn in July 2021, based on academic year (running from September to August).

Materials and Methods

The UK Health Security Agency (UKHSA) conducts enhanced national IMD surveillance in England. Hospitals routinely submit invasive isolates to the UKHSA Meningococcal Reference Unit (MRU) for confirmation, grouping and whole genome sequencing. The MRU also offers free PCR testing for suspected IMD cases.

Results

IMD cases declined after the 2015 introduction of MenB infant and MenACWY teenage national immunisation programmes, from 825 cases in 2015-16 to 534 (35% reduction) in 2018-19 before the COVID-19 pandemic emerged. Case-numbers fell to 420 in 2019-20 and 79 in 2020-21. After containment measures ceased, IMD cases increased to 219 cases in 2021-22, driven mainly by MenB (194/219, 89%) particularly in 15-24 year-olds (91/194, 47%). This MenB increase has continued into the first months of 2022-23 extending across all age groups but remaining relatively low in <10 year-olds when compared to pre-pandemic figures. MenCWY cases remain very low across all ages.

Conclusion

After reaching lowest recorded levels in 2020-21, cases of IMD re-emerged in England driven almost entirely by increases in MenB disease, initially in in teenagers and young adults who have the highest carriage rates (2), and then spreading across all age groups except in young children, who remain protected through the national infant MenB immunisation programme. MenCWY disease is rare because of the direct and indirect protection offered by the teenage MenACWY vaccination programme.

MAY 30, 2023

AMR, 09:30 - 10:50

Moderators: Jay Lucidarme; Thien-Tri Lam

OC 5 - Antibiotic-resistant Neisseria meningitidis serogroup Y and revising the prophylaxis guidance in the United States

Isha Berry[1], Amy B. Rubis[1], Rebecca L. Howie[1], Shalabh Sharma[1], Daya Marasini[1], Lucy A. McNamara[1], Henju Marjuki[1], Samuel Crowe[1]

[1]Meningitis and Vaccine Preventable Diseases Branch, Centers for Disease Control and Prevention, Atlanta, United States

Introduction

Close contacts of invasive meningococcal disease patients are at increased risk for disease and are recommended to receive prompt prophylaxis with any of the first-line antibiotic choices—rifampin, ciprofloxacin, or ceftriaxone. Historically, Neisseria meningitidis (Nm) isolates in the United States (US) have largely been susceptible to these antibiotics. In 2020, the Centers for Disease Control and Prevention (CDC) identified 11 ciprofloxacin- and penicillin-resistant (dual-resistant) Nm serogroup Y (NmY) isolates from cases occurring between 2019 and 2020 and requested that jurisdictions promptly submit all NmY isolates to CDC for antimicrobial susceptibility testing (AST).

Aims

To describe the epidemiology of dual-resistant NmY cases and the development of guidance for when ciprofloxacin should no longer be routinely used as prophylaxis.

Materials and Methods

Meningococcal disease cases reported through the National Notifiable Diseases Surveillance System with isolates submitted to CDC from January 2019 to December 2022 were described. NmY isolates were tested for resistance using broth microdilution. Whole-genome sequencing was used to confirm serogroups and screen for mutations known to confer antibiotic resistance. Stakeholder interviews were conducted with federal- and state-level subject matter experts to gather input on creating a threshold for changing prophylaxis guidance.

Results

During 2019–2022, 27 dual-resistant cases were reported, 16 of which occurred since February 2020. Eight dual resistant cases were reported in each of 2019, 2020, and 2021 despite a decline in overall Nm incidence from 0.11 cases/100,000 to 0.06 cases/100,000 during that time. Of the 27 total dual-resistant cases, 77.8% [21/27] were in Hispanic individuals, the median patient age was 23 years (range: <1–97), and 3.7% [1/27] were fatal. Cases were reported in 15 states and were primarily clustered in metropolitan areas. When presented with these findings, stakeholders recommended a low threshold for changing prophylaxis guidance, but did not reach consensus on what this threshold should be. Stakeholders also highlighted the need for implementation flexibility and rapid, transparent communication about AST results. Potential challenges identified included cross-jurisdictional coordination and increased burden on providers.

Conclusion

Despite the decreasing incidence of meningococcal disease in the US, cases of dual-resistant NmY continue to occur. CDC is developing guidance for when jurisdictions should discontinue ciprofloxacin for prophylaxis of close contacts based on local detection of ciprofloxacin--resistant cases. Ongoing surveillance for antimicrobial resistance among circulating NmY strains will be important to monitor this issue and inform prophylaxis recommendations.

OC 45 - Antibiotics resistance of Neisseria meningitidis in Spain: an issue still evolving?

Raquel Abad[1], Marina Montes[1], Elena Martín[1], Carmen Navarro[1], Cristina García Amil[1], Julio Vázquez[1]

[1]Instituto De Salud Carlos III, Majadahonda, Spain

Background

Continued surveillance to follow the susceptibility to drugs used in chemoprophylaxis or treatment of meningococcal disease is extremely useful. The aims of this study is to analyse trends in antibiotic resistance in Spain in the period from 2015 to 2022. The potential mechanism of resistance in those strains with infrequent resistance was genetically studied.

METHODS. One thousand one hundred and fifty eight strains isolated from patients in the period from 2015 to 2022 were included in the study, representing around 80–85% of the confirmed cases. The antibiotics tested were Penicillin, Cefotaxime, Ceftriaxone, Ciprofloxacin and Rifampicin. The MIC was determined using agar diffusion with E-test strips and the breakpoints were those recommended by the EUCAST. In cases where unusual or infrequent resistance was detected, the alleles corresponding to the genes associated with such resistance were analysed.

Results

No significant changes in MIC50 and MIC90 were observed over the years of the study and only a high proportion of strains showing resistance to penicillin was observed, with a range going from 2.6% in 2017 to 18.9% in 2019. In the rest of the antibiotics tested, only ciprofloxacin had a limited number (3) of resistant strains throughout the study, and only one anecdotal rifampicin-resistant strain appeared in 2016.

Four isolates showed a lower level of susceptibility (range from 0.064 to 0.125 µg/ml) to cefotaxime. Three of the strains (C ST11cc strains) had the 327 allele of the penA gene (associated with lower sensitivity to cefotaxime) and the other one (serogroup B isolate) had the 11 allele, which shares specific mutations with the 27 allele.

Three strains with resistance to quinolones each presented a different allele of gyrA (alleles 387, 92 and 388), all of them showing T91I alteration and were characterized as B ST1163/269cc, B ST14827/cc Non Assigned (NA) and B ST3496/213cc.

The rifampicin-resistant strain presented an alteration at H552Y (associated with resistance).

Finally, the strain 00673, isolated in 2020, and with a penicillin MIC > 32 µg/ml, turned out to be a producer of beta-lactamase, carrying the blaROB-1 gene inserted in the chromosome, being characterized as Y, ST3587/23cc.

Conclusion

The resistance in Spain of N. meningitidis to antibiotics used both in treatment and in contact prophylaxis seems to have a slow evolution, but the appearance of resistance mechanisms and expansion of some clones with resistance makes it necessary to maintain a close surveillance of the evolution of this issue.

OC 31 - Meningococcal antibiotic resistance: Molecular characterization of isolates from patients with Invasive Meningococcal Disease (IMD) in Greece.

Ioanna Spiliopoulou[1,2,3], Athanasia Xirogianni[3], Stelmos Simantirakis[3], Georgina Tzanakaki[3]

[1]European Programme for Public Health Microbiology (EUPHEM), European Centre for Disease Prevention and Control (ECDC), Solna, Sweden, [2]National Public Health Organization (NPHO), Athens, Greece, [3]National Meningitis Reference Laboratory, Department of Public Health Policy, School of Public Health, University of West Attica, Athens, Greece

Background

IMD is a life-threatening disease requiring prompt antibiotic treatment. Although antimicrobial resistance is rare, the emergence and spread of meningococcal antibiotic resistance has become a global concern, jeopardizing the effective treatment of IMD patients and their close contacts.

Aim/Methods

The aim of the study was to describe the susceptibility phenotypes and resistance mechanisms to penicillin, ciprofloxacin and rifampicin of invasive meningococcal isolates recovered in Greece from 2010 to 2021. A total of 192 isolates were analyzed. Serogroups were identified by slide agglutination test and molecular typing (Multilocus Sequence Typing (MLST), porA and fetA) was performed. Minimum Inhibitory Concentration (MIC) to penicillin, ciprofloxacin and rifampicin was carried out by E-test and the results were interpreted according to EUCAST guidelines. Further, penA, gyrA and rpoB genes were identified by PCR amplification and sequencing.

Results

Among the 192 isolates, MenB accounted for 84% (162/192), followed by MenY (6%; 12/192), MenC (5%; 10/192), MenW (4%; 7/192) and MenX (1%; 1/192). E-test revealed that 52% (99/192) were penicillin-susceptible, standard exposure (PenS), 37% (72/192) were penicillin--susceptible, increased exposure (PenI) and 11% (21/192) were penicillin-resistant (PenR). The vast majority of PenR isolates belonged to MenB (95%; 20/21), while 5% (1/21) belonged to MenW. Seventeen clonal complexes (cc) were identified: cc269, cc32 and cc23 were most prevalent among the PenS isolates, while cc213 and cc865 predominated among the PenR isolates. Forty penA alleles were identified. Isolates expressing penicillin susceptibility, either standard or increased exposure, that harboured penA27 and penA3 alleles were all associated with MenB cc269 and cc32, respectively. The penA1 allele was mostly associated to MenB cc32 (45%; 9/20), MenY cc11 and MenW cc11 (15%; 3/20, respectively), while penA22 allele was mostly associated to MenY cc23 (69%; 9/13). The PenR isolates harbouring penA9 allele were mostly associated to MenB cc865 (5/6; 83%) and MenW cc11 (1/6; 17%). The penA295 allele was found in all PenR MenB cc213 isolates, while penA25 was associated to PenR MenB cc162. The penA910 allele was found in 2 PenR MenB isolates belonging to ST-3129 (unassigned cc) recovered from an outbreak in a migration camp also resistant to ciprofloxacin. One rifampicin-resistant isolate expressing rpoB5 allele was identified belonging to MenB, ST-12983 (unassigned cc).

Conclusion

Resistance to ciprofloxacin and rifampicin remained rare during the 11-year period. Increased penicillin resistance was observed and associated with specific hyperinvasive clones, suggesting that genotypic monitoring of antibiotic resistance is essential.

OC 36 - Antibiotic susceptibility of invasive Haemophilus influenzae isolates in Germany: low rates of piperacillin/tazobactam and ciprofloxacin resistance

Thien-Tri Lam[1], Helene Duske[1], Lei-Lani Hohenadel[1], Manuel Krone[1], Heike Claus[1]

[1]University of Würzburg, Würzburg, Germany

Background

Antibiotic resistance in Haemophilus influenzae (Hi) rises globally. Piperacillin/Tazobactam (TZP) and ciprofloxacin (CIP) are important agents for the treatment of infections, although the use of fluoroquinolones has been restricted due to severe side effects. There are currently no data for TZP and CIP resistance in invasive Hi infections in Germany.

Aims/Methods

The aim of this study was to analyze the epidemiology of TZP and CIP resistance in invasive Hi cases in Germany.

All invasive Hi strains collected at the National Reference Laboratory for Meningococci and H. influenzae (NRZMHi) in 2019 in Germany were included in this study. Antibiotic susceptibility testing was performed by gradient agar diffusion (GAD) and results were interpreted according EUCAST guidelines. Resistance was verified by broth microdilution (BMD) and TZP resistance additionally by agar dilution (AD). Molecular analysis included PBP3 mutations for TZP resistance, and mutations in QRDRs (GyrA, GyrB, ParC, ParE) for CIP resistance.

Results

GAD resulted in the detection of 21 TZP resistant invasive Hi isolates out of 726 (2,9%). Upon verification by BMD and AD, only two resistant strains were ultimately identified with a MIC >0,25mg/l by at least two methods. Both were β-lactamase-producing amoxicillin--clavulanate-resistant (BLPACR) strains with PBP3 mutations characterized as group III-like+. Furthermore, out of the 21 TZP resistant strains in GAD, five β-lactamase-negative ampicillin-resistant (BLNAR) and one BLPACR strain showed relevant PBP3 mutations. Although the TZP resistance in these strains was not confirmed by a second phenotypic method, the mutations suggest a reduced affinity of β-lactam antibiotics to the PBP3 in these strains.

Using GAD, five isolates were identified as CIP resistant. Microdilution confirmed four cases, resulting in a prevalence of 0,55 %. All ciprofloxacin resistant strains showed at least one mutation in either GyrA or ParC. No mutations in QRDRs were found in any CIP susceptible control strains.

Conclusions

TZP as well as CIP remain effective agents to treat Hi infections. Resistance prevalences for both antibiotics were at very low rates in invasive Hi strains in Germany. A good correlation between GAD and BMD was found for CIP testing. However, using BMD, the number of TZP resistant strains may be underestimated. The mutations found in PBP3, GyrA and ParC have been described previously and are a possible explanation for the increased minimal inhibitory concentrations. Changing case numbers during the COVID19-pandemic warrant further epidemiologic surveillance that include antibiotic resistance.

Surveillance and strain characterisation 3, 11:15 - 12:55

Moderators: Dominique Caugant; Paula Mölling

OC 10 - Dynamics of the Neisseria meningitidis population structure revealed by whole genome sequence data from over sixty years of Dutch surveillance

Boas CL van der Putten[1,2,3], Sandra Man-Bovenkerk[1], Wieke Freudenburg-de Graaf[1,2], Arie van der Ende[1,2], Nina M. van Sorge[1,2]

[1]Department of Medical Microbiology and Infection Prevention, Amsterdam UMC location University of Amsterdam, Amsterdam, Netherlands, [2]Netherlands Reference Laboratory for Bacterial Meningitis, Amsterdam UMC location AMC, Amsterdam, Netherlands, [3]National Institute for Public Health and the Environment, Bilthoven, Netherlands

Background

The incidence of invasive meningococcal disease (IMD) has significantly decreased through a combination of natural decline of serogroup B since 2000 andsubsequent introduction of the Neisseria meningitidis serogroup C conjugate polysaccharide vaccine in 2002 and the tetravalent vaccine against serogroups ACWY in 2018. Currently, N. meningitidis serogroup B is the main cause of IMD in the Netherlands. Neither of the licensed recombinant protein vaccines against N. meningitis serogroup B is included in the national immunization program.

Aim

We aimed to identify shifts in the meningococcal population structure and predict MenB vaccine coverage for isolates collected between 1958-2020 using whole-genome sequencing (WGS) data.

Methods

From the collection of the Netherlands Reference Laboratory for Bacterial Meningitis, 2,231 invasive meningococcal isolates were selected for WGS: 1,582 from the period 1958-2010 and the

remaining 649 from 2015 onwards. Lineages, antigenic profiles, and vaccine coverage (gMATS and BAST methods) were predicted in silico through BIGSdb. For isolates with 'unpredictable' coverage, 50% was counted towards 'covered'.

Results

After quality control, 2,149 isolates were included for further analysis. Of these, 1311 (61%) were serogroup B and the median patient age was 6 years. Between 1965 and 1980 clonal complexes (CC) 8 and 1 comprised 50% of the population, but are currently very rare. Between 1985 and 2005, CC41/44 covered 40 to 50% of the isolates. CC11 has been present throughout this 60-year period and displayed at least three different capsular polysaccharides (B, C and most recently W). Predicted coverage of serogroup B meningococci by Bexsero and Trumenba strongly fluctuated over the years, ranging from 75% (late 1970s) to 95% (late 1980s) for Bexsero and 83% (1960's) to 95% (1990's) for Trumenba. Currently, the Bexsero coverage of MenB isolates from 0-4 year olds is estimated to be 78%. All major CCs are well covered by Bexsero on average, except CC213 (average coverage 49%).

Conclusion

The past sixty years showed rapid shifts in the meningococcal population structure. Consequently, MenB vaccine coverage fluctuates over time. This is particularly relevant in light of the aftermath of decreased transmission during the COVID-19 pandemic, which may have caused perturbations in the N. meningitidis population structure.

OC 32 - The emergence of new genetic lineage, ST-3753, of Neisseria meningitidis serogroup B in Auvergne-Rhône-Alpes region, France 2021-2022

Ala-Eddine Deghmane[1], Garance Terpant[2], Alexandra Thabuis[2], Anne-Sophie Barret[3], Eva Hong[1], Muhamed-Kheir Taha[1]

[1]Institut Pasteur, Paris, France, [2]Santé Publique France, France, [3]Santé Publique France, Saint-Maurice, France

Ala-Eddine Deghmane1, Garance Terpant2 et Alexandra Thabuis2 Anne-Sophie Barret3 Eva Hong1, and Muhamed-Kheir TAHA1

Introduction

After two years of decreased incidence of invasive meningococcal disease (IMD), cases seem to rebound with an increase in the incidence of IMD due to group B (IMDB) at national and local levels in France with a recent cluster of cases in the region Auvergne-Rhône-Alpes, France.

Aims

We aimed to characterize this local increase in incidence to inform the decision-making process in terms of cluster management.

Materials and Methods. Surveillance epidemiological and bacteriological data in France were used in combination with whole genome sequencing (WGS) to detect emerging meningococcal isolates causing IMD. Epidemiological characteristics of cases, genomic analysis of the isolates, and their coverage by vaccines were analyzed.

Results

During the 52 weeks from 15 august 2021 to 14 August 2022, we detected 28 IMDB cases in the Auvergne-Rhône-Alpes region. A local increase of IMDB isolates was detected with an incidence of 0.35 cases per 100,000 inhabitants versus 0.15 at the national level. Among these 28 isolates, 12 were identical and associated with a shift to 15-24 years of age. All 12 isolates belonged to a new sequence type ST-3753 of the clonal complex ST-41/44 (CC41/44). WGS clustered these isolates together and were separated from other isolates of CC41/44. These isolates were predicted to be covered by vaccines against group B meningococci. Epidemiological investigations identified two geographical clusters around Chambery (cluster 1) and Eastern Lyon (cluster 2). Vaccination was therefore recommended in these two areas targeting individuals 16-24 years old.

Conclusion

Combining real-time WGS with epidemiological surveillance offers a rapid and reliable tool to optimize the implementation of outbreak control measures.

OC 39 - Visual analytic developments on the PubMLST databases

Keith Jolley[1], Margaret Varga[1], Holly Bratcher[1], Martin Maiden[1]

[1]University of Oxford, Oxford, United Kingdom

Introduction

Visual analytics in the form of dashboards and interactive graphical breakdowns allow users to rapidly assimilate and understand the nature of complex datasets. We have recently introduced front-end and query dashboards that show the breakdown of field values within complete databases and within user-defined and public projects.

Aims

The aims are to provide easily-digested overviews of database contents and the dataset results returned from queries, to improve understanding and the user experience.

Methods and Results

Default dashboards can be defined for individual databases or projects and these are fully customizable with users able to:

1) modify the size and layout of individual visualizations and the selection of fields shown;

2) select how these are visualized with a choice of different charts including pie charts, doughnut charts, bar charts, treemaps, word clouds, lists, gauges, and geographical maps;

3) choose colour themes and individual colours for different elements.

Separate dashboards are also displayed following an isolate database query that show the composition of isolates within a returned dataset.

In addition, we have introduced high-resolution mapping that allows the values of individual geographic fields, such as town or city, to be linked to lookup tables of GPS coordinates so that isolation locations can be displayed, as well as exported to external tools such as Microreact.

Finally, an interactive Data Explorer tool has been developed that links to front-end dashboards and allows users to investigate how different fields relate to each other, for example showing how clonal complexes are distributed among capsule groups and countries. Links within the Data Explorer take users directly to a query page that returns datasets filtered by selected criteria.

Conclusion

The new functionality enhances the user experience of the PubMLST databases, providing improved understanding of dataset contents and guidance of how complex queries can be constructed.

OC 66 - Characterisation of meningococci in children fully vaccinated with 4CMenB over a 7-year period in England

Jay Lucidarme[1], Aiswarya Lekshmi[1], Xilian Bai[1], Lloyd Walsh[1], Stephen Clark[1], Laura Willerton[1], Andrew Walker[1], Helen Campbell[2], Sonia Ribeiro[2], Shamez Ladhani[2,3], Ray Borrow[1]

[1]Meningococcal Reference Unit, UK Health Security Agency, Manchester, UK, [2]Immunisation and Vaccine Preventable Diseases Division, UK Health Security Agency, London, UK, [3]Centre for Neonatal and Paediatric Infection, St George's, University of London, London, UK

Introduction

In September 2015, the UK introduced the meningococcal B (MenB) vaccine 4CMenB into its routine infant vaccine schedule at 2, 4 and 12 months. 4CMenB comprises four main peptide antigens that vary among meningococci in terms of their immunological cross-reactivity and expression. 4CMenB coverage of MenB isolates is determined using the Meningococcal Antigen Typing System (MATS). Genetic (g)MATS was developed with reference MATS data to estimate strain coverage based on genotypic data alone. MATS/gMATS are not validated for non-MenB strains but may provide insight into potential coverage. By September 2018, there were 12 culture-confirmed MenB cases in children receiving the national-recommended 2+1 schedule. Of these, five were MATS negative and seven were MATS positive for NHBA-only (n=4) or NHBA and fHbp (n=3).

Aims

To characterise meningococci from fully vaccinated children with confirmed invasive meningococcal disease up to the end of August 2022.

Materials and Methods

Cultures underwent genome sequence analysis with draft genomes deposited on PubMLST.org. Non-culture clinical specimens underwent Sanger sequence analysis for fHbp and PorA. gMATS/partial gMATS analysis was used to estimate 4CMenB coverage of culture/non-culture meningococci. Vaccine status was determined by UKHSA enhanced surveillance.

Results

There were 102 cases in fully vaccinated children (92 MenB, 7 MenW and three MenY).

For MenB, 37 were culture-confirmed and 55 were PCR-confirmed. Among culture confirmed MenB cases, 13 isolates were gMATS negative (not covered) and 19 were gMATS positive for fHbp + NHBA (n=10), fHbp (n=1), NHBA (n=7) or PorA (n=1). The remaining five MenB isolates were indeterminate for fHbp (n=2) or NHBA (n=3). Available MATS data largely concurred with gMATS.

Among the non-culture MenB cases, 3/32 with PorA data and 5/23 with fHbp data were gMATS positive. A further four were indeterminate for fHbp. The remainder with typing data were gMATS negative for the respective antigens.

All MenW (n=5) and MenY (n=2) isolates were gMATS indeterminate with potential coverage for NHBA only. With the exception of a single MenW case (gMATS indeterminate for fHbp), the non-culture MenW (n=2) and MenY (n=1) cases were gMATS negative for PorA and fHbp.

Conclusion

Half of culture-confirmed breakthrough MenB cases were considered 4CMenB-covered with 35% not covered. There were very few non-MenB cases and vaccine coverage of these was largely indeterminate. Antigenic distribution and timing of disease may provide insights into breadth and duration of immunity. Improved non-culture characterisation will serve to enhance these data.

MAY 31, 2023

Carriage studies, 9:30 - 10:50

Moderators: Georgina Tzanakaki; Stephen Clark

OC 54 - Genetic evolution in long-term carriage of Neisseria meningitidis within a Swedish carriage study

Sara Thulin Hedberg[1,2], Lorraine Eriksson[1,2], Olof Säll[2,3], Berhane A Idosa[1,2], Martin Sundqvist[1,2], Per Olcén[1], Hans Fredlund[1], Bianca Stenmark[1,2], Susanne Jacobsson[1,2], Paula Mölling[1,2]

[1]Dept Laboratory Medicine, Clinical Microbiology, University Hospital Örebro, Örebro, Sweden, [2]Faculty of Medicine and Health, Örebro University, Örebro, Sweden, [3]Department of Infectious Diseases, University Hospital Örebro, Örebro, Sweden

Introduction

A study of meningococcal carriage was conducted among students at Örebro University, Örebro, Sweden, showing an overall carriage rate of 9.1% (Säll et al). Sampling was performed at 5 occasions during 2018-2019 at four-month interval, including a pilot study.

Aims

The aim was to study the genetic evolution of persistent carriage of Neisseria meningitidis every fourth months up to 16 months.

Materials and Methods

The 241 verified N. meningitidis isolates (PCR positives + culture positives) were Illumina whole-genome sequenced (WGS), including three isolates from the earlier pilot study. From the analyzed WGS data, distance matrixes were created and calculated based on core-genome MLST (cgMLST) using BIGSdb, https://pubmlst.org/software/bigsdb.

Results

In total, 32 students were positive more than once and of these, 20 harboured the same strain, verified by WGS. The observed duration of carriage was 4 months (n=12 students), 8 months (n=6), 12 months (n=1) as well as 16 months (n=1). The student displaying carriage for 12 months was repeatedly positive on four consecutive occasions with a N. meningitidis genogroup B, ST-809, cc35 and the distance matrix showed 59 loci differences between the first and the latest isolates. The student with 16 months carriage participated only on the first two occasions (including the pilot study) and on the last occasion. This student was positive each time with a genogroup B, ST-7460, cc32 meningococci with a distance matrix of 36 loci differences between the first and the latest isolates.

Conclusion

Long-term carriage, of the same meningococcal strain for up to 16 months, was here be verified by WGS. To our knowledge, this is the longest duration of meningococcal carriage that has been reported. One limitation in this study is that the student in question didn´t participate in two of the sampling occasions, leading to a long time (12 months) between the second and third sample collection. However, due to relatively low prevalence of ST-7460 in the present population, and the genetic similarity between the isolates; it´s deemed likely that our findings is consistent with persistent carriage.

OC 63 - Adolescents prevention against meningitis in Europe

Elena MOYA[1]

[1]Confederation Of Meningitis Organisations, Bristol, United Kingdom

- European Coordinator of CoMO (Confederation of Meningitis organisations) since 2008.

- COMO 2017 Adolescents Survey

- Results in Ppoint presentation

- Conclusion MENINGOCOCCAL DISEASE : adolescents carry and transmit bacteria that may cause meningitis

- Young people belong to a high risk group that need protection

- Vaccination against serogroups ACWY is majority in Europe

- In France, adolescentes do not receive yet this protection

- CoMO demands a better protection for young people in France

- WHO Global Plan to DefeatMeningitis 2030 encourages all member

states in Europe to implement vaccination against meningitis for all aged groups. Meningitis can affect anyone at any age

OC 49 - Genetic variants of Neisseria meningitidis and outcome of infection in mice

Lorraine Eriksson[1], Cecilia Klanger[1], Ala-Eddine Deghmane[2], Bianca Stenmark[1], Sara Thulin Hedberg[1], Hans Fredlund[1], Muhamed-Kheir Taha[2], Paula Mölling[1]

[1]Department of Laboratory Medicine, Faculty of Medicine and Health, Örebro University, Örebro, Sweden, [2]Institut Pasteur, Invasive Infections Unit, Paris, France

Background

Genetically similar isolates of Neisseria meningitidis can cause either carriage or invasive disease, and so far no specific genetic markers have been identified to predict the phenotypic outcome. In order to identify genetic variants that are associated with invasive or carriage isolates, a genome wide association study (GWAS) was performed on isolates from a Swedish carriage study, and invasive isolates during the same time period. The GWAS study identified genetic variants of porB, tspB, and pilE/S and two non-synonymous single nucleotide polymorphisms (SNP; glmU S373C and fkbP D33N) associated with invasiveness or carriage.

Aims/Methods

The aim was to investigate how invasive and carriage isolates were able to cause infection in transgenic mice, with a focus on variants of porB and tspB. In addition, expression of the pilE/S will be compared between the isolates.

BALB/c mice were infected with 24 N. meningitidis isolates (13 invasive, 11 carriage) that expressed different variants or absence of porB, tspB, pilE/S and the two non-synonymous SNP's. The outcome of infection was determined by bacterial amount (CFU/mL) and cytokine levels (TNF-α, IL-6 and KC). Two isogenic mutants were created where porB was replaced with an erythromycin cassette, and used to infect mice. The outcome of infection was compared between original- and mutant isolates.

Further studies to create isogenic mutants of porB, tspB and the SNP´s are ongoing. In addition the expression of pilE is investigated by droplet digital PCR (ddPCR) targeting pilE class 1 and 2.

Results

The invasive isolates caused a more severe infection in transgenic mice than carriage isolates. Significant differences were observed 24 h after infections between mice infected with carriage and invasive isolates in CFU/ml ($p=<0.001$), temperature ($p=<0.05$), TNF-α ($p=<0.05$), IL-6 ($p=<0.01$) and KC ($p=0.01$). When comparing the first two isogenic porB mutants with the original isolates the only significant difference was found in temperature variation (< 1° C) at 3 h post-infection. Further studies are ongoing with additional isogenic mutants. Preliminary results of the pilE ddPCR indicate a difference in expression of pilE between isolates.

Conclusion

Invasive isolates of N. meningitidis have a greater ability to cause a more severe outcome of infection in transgenic mice than carriage isolates. This phenotype may be multifactorial and further investigation may be required to explore the role of porB, tspB, pilE/S and significant SNP's

Vaccines, strain coverage and seroprevalence, 11:15 - 12:55

Moderators: Georgina Tzanakaki; Paola Stefanelli

OC 56 - Rationale for a Pentavalent Meningococcal Serogroup ABCWY Vaccine in Europe: A Review of Epidemiologic and Clinical Data

Jason D. Maguire[1], Lefteris Zolotas[2], Beth Moughan[1], Paula Peyrani[1], Paul Balmer[1], Jamie Findlow[3], William C. Gruber[4], Annaliesa S. Anderson[4], Johannes Beeslaar[2]

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Introduction

Invasive meningococcal disease (IMD) is dominated by serogroups A, B, C, W, and Y, but currently available vaccines target serogroups ACWY or B only using different schedules.

Aims

We present the potential utility of a pentavalent MenABCWY vaccine as a solution to the challenges of the evolving IMD epidemiology.

Materials and Methods

The global IMD burden was assessed through a literature review of surveillance reports and PubMed articles published during January 2010-June 2020. Clinical data were derived from the MenABCWY clinical development program covering 3 phase I/IIb/III studies in >4,000 adolescents/young adults. Immunogenicity evaluations utilized serum bactericidal assays using human complement (hSBA) against serogroup A/C/W/Y strains and 4 diverse, vaccine--heterologous B strains. hSBA titers were defined by the proportion of participants achieving seroprotective hSBA titers (≥1:8 or ≥1:16 depending on strain) and ≥4-fold rise from baseline (seroresponse). Safety was also evaluated.

Results

Surveillance reports and publications from 77 countries indicated that IMD incidence during 2010-2019 was generally low (<3 per 100,000) but was characterized by unpredictable shifts in disease-causing serogroups and sporadic outbreaks. Incidence peaked among infants and young children, with secondary peaks in adolescents/young adults and sometimes older adults. Serogroups ABCWY caused the vast majority of IMD; serogroup B dominated in many regions and some regions underwent increases in serogroups W and Y.

Clinical data showed that following 2 MenABCWY doses at 0,6-month, 93.3%-97.8% of ACWY-naïve and 68.1%-95.9% of all participants achieved hSBA seroresponses for serogroups A/C/W/Y and serogroup B test strains, respectively, which were noninferior (at −10% margin for difference across groups) to 1 MenACWY-CRM dose and 2 MenB-FHbp doses (0,6-month) respectively. Most (78.3%) achieved noninferior seroprotective hSBA titers against all 4 B strains combined. Noninferior A/C/W/Y hSBA seroresponses were observed in ACWY-experienced participants. Four-year immunopersistence was similar to the comparator. After the 4-year booster dose, 100% achieved seroprotective hSBA titers for A/C/W/Y and the percentages achieving seroprotective hSBA titers for B test strains were higher after boosting than after the primary series. Seroresponses following a MenABCWY 0,12-month schedule were higher

compared to a 0,6-month schedule for all 5 serogroups. One MenABCWY dose was noninferior to one MenACWY-CRM dose regardless of ACWY experience. MenABCWY was well-tolerated. No safety concerns were identified.

Conclusion

MenABCWY was safe, well tolerated, and highly immunogenic and could help address challenges in evolving IMD epidemiology and existing vaccination schedules by providing adolescents/young adults with comprehensive protection using a single vaccine. Funded by Pfizer.

OC 16 - Evaluating the effect of targeted strategies as control tools for hypervirulent meningococcal C outbreaks.

Giorgio Guzzetta[1], Marco Ajelli[2,1], Alessandro Miglietta[3,4], Cecilia Fazio[4], Arianna Neri[4], Stefano Merler[1], Giovanni Rezza[5], Paola Stefanelli[4]

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Objectives

In 2015-2016, an outbreak caused by an ST-11 cc-11 hyperinvasive meningococcus C (MenC) strain caused 62 invasive meningococcal disease (IMD) cases in Tuscany, Italy (1-3). We estimated key outbreak parameters and assessed the impact of interventions.

Materials and Methods

We developed an individual-based model of MenC transmission, accounting for transmission in households, schools, discos/clubs, and the general community and informed by detailed data derived from epidemiological investigations and implemented control measures.

Results

The reproduction number of the outbreak was 1.35 (95%CI: 1.13-1.47) and the IMD probability was 4.6 every 1,000 new carriage episodes (95%CI: 1.8-12.2). Performed interventions (chemoprophylaxis and vaccination of close contacts of IMD cases, and widespread age-targeted vaccination) were effective in reducing the reproductive number, putting an end to the outbreak. Case based interventions (including ring vaccination) alone would have been insufficient to achieve outbreak control. The definition of age groups to prioritize vaccination has a critical impact on the effectiveness and efficiency of control measures.

Conclusions

There are no effective alternatives to large-scale reactive vaccination during outbreaks of highly transmissible meningococcal strains. Age-targeted campaigns can increase the magnitude of vaccination effectiveness. These results can be instrumental to define effective guidelines for the control of future meningococcal outbreaks caused by hypervirulent strains.

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OC 9 - Epidemiological basis for vaccination against invasive meningococcal disease in the Czech Republic

Paula Kriz[1], Michal Honskus[1,2], Jana Kozakova[1]

[1]National Institute of Public Health, Prague, Czech Republic, [2]Third Faculty of Medicine, Charles University, Prague, Czech Republic

Introduction

Due to the high case fatality rate of invasive meningococcal disease (IMD) and the high percentage of lifelong sequelae, it is important to vaccinate against this disease. The vaccination strategy in each country should be based on valid epidemiological data. Accurate epidemiological data on IMD in the Czech Republic are provided by the IMD surveillance programme initiated by the National Reference Laboratory for Meningococcal Diseases (NRL) in 1993.

Aim

Presentation of the analysis of IMD surveillance data in the Czech Republic for the period 1993–2020, which are the basis for the vaccination strategy.

Materials and Methods

The IMD surveillance data merge NRL data and infectious disease reporting data with the

exclusion of duplication. The surveillance IMD data include molecular characterisation of Neisseria meningitidis, are internationally comparable and are reported to international databases.

Results

IMD morbidity in the Czech Republic has been on a downward trend in recent years, but the age-specific morbidity of children under 1 year of age has remained high for a long time. The second and third risk groups are adolescents aged 15-19 years and children aged 1-4 years. The total IMD case fatality rate over the entire surveillance period is on average 10%, but unlike the gradually decreasing morbidity, there is no decrease in the case fatality rate. Most IMD cases are caused by serogroup B, followed by serogroup C, serogroup Y and serogroup W. The molecular data of IMD isolates showed the most frequent representation of eight clonal complexes: cc11, cc44/41, cc32, cc267, cc23, cc18, cc35 and cc865. The results of the molecular data analyses showed sufficient coverage of Czech N. meningitidis isolates with MenB vaccines. Recommendations for IMD vaccination in the Czech Republic are continuously updated and are available on the website of the Czech Vaccination Society and at the NRL website. In recent years, the Czech Republic has succeeded in implementing legislation to provide the vaccination free of charge with the MenB vaccine and the ACWY conjugated vaccine to high risk groups, both in terms of health (patients with immunological disorders) and age (young children and adolescents).

Conclusion

The analysis of long-term IMD surveillance data confirms that the current vaccination strategy, i.e. vaccination of young children and adolescents with a combination of the MenB vaccine and quadrivalent (ACWY) conjugate vaccine, best corresponds to the epidemiological situation of IMD in the Czech Republic.

OC 20 - A trend of lower seroprevalence against the capsular polysaccharide of Haemophilus influenzae serotype b in 2-4 year olds compared to older cohorts eligible for vaccination; a population-wide seroprevalence study in the Netherlands

Anneke Steens[1], Jesca Brouwer[1], Fiona van der Klis[1], Hester de Melker[1], Gerco den Hartog[1]

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Introduction

Vaccination against Haemophilus influenzae serotype b (Hib) has been part of the national immunization programme (NIP) since 1993. Various vaccines have been used including monovalent (1993-2002), pentavalent (DTPw-IPV/Hib in 2003-2004, DTPa-IPV/Hib in 2005-2011) and hexavalent vaccines (DTPa-HBV-IPV/Hib; since 2011). At the time of study, vaccinations were offered at 2, 3, 4 and 11 months of age. The vaccine coverage has been constantly high (≥93%).

The incidence among children <5 years has increased in the Netherlands since 2012. This might partly be explained by changes in immunity as a result of changes in exposure or in the kind of NIP vaccine.

Aims

We aimed to study levels of anti-polyribosyl-ribitol phosphate (PRP; capsular polysaccharide of Hib) IgG and seroprevalences by age-cohorts.

Materials and methods

Sera from participants from a population-based serosurvey (PIENTER-III) performed in 2016/2017 were tested for anti-PRP IgG concentrations by Multiplex Immuno assay. N=5552 participants, aged 0-89 years, were included. We determined seroprevalence, i.e., the percentage above the cut off for protection for ≥0.15 µg/mL (providing at least short-term protection) and >5 µg/mL (defined to provide protection against colonisation). We performed weighted analyses to account for the two-stage cluster sampling design.

Results

The seroprevalence using the ≥0.15 µg/mL cut off was highest for those aged 12-17 and 18-23 months (each 94% [95%CI 85-100]), reflecting the response to the booster at 11 months. Despite longer time since vaccination, the seroprevalence among those aged 2-4 years (76% [69-82]; born 2011-2015) was non-significantly lower than for older vaccinated age groups (all point estimates ≥79%, overlapping 95CIs); this was especially seen compared to 9-10 year (87% [80-95]; born 2005-2008) and 15-18 year olds (84% [77-90]; born 1997-2002). Seroprevalence using the ≥5 µg/mL cut off was significantly lower in 2-4 year olds (8.7% [5.2-12.2]) than in older age groups (point estimates between 15-25%).

Conclusion

It is remarkable that those aged 2-4 years old (born 2011-2015) have (slightly) lower seroprevalence than older age groups that were eligible for vaccination, despite longer time since vaccination for the latter. We cannot disentangle whether this results from differences in vaccination between birth cohort/age groups and/or in exposure. Lower seroprevalence at the cut off ≥5 µg/mL may lead to more transmission. Further studies should investigate whether the observed seroprevalences are related to the increase in Hib incidence in children aged <5 years since 2012.

OC 41 - Evolution of Haemophilus influenzae type b (Hib) and vaccine failure cases in France: impact of vaccination schedules

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Background

In 2013, France modified its Haemophilus influenzae b (Hib) vaccination schedule to remove one dose at 3 months of age and change the age of the booster dose from 16 to 11 months. During the COVID-19 pandemic, most respiratory-transmitted diseases decreased as a result of containment measures. In this work, we aimed to provide the evolution of invasive Hib disease between the pre-and post-COVID-19 pandemic and explore the immune response of vaccine failure cases in France during the period 2017-2022.

Methods

The numbers and proportions of Hib invasive isolates during the period 2017–2022 were analyzed. The vaccine failure cases were explored by measuring the concentration of anti-polyribosyl--ribitol phosphate (PRP) IgG using specific ELISA in the sera of patients at the admission and at least one month after the onset of the disease. Anti-Hib antibodies-dependent opsonophagocytosis and complement activation assays were performed to monitor the functionality of these antibodies.

Results

During the period 2017-2022, the number of Hib invasive disease increased, particularly in children under 5 years-old, despite the measures implemented to stop COVID-19. Several cases of vaccine failure were registered with a proportion significantly higher in toddlers vaccinated according to the current scheme (2+1). The increased vaccine failure was associated with a decline in anti-PRP IgG response after the last dose to levels below the protective threshold (1 µg/ml). These levels correlated with reduced antibody-dependent opsonophagocytosis and complement activation. However, the levels of bactericidal antibodies increased significantly 1 month after the admission suggesting a secondary immune response to the Hib.

Conclusions

The simplification of the vaccination to a 2 + 1 scheme seems to reduce the level of anti PRP IgG. Hib antibodies wane rapidly after the 11 months booster and may not be enough to ensure long term protection. Surveillance of cases and monitoring of titres need to be continued to informe future vaccination Policy.

1 JUNE, 2023

Epidemiology, 9:30 - 10:50

Moderators: Nina M. van Sorge; Suzana Bukovski

OC 17 - Epidemiology of invasive meningococcal disease in Belgium

Wesley Mattheus[1], Nathalie Goeders[1], Stéphanie Jacquinet[2]

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Background

In Belgium, invasive meningococcal disease (IMD) cases are under mandatory reporting to regional health authorities. Laboratories are requested to send the isolates or culture-negative samples to the Belgian National Reference Centre for Neisseria meningitidis (NRC-NM) for confirmation and further typing.

Aims

The aim is to describe the current epidemiological situation of IMD in Belgium during and after the COVID-19 pandemic.

Materials and Methods

The study included all laboratory confirmed invasive meningococcal cases received at the NRC-NM between 2020 and 2022. Identification of isolates was confirmed by biochemical test and serogroup determined by slide-agglutination. Further characterization (porA, FetA, MLST) was derived from Whole Genome Sequencing data (WGS, Illumina).

Results

Between 2020 and 2022, the NRC-NM confirmed 122 cases of IMD in Belgium. The annual incidence varied from 0.48 per 100,000 population (55 cases) in 2020, 0.21 (24 cases) in 2021 to 0.37 (43 cases) in 2022. This is significantly lower than the long term average annual incidence of 0.96 per 100,000 population observed pre-COVID-19 pandemic (2010-2019). As in previous years, infants under 1 year of age showed the highest incidence, although a decreasing trend was observed (8.54 in 2020, 3.52 in 2021 and 2.54 in 2022). A similar trend was observed for children between 1 and 4 years (2.25 in 2020, 1.45 in 2021 and 0.84 in 2022). For the other age groups incidences remained low, yet stable during the 3-year period. The majority of IMD cases was caused by meningococci of serogroup B (MenB, N=70; 57,4%), followed by serogroup W (MenW, N=26; 21,3%), serogroup Y (MenY, N=18; 14,8%) and serogroup C (MenC, N=8; 6,6%). MenY was predominantly observed in elderly with 55,6% of total MenY cases in the age group above 65 years of age. IMD cases were genetically diverse with among 120 isolates analyzed by WGS, 56 different Sequence Types (ST) found, of which 36 ST were only observed once. The isolates were clustered into 17 different Clonal Complexes (CC) with 39 isolates that did not belong to any currently assigned CC. The hyperinvasive complexes CC269 (N=12), CC41/44 (N=12), CC11 (N=11) and CC32 (N=10) represented only 37,5% of the cases.

Conclusion

IMD in Belgium decreased during the COVID-19 pandemic with incidence levels reduced to one

fifth of pre-pandemic years, yet an upward trend was observed near the end of 2022. The IMD cases were genetically diverse.

OC 21 - Implementation of a protocol for genomic-based surveillance of invasive meningococcal disease in EU/EEA Member States

Jessica Beser[1], Kim Brolin[1], Priyanka Nannapaneni[1], Keith Jolley[2], Erik Alm[1], Sabrina Bacci[1], Daniel Palm[1]

[1]European Centre for Disease Prevention and Control (ECDC), Sweden, [2]Department of Zoology, University of Oxford, United Kingdom

Introduction

Invasive meningococcal disease (IMD) is notifiable and under surveillance in EU/EEA. In 2021, 624 cases of IMD were notified in the EU/EEA from 26 countries which corresponds to a notification rate of 0.14 per 100,000 population. Vaccines are available for primary prevention of disease caused by the most common serogroups of Neisseria meningitidis. Molecular typing can be used to categorize N. meningitidis into serogroups as well as different sequence types and clonal complexes, thereby providing useful information for surveillance, outbreak detection and to inform vaccination policies. We present here a protocol of genomic-based surveillance of IMD, based on the strategy outlined in the 'ECDC strategic framework for integration of molecular and genomic typing into European surveillance and multi-country outbreak investigations'[1].

Aims

The aim of the protocol for genomic-based surveillance of IMD in EU/EEA is to monitor the distribution of variants of N. meningitidis causing invasive disease in the EU/EEA by time, place and person for shorter term outbreak investigation and control, and longer-term surveillance monitoring.

Materials and Methods

The protocol includes the integration of the epidemiological information submitted by countries to The European Surveillance System (TESSy)[2] with molecular data submitted to the European Meningococcal Epidemiology in Real Time (EMERT) II database[3] within the PubMLST Neisseria database. Both the finetyping data as well as cgMLST data will be used to generate signals based on pre-defined cluster definitions. Public data being submitted to PubMLST database from EU/EEA countries will also be included in the analysis. ECDC will conduct regular monthly cross-border signal analysis. Detected clusters will be communicated and visualised in the ECDC EpiPulse system[4].

Results

A summary of regular cross-border signal analysis will be communicated to the national public health institutes and laboratories through EpiPulse for joint assessments and potential public health action. Longer term trend analysis at the EU/EEA level will be conducted in collaboration with country participants. The pilot protocol will be re-assessed after two years, when lessons learned will be incorporated.

Conclusion

This system integrates both public data as well as data collected in TESSy from EU/EEA countries, which is important for the continuous monitoring of circulating invasive clones over time. By providing data for public health action, the project adds value to EU/EEA surveillance of IMD and contribute to improved public health in Europe.

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[3]https://pubmlst.org/projects/emert

[4]https://www.ecdc.europa.eu/en/publications-data/epipulse-european-surveillance-portal-infectious-diseases

OC 35 - Molecular epidemiology of Haemophilus influenzae invasive disease in Portugal, 2019-2022

Andreia Frederico[1,2], Célia Bettencourt[2], Maria Paula Bajanca Lavado[2], on behalf of The Portuguese Group for the Study of Haemophilus influenzae Invasive Infection[3]

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Background

Haemophilus influenzae is an exclusively human pathogen responsible for severe invasive disease in both children and adults.

National Reference Laboratory for Haemophilus influenzae, based at the NIH, in Lisbon, have been responsible for surveillance of H. influenzae invasive disease, since 1989.

After the implementation of Hib vaccine, in 2000, we are assisting in changes in epidemiology of disease, with a shift in the predominant serotype from Hib to non-encapsulated H. influenzae (NTHi) and non-b serotypes (1-3).

Aim / Methods

We aim to characterize H. influenzae invasive isolates recovered in Portugal, in last four-year period (2019-2022) and compare results with previous studies from our laboratory.

From January 2019 to December 2022, 171 invasive isolates (21-LCR and 140-blood cultures) were

characterized: 58.5% from male, 33.3% from children and 43.9% from adults > 65 years old.

Serotyping was performed by PCR, as previously described (4).

Beta-lactamase production was assessed with nitrocefin. Antibiotic susceptibility was determined according to EUCAST guidelines (5).

Mutations in the ftsI gene were identified as previously described (6).

Genotyping was performed by MLST (7) and ST was assigned in PubMLST (https://pubmlst.org/organisms/haemophilus-influenzae/) (8).

Results

NTHi isolates (65.5%; 112/171) were mostly responsible for invasive disease. Among encapsulated isolates (34.5%; 59/171), 33.9% were Hia (20/59), 32.2% hib (19/59), 1.7% Hic (1/59), 8.5% Hie (5/59) and 23.7% Hif (14/59).

Most strains were susceptible to the antibiotics studied, with 10.5% (18/171) of the isolates being β-lactamase producers. Mutations on ftsI gene characterized 4.6% (15/103) isolates as BLNAR.

MLST profiles revealed high genetic variability, as expected, with 42 different STs among 63 NTHi isolates (66.7%). Of these, ST1034 was prevalent (n=6), with five isolates being BLNAR IIb, and ST165 with four isolates being β-lactamase producers.

In contrast, encapsulated isolates were clonal with all Hib assigned to ST6, Hia to ST-23 complex (ST23, ST1352, ST1511), Hic to ST7, Hie to ST18 and Hif to ST-124 complex (ST124, ST864).

Conclusion

Comparing these results with previous studies from our laboratory (2002-2018), we emphasize a global emergence of encapsulated isolates, from 22% to 34%, especially due to an increase in Hia, from 2.4% to 11.7%. Hie and Hif also increased, from 1.5% and 3.1% to 2.9% and 8.2%, respectively, while Hib decreased, from 13.5% to 11%.We characterized, in 2022, a Hic for the first time, in our country.

Surveillance of H. influenzae invasive disease should be continue, given the evolving dynamics of this pathogen and the increase of non-b serotypes.

OC 46 - Invasive Haemophilus influenzae diseases in Poland, 1997-2022

Alicja Kuch, Marlena Kiedrowska[1], Patrycja Ronkiewicz[1], Agnieszka Gołębiewska[1], Izabela Wróbel-Pawelczyk[1], Kinga Błaszczyk[1], Waleria Hryniewicz[1], Anna Skoczyńska[1]

[1]National Reference Centre for Bacterial Meningitis, National Medicines Institute, Warsaw, Poland

Introduction

Haemophilus influenzae is responsible for respiratory tract infections as well as invasive infections as e.g. meningitis, sepsis and epiglottitis. The majority of isolates are noncapsulated (non-typeable, NTHI) but encapsulated ones are also present and belong to six capsular types from a to f. In Poland H.influenzae serotype b (Hib) mass vaccination has started in 2007.

Aims

To characterise the invasive H.influenzae isolates from 1997 to 2022 in Poland.

Materials and Methods

The study was performed on all H. influenzae isolates collected by the National Reference Centre for Bacterial Meningitis between January 1997 and December 2022 during the routine monitoring of bacterial invasive infections in Poland. All strains were identified according to standard procedures. PCR reactions were run to confirm species identification, serotype determination, and to detect capsule-specific genes and changes in ftsI gene [1-7]. MICs of antimicrobials were evaluated by E-test and microdilution methods8. The data were interpreted using EUCAST clinical breakpoints guidelines [8.]Beta-lactamase production was detected by nitrocefin assay.

Results

During the study, 996 invasive H.influenzae isolates were collected. Until 2007 most of them (73.5%) were recovered from children below 5 years and were characterized as Hib (92%). Ampicillin resistance was mostly associated with beta-lactamase production (13.0%) and BLNAR phenotype [beta-lactamase positive, ampicillin resistant] (1.2%).

Following the introduction of routine Hib vaccination in the Poland, between 2008 and 2022, most of H.influenzae invasive infections were mainly diagnosed in patients above 10 years of age (73.6%). An overall drop in Hib cases (7.9%) was registered and the majority of the cases (82.1%) were caused by non-typeable H.influenza strains (NTHI). HIf (H. influenza serotype f) was the most frequent capsular type (49 cases; 7.4%) followed by H.influenzae serotype e (14 cases; 2.1%). Three isolates of serotype a (Hia) and d (Hid) were for the first time detected in 2017 and 2019, respectively (0.25% each).

Ampicillin resistance was correlated with beta-lactamase production (11.1%) and BLNAR phenotype (9.7%). There were only six isolates with BLPACR phenotype [beta-lactamase positive amoxicillin-clavulanic acid resistance] (0.6%) between 2010 and 2019.

Conclusion

After the introduction of the Hib vaccine into the Polish National Calendar a significant decrease in infections due to H. influenzae type b was observed. At the same time, a shift in patients' age toward the elderly and an increase in infections caused by non-Hib isolates were found. NTHI, Hif, Hie, Hia, and Hid are becoming emerging serotypes therefore should be monitored.

Surveillance and Strain characterisation 4, 11:15 - 12:55

Moderators: Ala-Eddine Deghmane; Julio Vazquez

OC 24 - Characterization of meningococcal disease outbreaks in the United States, 2014-2018.

Gabrielle Amore Lee Cooper[1], Nicole Brown[1], Amy Rubis[1], Sarah Meyer[1], Lucy McNamara[1]

[1]National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, United States

Introduction

Despite decades of declining incidence of meningococcal disease in the United States, meningococcal disease outbreaks are still of public health concern. During 2009 – 2013, 36 outbreaks occurred in the United States in both organization and community settings.

Aims

The goal of this analysis is to describe characteristics of meningococcal disease outbreaks in the United States during 2014-2018.

Materials and Methods

Cases reported through the National Notifiable Diseases Surveillance System (NNDSS) and additional data sent by state health departments were used to identify outbreak cases and response measures. Outbreaks were defined as 2-3 cases within an organization during a 3-month period, an incidence of meningococcal disease above the expected incidence in a community during a 3-month period, or ≥2 cases of meningococcal disease that occurred in the same family or household during a 24-month period.

Results

Twenty-five meningococcal disease outbreaks were reported in the United States during 2014-2018. Outbreaks occurred in organization (15), community (7), and household settings (3) and included populations such as college/university students, men who have sex with men (MSM), and persons experiencing homelessness (PEH). Outbreak cases predominantly serogroup B and C, accounted for 6.2 percent (115/1853) of all meningococcal disease cases reported during 2014-2018. Twelve of 15 (80%) organization-based outbreaks were due to serogroup B. Serogroup C accounted for 2 of 3 family/household outbreaks, 2 of 3 PEH outbreaks, and all 4 MSM outbreaks. Community outbreaks had longer median durations (188 days) compared to family/household and organization outbreaks (136 days and 10 days, respectively). Of the 7 family/household outbreak cases, only 2 occurred within 14 days of each other. The median number of days between consecutive cases in family/household outbreaks was 121.5 days. A public health intervention was implemented in 19 of 21 outbreaks for which information was available: mass vaccination campaign alone was conducted in 12 outbreaks, expanded chemoprophylaxis alone in 2, and both in 5.

Conclusion

Similar to previous reports, we identified outbreaks of meningococcal disease in a variety of settings and populations; however, we observed more MSM and PEH outbreaks than 2009-2013. This is also the first time family/household outbreaks have been systematically characterized in the United States. We found that family/household outbreaks had a median of 121.5 days between consecutive cases. This finding suggests that household contacts of meningococcal disease patients may be at increased disease risk beyond direct secondary transmission.

OC 11 - Core Genome Multilocus Sequence Typing Development and Validation for Haemophilus influenzae

Made Ananda Krisna[1,2,3], Keith Jolley[3], Alexandra Boubour[4], Raph Hamers[1,2], Angela Brueggemann[4], Odile Harrison[3,4], Martin C. J. Maiden[3]

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Introduction

Haemophilus influenzae (Hinf) is part of the human nasopharyngeal commensal microbiota and a human pathogen causing invasive disease. The high genetic diversity observed in Hinf, in part due to frequent horizontal gene transfer (HGT) events, necessitates novel analytic approaches that discriminate among variants and minimise bias to evaluate bacterial population structure. Core genome MLST (cgMLST) is a high-resolution typing approach that enables the evaluation of bacterial population structure for public health-related purposes such as outbreak confirmation and non-serotype b Hinf (non-Hib) vaccine development.

Methods

A cgMLST scheme for Hinf was developed using several bioinformatic tools including PIRATE, chewBBACA, Panaroo, and the BIGSdb tool Genome Comparator. These tools characterise the pangenome which will also contain paralogous genes which were specifically detected and removed through paralog exclusion pipelines. A workflow combining these tools was developed and applied to a dataset of completed, reference (N = 14) and draft Hinf genomes (N = 1,059). Draft genomes were obtained from both clinical (N= 531, 53.5%) and carriage (N=55, 5.5%) samples, and for 407 (41%) samples the source were unknown. They were selected based on geographic region and capsule genotype frequency (N= 585, 58.9% lacked a capsule known as non-typeable Hinf (NTHi).

Results

After paralog exclusion, initial analyses identified 1,017 to 1,309 core genes. Variation in annotation and paralog definitions employed by each software package resulted in different

lists of core genes. Validation using an independent dataset (N = 1,495) identified 1,167 core loci. Validating dataset is an important step in sequence typing development to ensure reproducibility and eliminate sampling bias. This dataset has similar geographic and capsule genotype frequencies, with fewer originating from clinical isolates (N = 474, 30.4%). Phylogenetic analyses generated using both core genome allelic profile clustering and nucleotide sequence alignment show a more diverse population structure of Hinf than previously described, without any apparent lineages or sublineages.

Conclusion

Genomic comparison using cgMLST facilitates Hinf genomic analyses and enhances our understanding of this pathogen. Our findings indicate that Hinf is less clonal than expected with evidence for a panmictic population structure, a challenge for non-Hib vaccine development.

OC 12 - Comparative genomic characterization of invasive non-typeable Haemophilus influenzae (NTHi) in Germany in 2010/11 and 2019-2021

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Background

Hib vaccine reduced the burden of invasive Haemophilus influenzae (Hi) disease massively. However, the incidence of non-typeable Hi infections (NTHi) increased in countries with a Hib vaccine program. Although usually sporadic, clusters of invasive NTHi infections have been reported occasionally.

Aim/Methods

In this study we compared recent invasive NTHi isolates with isolates from a decade ago to investigate (I) if there is clonal clustering among usually genetic diverse NTHi; (II) rates of antibiotic resistance to selected reagents; (III) if invasive NTHi have a specific profile of surface and adherence associated virulence factors compared to carriage isolates.

Invasive NTHi from the Federal State of Baden-Wuerttemberg 2010/2011 and 2019/2020/2021 were analyzed to compare two different periods 10 years apart. Whole genome sequencing and phenotypic antibiotic susceptibility testing was performed on all strains. Furthermore, whole genome sequenced carriage isolates from an earlier study were included for comparative genetic analysis. Genomes were analyzed using MLST and a previously developed cgMLST scheme. Simpson's diversity index from sequence types (ST) was calculated. Resistance genes were compared to the phenotypic resistance patterns. The presence of virulence factor genes in the genomic sequences was identified using the virulence factor database (VFDB, http://www.mgc.ac.cn).

Results

A total of 220 invasive strains (50 from 2010/11 and 170 from 2019-21) were analyzed. In total, 99 STs were identified, of which 23 occurred in both time periods The most frequent STs were ST12 (n=18), ST103 (n=14), ST3 (n=7), ST145 (n=7), and ST203 (n=6). Other STs counted five or less isolates. Ten clonal clusters were found, the largest consisted of six isolates (ST103). Simpson diversity index showed no relevant reduction of genetic diversity from 2010/11 (0.989) to 2019-21 (0.977).

Approximately 23% of the isolates were ampicillin resistant, 15% were BLPAR (6% of them BLPACR) and 8% BLNAR. Cefotaxime and rifampicin resistance rates were low (<1%).

Results of virulence factor comparison will be reported on the conference.

Conclusion

Although there was no significant reduction of genetic diversity, we found 10 clusters of NTHi, of which transmission events could not be confirmed epidemiologically. The dominant ST 103 is known for containing TEM-type β-lactamase.

The results confirm that invasive NTHi infections continue to be sporadic events, even though case numbers have increased substantially over the years. However, further continuous surveillance should be carried out to observe future developments of the disease.

OC 60 - Molecular epidemiology of an emerging invasive Neisseria meningitidis sequence type, ST-9316

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Introduction

Invasive meningococcal disease (IMD) caused by Neisseria meningitidis remains a public health problem, with mortality rates as high as 10%, even in high-income countries. In 2010 new sequence type ST-9316 was reported in Poland which has subsequently become widespread in the country, with incidence reaching 33% of all reported cases in 2021. This sequence type is mostly associated with serogroup B and W but isolates of serogroup C and Y were also observed, indicating a possible capsule switching event. Further analysis of the epidemiological and molecular features of ST-9316 is required,translating to public health benefits in Poland and other European countries.

Aims

This investigation aimed to:

1. Perform epidemiological analysis on ST-9316 prevalence and case dynamics in Poland;

2. Undertake an in-depth analysis of ST-9316 genome data to establish the extent of this potentially new clonal complex;

3. Identify capsule switching events and other potential virulence factors;

4. Infer potential cross-protection of existing vaccines against ST-9316.

Materials and Methods

Whole genome sequencing was used to obtain genomic data from isolates collected in Poland between 2010-2022 (n=184). Data was curated and uploaded into PubMLST for further analysis. Bioinformatic tools such as PIRATE, Genome Comparator, RAxML and ClonalFrameML were used to align and compare all complete genomes of ST-9316 and close locus variants uploaded to PubMLST from all countries (N=177) and produce phylogenetic trees and recombination analysis. Further analysis was focused on specific metabolic features shared by ST-9316, such as the absence of functional hmbR gene. MenDeVAR tool was used to assess the reactivity of Bexsero® and Trumenba® vaccines against ST-9316 antigenic variants.

Results

RAxML and ClonalFrameML recombination analysis enabled the establishment of a new clonal complex. PubMLST analysis highlighted metabolic differences between ST-9316 and other common clonal complexes in Poland (including ST-11), most notably an altered iron metabolism due to loss of functional hmbR gene responsible for haemoglobin binding. Analysis suggested a capsule switching event which resulted in emergence of W serogroup ST-9316 from the original B serogroup. This was linked to an increase in incidence of W-IMD in children under the age of 4, with nearly all cases attributed to ST-9316.

Conclusion

Molecular epidemiology plays an important part in surveillance of meningococcal disease in both high and low-income countries. Understanding N. meningitidis virulence factors and trait acquisition results in better predictions of the dangers associated with newly emerging clonal complexes such as ST-9316.

PO 44 - Comparative genome analysis of Chilean clonal complex 11 Neisseria meningitidis isolates.

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Background

Invasive meningococcal disease (IMD) is an important public health problem. Since 2012, serogroup W cc11 have been the main cause of IMD in Chile, considered highly virulent. Aim: To analysis of whole genome sequence (WGS) data for Chilean cc11 meningococcal isolates and compare with public database.

Methods

From 2016 to 2019, 42 genomes of meningococcus from children with IMD were sequenced. Sixteen were cc11 and were included in core genome MLST (cgMLST) approach with 1054 genomes selected from PubMLST.org database and visualized on phylogenetic networks.

Results

A total of 1070 cc11 genomes of MenB (3.6%), MenC (35.9%), MenW (59.4%) and MenY (1.1%) since 1964 to 2021 were included. Two lineages were identified (11.1 and 11.2). Lineage 11.1 comprised serogroups B, C, W and Y and were distributed into 5 sublineages (sub). The 1st sub. included only MenB and MenC from Europe, USA, Canada, and South America (Venezuela, Brazil, and Argentina) from 1969 to 2018. The 2nd sub. formed by MenW from South Africa, UK and one Chilean strain, from 1975 to 2014. The 3rd sub. and 4th sub. conformed a bifurcation, 3rd sub. included only MenW descendant of Hajj outbreaks from Africa, UK, and France from 2000-2014, meanwhile 4th sub. That we called "American/UK strains", included MenW and MenY strains which formed 4 clusters from 2008-2019: newest Brazilian strains; The UK, USA and Mexico; a cluster formed by Argentina, Chile (from this study), and USA strains; and a second group of Brazilian with old and new strains. The 5th sub. was formed by MenW from China, UK, South African and Brazilian strains from 1996-2019. Lineage 11.2 were constituted solely by MenB and MenC, grouped in 4 sublineages: 1st North American strains (2009-2019); 2nd USA, Mexico, UK, France, and Colombia (2007-2019); 3rd had old strains from Western Europe and South Africa (1996-2013); and 4th included Western Europe, Canada and South Africa (1993-2005).

Conclusion

We showed a geo-temporal distribution of some cc11 strains described in the last 60 years with similar distribution as informed by other authors. Chilean strains clustered in lineage 11.1 closely related to Argentina and USA isolates. For the first time, we report the presence of MenY (since 2015) within this lineage. This find leads us to think that capsular switching events may be occurring, which could be explain due to the presence of very similar cps genes loci shared by serogroups B, C, W and Y.

POSTERS

PO 0 - 4CMenB: 10-Year Anniversary Journey and Beyond

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Introduction

The 4-component meningococcal serogroup B (MenB) vaccine (4CMenB), first licensed in 2013 in Europe, is now registered in 50 countries for prevention of MenB invasive meningococcal disease (IMD). 4CMenB is included in various national (Andorra, Czech Republic, France, Ireland, Italy, Lithuania, Malta, New Zealand, Portugal, San Marino, Spain, UK) and regional (Australia) immunisation programmes.

Aim

Present 4CMenB 10-year development journey, from clinical trials to real-world use, and highlight future prospects.

Methods

Data generated using established laboratory and clinical trials endpoints together with real-world use are summarised to demonstrate consolidated evidence on vaccine effectiveness (VE).

Results

4CMenB licensure relied on safety and immunogenicity generated by human complement serum bactericidal antibody (hSBA) assay against 4 indicator strains.1 Its clinical development programme established protective hSBA titres, acceptable safety and tolerability in infants, children, adolescents and adults when administered alone and/or with routine childhood vaccines, including MenACWY.2,3 At the time of development, assessment of VE was not feasible with hSBA against broad panels of MenB isolates because of wide diversity in MenB antigens. Therefore, the meningococcal antigen typing system (MATS) was developed to estimate 4CMenB strain coverage. The genetic MATS (gMATS) complements MATS in predicting 4CMenB coverage.4 MATS strain coverage estimates in Europe, North America, Brazil and Australia range from 66% to 91%,4-10 although MATS (and gMATS) does not account for synergistic effects of simultaneous binding of antibodies to multiple antigens.11 Real-world data from various countries show VE of 59–94%,12-14 with evidence of protection also against non-B serogroups and gonococcal infections.14,15 New developments include the investigational MenABCWY vaccine that incorporates 4CMenB antigens and an innovative assay, enc-hSBA,16 in which endogenous complement in each vaccinee's serum is preserved. In a phase 3 study, enc-hSBA was used against 110 representative MenB strains to measure 4CMenB and MenABCWY VE to proxy real-world conditions, reflecting both breadth of coverage across study population and robustness of vaccine responses at subject level.

Conclusion

Real-world experience gained over last decade confirms the effectiveness of 4CMenB against MenB IMD. An innovative approach (enc-hSBA on 110-strain panel) should enable more accurate MenB VE assessment in clinical settings.

Funding: GlaxoSmithKline Biologicals SA.

PO 1 - Clinical validation of the new direct real time duplex PCR assay for the serogrouping of Neisseria meningitidis serogroups E (29E or Z`) and Z

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Introduction

Invasive meningococcal disease (IMD), including meningitis and septicemia, caused by Neisseria meningitidis (Nm) is a major public health concern. Among the 12 defined serogroups, IMD cases are mainly associated with serogroups A, B, C, W, X and Y. Recently, IMD caused by Nm serogroups E (formerly 29E or Z`) and Z, for which a rapid and reliable detection method was not available, have been reported in some European countries.

Aims/Methods

We used a total of 245 specimens for the clinical validation, including 114 (97 NmE and 17 NmZ) positive and 131 negative specimens. The specimen types used for the validation included 40 CSFs, 107 crude DNA preps from isolates, and 98 mocked CSF specimens prepared by spiking CSF with crude DNA preps from NmE (n=49), NmZ (n=9) or non-NmE/Z (n=40) clinical isolates collected as a part of CDC surveillance programs during 2006-2019 and previously serogrouped by whole genome sequencing and/or slide agglutination. The lower limit of detection (LLD) yielding a Ct value of 35, was determined following a previously published protocol. Cross-detection with closely related species (analytic specificity) was evaluated by testing 36 different bacterial species. Sensitivity was defined by the proportion of true positive specimens with positive drt-PCR results out of all specimens with a positive drt-PCR result. Specificity was defined as the proportion of true negative specimens with a negative drt-PCR result out of all specimens with a negative drt-PCR result.

Results

The sensitivity and the specificity of the duplex assay was 100% for both NmE and NmZ. The lower

limit of detection (LLD), defined as CFU/mL yielding a Ct value of 35, for the NmE assay was 164 CFU/mL, while that for NmZ assay was 424 CFU/mL. The assay did not show any cross detection with closely related bacterial species.

Conclusion

Clinical validation of the new duplex drtPCR assay demonstrated high sensitivity and specificity of this test method. This direct method reduces the time and cost of processing CSF specimens and aids in the timely detection of Nm serogroups E and Z to inform appropriate public health action.

PO 2 - Azithromycin resistance detected in invasive Neisseria meningitidis strains isolated in Germany 2019 - 2021

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Background

Azithromycin has been shown to eradicate meningococcal colonization, is easy to applicate and has a good safety profile. Thus, it is recommended in some countries as one of few antimicrobial substances for the post-exposure prophylaxis of close contacts to an invasive meningococcal disease (IMD) case. Among 200 invasive Neisseria meningitidis isolates from Germany from the years 2006 to 2018, no azithromycin resistant isolate was detected [1].

Aim/Methods

Minimal inhibitory concentrations (MIC) of all cultured IMD isolates sent to the German National Reference Laboratory for Meningococci and Haemophilus influenzae in the years 2020 and 2021 as well as a selection of the isolates from 2019 were determined by broth microdilution according to the methods and interpreted according to the standards of the Clinical and Laboratory Standards Institute. Isolates are judged susceptible against azithromycin if the MIC was 2 mg/L or below.

Results

225 IMD isolates were tested with three isolates not been able to grow in the used media, one from each year. While 2 of the 105 isolates from 2019 (1.8%) showed azithromycin resistance, all 74 tested isolates from the year 2020 were azithromycin susceptible. From the year 2021, two out of 46 isolates tested repeatedly resistant (4.3%) with a MIC between 4 and 16 mg/L.

Conclusion

Since 2019, azithromycin resistant N. meningitidis isolates were detected in Germany. This fact puts the use of azithromycin as post exposure prophylaxis for close contacts of IMD cases into perspective. When azithromycin prophylaxis is recommended, reference laboratories are advised to monitor the emergence of azithromycin-resistant meningococcal strains.

PO 4 - Meningococcal disease in Italy: microbiological characterization from National Surveillance data, 2017-2022

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Introduction

In Italy, the National Surveillance System for Invasive meningococcal disease (IMD) is coordinated by the Istituto Superiore di Sanità (ISS). Italy shows a low incidence for IMD compared to the overall incidence reported by ECDC for EU/EEA Member States.

Aims

Based on the data collected, this analysis aims to describe the main genotypic characteristics and the antibiotic susceptibility profiles of Neisseria meningitidis identified in Italy from 2017 to 2022.

Materials and Methods

Bacterial isolates and biological samples from IMD cases were sent and analysed at ISS. The antibiotic susceptibility for cefotaxime, ceftriaxone, ciprofloxacin, meropenem, penicillin and rifampicin was assessed according to the European Committee on Antimicrobial Susceptibility Testing. Bacterial isolates were analysed by whole genome sequencing using the Neisseria.org website.

Results

In Italy, from 2017 to 2022, the annual incidence of IMD decreased from 0.33 to 0.09 cases per 100,000 inhabitants. Serogroups B (51%) and C (27%) were the prevalent. Serogroup B increased from 42% in 2017 to 83% in 2022 and determined an outbreak of 5 cases in 2018. Serogroup C decreased from 27% in 2017 to 9% in 2022 and caused an outbreak of 6 cases in 2019/2020. Among serogroup B, 16 different clonal complexes (ccs) were identified: cc162 was the predominant. Among serogroups C and W, cc11 prevailed, while cc23 characterized mostly serogroup Y meningococci. All isolates were susceptible to cefotaxime, ceftriaxone and meropenem. Five isolates were penicillin resistant and 67% showed a reduced susceptibility to penicillin. Two meningococci resistant to rifampicin and one resistant to ciprofloxacin were also identified.

Conclusion

In Italy, incidence of IMD remains low, however two outbreaks were detected during the

period. A drastic decrease in the IMD incidence caused by the COVID-19 emergency was observed. Serogroup B increased its proportion during the last six years and was characterized by a high molecular heterogeneity. Resistance to antibiotics for therapy or chemoprophylaxis does not represent currently an issue. However, in Italy sporadic meningococci resistant to antibiotic were identified. Continued surveillance of N. meningitidis is essential for the appropriate public health interventions.

PO 6 - Prediction by genetic MATS of 4CMenB vaccine coverage of invasive meningococcal serogroup B (MenB) isolates circulating in Taiwan between 2003 and 2020

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Introduction

Among 165 invasive meningococcal disease (IMD) isolates collected in Taiwan in 2003–2020, 134 were identified as MenB.[1] The Meningococcal Antigen Typing System (MATS), a sandwich ELISA method for testing viable isolates, and genetic MATS (gMATS), a genome-based tool for viable and non-viable isolates, are used to predict 4CMenB vaccine coverage of MenB isolates.

Aim

To characterise the 134 MenB isolates from Taiwan by whole genome sequencing and vaccine antigen genotyping, to predict 4CMenB coverage using gMATS.

Methods

Whole genome diversity of the isolates was characterised via phylogenetic relationships with 502 MenB isolate genomes downloaded from PubMLST (https://pubmlst.org/neisseria/). gMATS coverage was estimated via individual associations between antigen genotypes and MATS coverage for each 4CMenB component.

Results

Of the 134 MenB isolates, 32.8% were from children aged <5 years, while 29.9% and 37.3% were from individuals aged 5–29 and ≥30 years, respectively. Most of the isolates belonged to three global hyperinvasive clonal complexes (cc): cc4821 (27.6%), cc32 (23.9%) and cc41/44 (14.9%). Predicted 4CMenB vaccine coverage by gMATS was 62.7% (lower/upper limit: 27.6%/97.8%). Overall, 2.2% of isolates were not covered, 27.6% were covered and 66.4% were unpredictable by gMATS (3.7%: data not available). gMATS coverage estimates by age group were 66.1% (<12 months), 50.0% (12–23 months), 42.9% (2–4 years), 63.8% (5–29 years) and 64% (≥30 years). In the analysis of antigen coverage, gMATS coverage estimates and percentages of isolates predicted as covered/not covered were highly variable, depending on the group considered. Vaccine coverage estimates were higher for isolates with two or more gMATS-positive antigens than for isolates positive for one antigen.

Conclusion

Analysis of 134 MenB isolates from Taiwan shows overall 63% (lower/upper limit: 27.6%/97.8%) coverage of 4CMenB by gMATS, in line with estimates from other countries (58–88%), with predictable coverage for 30% of isolates. These are likely to be underestimates as the gMATS calculations do not take into consideration synergistic mechanisms associated with simultaneous binding of antibodies elicited by multicomponent vaccines, such as 4CMenB, to multiple antigenic targets, or the contribution of all outer membrane vesicle components.

Reference:

1. Chiou et al. Microbiol Spectr. 2022;10:e00882-22

PO 7 - Invasive nongroupable and capsular group E Neisseria meningitidis isolated in Italy, 2005-2022

Vacca P[1], Cecilia Fazio[1], Arianna Neri[1], Luigina Ambrosio[1], Anna Carannante[1], Florigio Romano Lista[2], Silvia Fillo[2], Andrea Ciammaruconi[2], Antonella Fortunato[2], Paola Stefanelli[1]

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Background

The polysaccharide capsule is one of the major virulence factor of Neisseria meningitidis1. The majority of invasive N. meningitidis isolates are encapsulated, with serogroups A, B, C, Y, W and X being the most responsible of invasive diseases. In contrast, the nongroupable (NG), including the capsul null locus (cnl), and those belonging to other serogroups (e.g. E, H, L, Z) are generally identified in healthy carriers. Although rare, invasive diseases caused by those meningococci have been documented, mostly in immunocompromised patients.

Aim

The aim was to describe and characterize the invasive NG and serogroup E meningococci collected in Italy from 2005 to 2022.

Methods

Bacterial isolates and biological samples from invasive cases are collected and characterized at the Department of Infectious Diseases of Istituto Superiore di Sanità. Serogroup was molecularly determined. Genotypic profiles and genomic comparation were obtained using PubMLST platform (http://pubmlst.org/neisseria/). Antimicrobial susceptibility was determined by MIC Test Strip Method and interpreted according to the EUCAST breakpoints.

Results

From 2005 to 2022, 13 invasive meningococcal diseases (IMD) caused by 7 NG, 4 cnl, and 2 serogroup E meningococci were reported in patients with a range of age from <1 to 68 years. Two

patients were vaccinated against meningococcal serogroups A, C, W, Y. Sepsis and meningitis were the main clinical presentations. All patients survived, except for one. Meningococci showed different genotypic profiles belonging to clonal complexes: cc23, cc60, cc175, cc1136, and cc1157. Genomic comparison with an international collection of NG, cnl and capsule group E genomes from invasive and carriage meningococcal isolates available on PubMLST database confirmed clustering by clonal complexes, with intermixed invasive and carriage genomes.

No antimicrobial resistant phenotype were observed in these meningococci; however, for 2 isolates MIC values for penicillin and rifampicin were close to the resistant breakpoints.

Conclusion

Invasive meningococcal isolates belonging to nongroupable and more rare capsular groups have to be monitored and analysed in order to evaluate changes in the genomic and phenotypic patterns.

PO 8 - Whole genome analysis of Neisseria meningitidis isolates from the Czech Republic over 28 years and estimate of their theoretical coverage by MenB vaccines

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Introduction

Invasive meningococcal disease (IMD) belongs among the most dangerous infectious diseases in the world. Several polysaccharide conjugate vaccines against serogroups A, C, W and Y are available and two recombinant peptide vaccines against serogroup B (MenB vaccines) have been developed: MenB-4C (Bexsero) and MenB-fHbp (Trumenba). Since the genes encoding MenB vaccine antigens are present across isolates of all other serogroups, MenB vaccines have the potential to provide protection also against isolates of other serogroups.

Aim

Our study presents an analysis of whole genome sequencing (WGS) data of 369 Neisseria meningitidis isolates from IMD from the Czech Republic for the period 1993–2020. The aim of this study was to define the population of the N. meningitidis and to estimate the theoretical coverage of isolates by MenB vaccines.

Methods

The Illumina MiSeq platform was used for WGS. The genome assembly from raw data was performed using the Velvet de novo Assembler software. Genomes were submitted to the PubMLST database and characterized at MenB vaccine antigen genes. The theoretical coverage of a given isolate by both MenB vaccines was determined using the Meningococcal Deduced Vaccine Antigen Reactivity Index (MenDeVAR).

Results

The coverage by Bexsero vaccine was determined in 44.2% MenB isolates, 3% were marked as not covered, and the remaining 52.8% isolates carried variants of MenB antigen genes, for which data were not available in the PubMLST database presently. For the Trumenba vaccine, the coverage was determined for 49.8% isolates, 1 isolate was defined as not covered by the vaccine, and for 49.8% isolates data were missing. For MenC, W, and Y isolates, 25% were defined as covered by Bexsero vaccine, 1 isolate was defined as not covered, and for the remaining 74.4% isolates, data were not yet available. There were 30.8% isolates that were defined as covered by Trumenba, and for the remaining 69.2% data were missing. If half of the isolates for which MenDeVAR index data are missing from the PubMLST database were covered by the vaccines, the theoretical Bexsero vaccine coverage would be 70.6% (for MenB) and 62.2% (for MenC, W, Y). For the Trumenba vaccine, under the same assumptions, the theoretical coverage would be 74.6% (for MenB) and 65.7% (for MenC, W, Y).

Conclusions

Our results demonstrated sufficient coverage of Czech population of N. meningitidis with MenB vaccines and, together with surveillance data, were the basis for updating recommendations for vaccination against invasive meningococcal disease.

PO 23 - Comparison of the impact of ampicillin and cefuroxime on mutation emergence in Haemophilus influenzae using whole genome sequencing

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Background

Treatment of infections caused by Haemophilus influenzae is based on beta-lactam antibiotics. Usually, two main mechanisms are responsible for resistance to this antibiotic class: production of beta-lactamase and structural alteration of the penicillin-binding protein (PBP3) encoded by ftsl gene (rPBP3 strains). Other mechanisms that could lead to resistance have been speculated, such as overexpression of the efflux pump AcrAB (caused by mutations in the regulatory gene acrR) or porin defects. It was shown that exposure to beta-lactams has stimulating effect on increase of rPBP3 H. influenzae strains. According to the results of regular surveillance of antibiotic resistance in H. influenzae, the prevalence of H. influenzae rPBP3 strains increased during the same time period as cefuroxime consumption doubled in the Czech Republic. The aim

of our study was to compare the mutations induced by ampicillin and cefuroxime using whole genome sequencing (WGS) with a focus on resistance to beta-lactam antibiotics.

Methods

To investigate whether ampicillin and cefuroxime differ at de novo generating mutations we used five beta-lactam susceptible wild-type haemophili and these strains were serially passaged for 30 days in medium containing either ampicillin or cefuroxime. Prior and after the experiment, minimal inhibitory concentration (MIC) according to EUCAST was determined and WGS was performed. The isolates were sequenced using PacBio platform and annotated with PROKKA. Changes in coding sequences that occurred after 30 passages were identified by blasting against local database created from the coding sequences of the sample before passaging.

Results

After 30 days of an experiment, MIC of ampicillin increased 4-32 fold (mean value 13.6) and MIC of cefuroxime by 8-32 fold (mean value 20). WGS have shown many de novo generated mutations in various genes. Mutations in ftsI gene was found, furthermore, mutations that could influence resistance, such as mutations in efflux pump and porin genes, will also be investigated.

Conclusions

Exposure to cefuroxime resulted in generating different mutation comparison to exposure to ampicillin in H. influenzae. Cefuroxime has a higher effect on increasing MIC than ampicillin.

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PO 25 - Invasive Haemophilus influenzae isolates in Germany 2019 to 2023: laboratory surveillance report

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Background

The National Reference Laboratory for Meningococci and H. influenzae (NRZMHi) performs laboratory surveillance of invasive H. influenzae in Germany. The period 2019-2022 is marked by the COVID19 pandemic, which lead to substantial changes in the case numbers of respiratory infections.

Aim/Methods

The aim was to present epidemiologic data from 2019 to 2022.

Isolates from blood and cerebrospinal fluid (CSF) are defined as invasive and must be notified in Germany, but submission to the NRZMHi is voluntary. The NRZMHi performed species confirmation, serotyping and susceptibility testing of ampicillin and cefotaxime on all submitted isolates.

Results

From 2019 to 2022, invasive Hi was confirmed in 2202 cases; 2091 isolates derived from blood, 101 from CSF only, and 10 from both blood and CSF. The coverage of the laboratory surveillance was estimated by comparing NRZMHi submissions to registered cases in the statutory notification and ranged from 76% (2019) to 80% (2022).

The majority of isolates were non-typeable H. influenzae (NTHi, 1718 isolates, 78.0%), followed by Hif as the most frequent capsular serotype (282 cases; 12.8%). Hib and Hie were at comparable levels with 72 cases (3.3 %) for Hie and 68 cases for Hib (3.0%). Compared to previous years, Hia (59 cases, 2.7%) was found more frequently 2019-2022. Hic and Hid were each found once in 2019 (0.05%). Among the analyzed cases, patients most affected were aged > 40 years (1870 cases; 84.9 % of all cases). A significant percentage of cases (179 cases; 8-1%) was found in children aged <5 years.

Ampicillin susceptibility testing revealed 934 (42.2%) ampicillin resistant Hi (MIC > 1 µg/ml), 277 (12.6%) showed β-lactamase production. Cefotaxim resistance was found in 27 tested isolates (1.2%).

Conclusion

The epidemiology of invasive Hi infections in Germany in the reporting period was strongly affected by the COVID19 pandemic. Whereas case numbers 2019 and in the beginning of 2020 were at levels similar to previous years, reduced mobility and public interventions during the pandemic lead to a marked reduction of invasive Hi infections. In spite of low case numbers, the proportion of Hia cases continued to high compared to previous years. Reduction of invasive cases did not affect neonatal infections due to NTHi suggesting that transmission by airborne droplets was prevented during the COVID19 pandemic. Case numbers have markedly risen again with increased mobility by the end of 2022.

PO26 - Invasive Meningococcal Disease in Greece: A 4 year epidemiological data (2019-2022)

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Background

Surveillance of Invasive Meningococcal Disease (IMD) is mandatory in Greece and is performed through the mandatory notification system. Clinical records are reconciled with laboratory

records on a national scale.

Aim/Methods

The study presents the epidemiological data for the time period 2019-2022.

A total of 62cases of IMD were notified in Greece for the 4-year studied period (32, 21, 4 and 5 cases for 2019,2020,2021,2022 respectively). Clinical samples (CSF, blood) and cultures were sent to the Reference Laboratory for further identification by conventional and molecular methods.

Results

The average annual incidence was 0.14/100 000 for 4 years; with a dramatic decrease during the COVID-19 pandemic years (2021 (0.04) & 2022 (0.05) In regards to the age, a decline in the average incidence was observed in all age groups as follows: 3.19 (in infants <1 year) and 0.5 (1-4 years), 0.14 (5-14 years), 0.32 (15-19 years) and 0.07 (>20 years) per 100 000 population. The case fatality rates (CFR) were 9.4 for 2019 while there were no fatal cases during the following years (2020-2022).

Among the 62 laboratory confirmed IMD cases, MenB was identified in 62.90 % (39/62) followed by MenY (9.7%; 6/62), MenC 6.4% (4/62) and MenW (1.6%; 1/62).

The highest average incidence rate for serogroup B was observed in age groups of <1 and 1–4 (average incidence 6.94 and 1.93 /100 000 respectively). The 6 MenY cases were related to the age groups of 20-60 years (n=5), 0-4 years (n=1), all belonging to 23 cc.

The most predominant clonal complexes were 41/44cc and 162cc. However, a new sequence type 3129 (ST-3129) was isolated from a migration camp during an outbreak in early 2020 related to MenB and by the use of 'gene-by-gene" approach clustered closely with isolates from China. The most predominant PorA combinations were 22-14 and 7-2,4 for VR-1, VR-2 respectively.

Finally, the highest percentage of reduced susceptibility to penicillin was found in the strains isolated during 2019 (73.3%). Resistance to ciprofloxacin was found for the first time in Greece in 2 isolates expressing a new gyrA allele (gyrA346) harbouring the T90I amino acid substitution

Conclusions

A dramatic decrease in IMD incidence was observed during the past two years due to COVID-19 pandemic. MenB was the most predominant, while MenY and MenW cases remain low most probably due to the implementation of the MenACYW vaccination program in adolescents, since 2011.

PO 27 - Haemophilus influenzae meningitis in Greece: 10 year of continuous surveillance (2013-2022).

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Introduction

Due to mass vaccination programs implemented in all European countries, the incidence of meningitis due to H.influenzae type b remains low. However, concern exists for the long-term effectiveness and possible disease replacement by other H. infuenzae serotypes. Therefore, continuous surveillance and monitoring is of high public health importance.

Aim/Methods

The study presents a 10 year continuous surveillance of meningitis cases due to H. influenzae in order to monitor possible serotype replacement. All H. influenzae meningitis cases recorded and confirmed either by culture or PCR during a 10-year period (2013-2022) were included. Strains were cultured in chocolate agar and DNA was extracted from clinical samples (CSF and whole blood) (MagCore HF16 Automated Nucleic Acid Extractor, RBC Bioscience). Two multiplex-PCR assays were employed for the identification of H.influenzae (hel gene) and Hib (bexA gene), and further identification of serotypes a, c, d, e, f by a multiplex-PCR assay.

Results

Of 65 H. influenzae laboratory confirmed cases during the study period, the majority (87.7%; 57/65) were solely confirmed by PCR assays, while 12.3% (8/65) were culture-confirmed. A predominance of non-b serotypes, mainly non-typeable (NTHi) was evident throughout the study period. Eleven (11) cases were caused by Hib, while 54 cases were caused by non-b H. influenzae (average incidence 0.01 and 0.05 per 100.000 population respectively). Among them, serotype f was identified in three cases and serotype a in only one case, while the remaining were NTHi. The few Hib cases identified annually were mostly observed in children (63.6%; 7/11) of which four in infants, two in 1-4 y.o. and one in 5-14 y.o.) and only 36.4% (4/11) in adults. Although the majority of NTHi cases (56.0%; 28/50) were recorded in adults >30 years of age, the rest 44% pertained to children up to 14 y.o, while, it is noteworthy that 17 NTHi cases were recorded in children 0-4 y.o. of which 35.3% (6/17) in infants.

Conclusions

Despite the reduction of Hib disease, the predominance of NTHi cases, highlights the need for constant awareness and closer surveillance of H.influenzae infections. Molecular techniques play an important role in the diagnosis and typing of culture-negative cases, allowing better epidemiological monitoring.

PO 38 - Reduction in invasive Neisseria meningitidis disease during the COVID-19 pandemic in Finland

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Background and Aims

Incidence of invasive bacterial disease has decreased worldwide during the COVID-19 pandemic (1, 2). We investigated changes in invasive meningococcal disease (IMD) in Finland in 2017-2022.

Materials and Methods

Notification of IMD is mandatory in Finland and all clinical microbiology laboratories report isolations of N. meningitidis or detection of bacterial specific nucleic acid from blood or cerebrospinal fluid into National Infectious Diseases Register (NIDR), a population-based electronic surveillance system maintained by the Finnish Institute for Health and Welfare (THL). Meningococcal isolates are requested to be sent to the THL's specialist microbiology laboratory, where their species and serogroup is confirmed, and they are further characterized using whole genome sequencing (Illumina) and sequence analysis tools available at the PubMLST website (pubmlst.org). In the present study, we analysed IMD surveillance data collected at THL from January 2017 to December 2022.

Military conscripts in Finland have been offered meningococcal ACWY (MenACWY) polysaccharide vaccine since 1974, which was replaced by the MenACWY conjugate vaccine in 2018. As already planned before the pandemic, MenACWY conjugate and MenB protein vaccines were introduced into national vaccination programme for medical risk groups in August 2020.

Results

During 2017-2019, sixteen laboratory-confirmed IMD cases were notified annually into NIDR (incidence rate, IR, 0.29 per 100,000 population), of which majority were caused by serogroups Y, B and C. Following the introduction of COVID-19 nonpharmaceutical interventions in mid-March 2020, IMD incidence decreased markedly and remained low until March 2022. Decrease was observed in all age groups and in all major serogroups. Incidence decreased by 69% (IR 0.09) in 2020 and 90% (IR 0.03) in 2021 compared to the average incidence in the three previous pre-pandemic years from 2017 to 2019. Since April 2022, the number of cases caused by serogroups B and Y has increased, but the IR was still markedly lower (0.13) than in the pre-pandemic years.

Conclusion

The incidence of IMD has been declining in Finland for more than two decades. Since 2020, COVID-19 control measures further reduced the incidence until spring 2022, after which an increase in incidence has been observed following the lifting of nonpharmaceutical interventions. The re-emergence of IMD needs to be monitored closely.

PO 40 - Haemophilus influnezae ability to form biofilms may be linked to virulence in non-typable isolates

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Nouria Belkacem, Eva Hong, Ala-Eddine Deghmane and Muhamed-Kheir Taha

Introduction

Non-typeable Haemophilus Influenzae (NTHi) is responsible for invasive infections that are encountered frequently in older adults but encountered in all age groups. Biofilms represent a protective mechanism that enhances bacterial resistance to clearance. Biofilm formation by Hi has been studied in only a limited number of strains, and a repertoire of genes and bacterial surface structures have been implicated in biofilm formation and maturation. These include type IV pili over-expression, the presence of fimbriae, quorum sensing, the presence of outer membrane proteins P2 and P5, and the presence of phosphorylcholine and sialic acid in the lipooligosaccharide molecule.

Aim

To understand the relationship between biofilm formation and virulence.

Materials and Methods

We analyzed the ability of NTHi and typeable isolates to form biofilms using plate assay with crystal violet staining. WGS was used to characterize Hi according to schemes of genes involved in biofilm formation.

Results

Invasive NTHi isolates trend towards higher biofilm indices than invasive typeable isolates regardless of age or clinical forms.

Conclusions

NTHi isolates lack capsule and biofilm formation may enhance NTHi survival upon acquisition and contribute to bacterial growth and invasiveness.

PO 42 - Haemophilus influenzae resistance to beta lactams in France

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Introduction

Haemophilus influenzae is a prevalent agent of respiratory infections including acute otitis media (AOM). Amoxicillin is usually used s the first-choice antibiotic leading to high antibiotic prescriptions and may contribute to the development of bacterial resistance to antibiotics.

Aim

The objective of this work was to describe and analyse antibiotic resistance of H. influenzae from 2017 to 2021 in France.

Materials and Methods

We characterized H. influenzae isolates transmitted to the French national reference centre for H. influenzae between 2017 and 2021. We included all the 608 non-invasive respiratory isolates. Resistance rates to the main antibiotics were described. The relationship between resistance rate, age, and sex of patients and germ serotype was investigated.

Results

Isolates were mainly from alveolar lavage (29.3%), expectoration (22.9%), or sputum (15%). Resistance to amoxicillin (61.4%), amoxicillin/clavulanic acid (47.4%), and cefotaxime (39.3%) was high and correlated with the presence of beta-lactamase and/or modifications of ftsI gene encoding the penicillin-binding protein 3. Resistance to sulfamethoxazole/trimethoprim (33.2%) was more moderate. There were no significant differences according to serotype, age, or gender.

Conclusion

The benefit/risk balance of first choice use of amoxicillin and even of amoxicillin/clavulanic acid in AOM is questionable in view of the significant resistance to H. influenzae. The use of sulfamethoxazole/trimethoprim could be an alternative but may still need further evaluation.

PO 47 - Meningococcal disease caused by Neisseria meningitidis sergroup W in Poland, 2014-2022

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Introduction

Neisseria meningitidis serogroup W (MenW) has for many decades been an infrequent cause of meningococcal disease; however, following a MenW outbreak after the Hajj in 2000, and recently, MenW disease started to be common in some regions, including Europe.

Aims

The objective of the study was characterize invasive meningococcal disease epidemiology caused by MenW in Poland, between 2014 and 2022.

Materials and Methods

The study included all invasive meningococcal cases confirmed by the National Reference Centre for Bacterial Meningitis (NRCBM) between 2014 and 2022. For all isolates serotyping and whole genome sequencing were performed. A PCR technique was used for meningococcal identification directly from clinical materials in the case of a negative culture.

Results

From 2014–2022, 1349 IMD cases were reported to the NRCBM. Among them, 99.5% had a serogroup result including 97 (7.2%) MenW. Between 2014 and 2017 MenW was responsible for 3.5% (range from 2.2 to 4.4%) infections, however in 2018, 2019 and 2020 the percentage increased significantly to 9.8%, 11.4% and 19.2%, respectively. In 2021 MenW accounted for 11.6% of cases and in 2022 for 7.5%. Over half of the cases occurred in children under four years old (52.6%) and the median age was 2 years. The overall male to female ratio was 1.53 (58:38). Case fatality ratio (CFR) for MenW cases with known outcome was 33.9% (21/62). MLST were available for 81 isolates. Among them, the most represented was ST-9316 and its single or double locus variants (60.5%), including two isolates of ST-167cc and two of ST-865cc. Almost all of these isolates had VR1/VR2 porA combination of 5-2/10-1 and fetA variant F5-8. Twenty five isolates (30.9%) belonged to ST-11cc. In infants, most of cases MenW were caused by meningococci of ST-9316 and its variants (86.4%). CFR for ST-9316 and its variants cases with known outcome was 55.5%, whereas for ST-11cc cases - 38.9%.

Conclusion

Between 2018 and 2020 the NRCBM notified a significant increase of MenW disease in Poland, with high CFR. Despite the observed decrease in MenW in the last two years, IMD cases should be closely monitored since changes in meningococcal epidemiology may occur rapidly.

PO 48 - Invasive meningococcal disease in Poland

Anna Skoczyńska[1], Marlena Kiedrowska[1], Agnieszka Gołębiewska[1], Patrycja Ronkiewicz[1], Izabela Wróbel-Pawelczyk[1], Kinga Błaszczyk[1], Alicja Kuch[1], Waleria Hryniewicz[1]

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Background

Neisseria meningitidis is a leading etiologic agent of severe invasive disease characterized by rapid onset, of which meningitis and septicaemia are the most common and important manifestations.

Aim

To characterise invasive meningococcal disease (IMD) epidemiology in Poland during last years, based on laboratory confirmed cases.

Methods

In Poland, population-based vaccination against meningococci was not introduced so far. All invasive meningococcal cases confirmed by the National Reference Centre for Bacterial Meningitis (NRCBM) between 2019 and 2022 were studied. Serotyping, antimicrobial

susceptibility testing, and whole genome sequencing were performed for all isolates.

Results

Between 2019 and 2022, the NRCBM identified 432 of laboratory confirmed IMD cases (317 by culture and 115/26.6% by PCR); 167, 99, 86, and 80 cases in consecutive years respectively. In 2019 the overall IMD incidence was 0.43/100,000 and in patients under one year of age, 10.80, ranging between regions from 0 to 22.47/100,000. A serogroup was defined for 429 (99.3%) cases. The majority of infections were caused by meningococci of serogroup B (MenB, n=279; 64.6%), followed by serogroup C (MenC, n=89; 20.6%), W (n=54, 12.5%) and Y (n=7, 1.6%). The percentage of MenW increased from 11.4% in 2019 to 19.2% in 2020 and then decreased to 11,6% in 2021 and 7.5% in 2022. According to the 2022 EUCAST criteria only one isolate of serogroup C, ST-11 was resistant to penicillin with MIC=0.38 mg/L. All meningococci were susceptible to cefotaxime, chloramphenicol, rifampicin and ciprofloxacin.

Amongst 273 meningococci 108 STs were found, although 81 of them were represented by one isolate only. Almost 60% of isolates represented 21 clonal complexes (cc), with the most common 32/ET-5cc (16.9%), ST-41/44cc (9.2%) and ST-11cc (7.0%). The remaining meningococci did not belong to any cc; amongst them, 43.9% were of ST-9316. Among MenB isolates 21 ccs were found; the most common were representatives of ST-32/ET-5cc (27.5%) and ST-213cc (7.8%). MenC meningococci belonged to nine ccs; the most frequent were ST-103cc (23.2%) and ST-41/44cc (19.6%). Among MenW the most common were isolates of ST-11cc and of ST-9316 (36.4% each).

Conclusions

Poland is one of the European countries with a low IMD incidence rate. In the COVID-19 pandemic years, 2020-2022, in Poland as in other countries, about 50% fewer IMD cases were confirmed. ST-9316 and clonal complexes of ST-32/ET-5cc and ST-41/44cc are well established in our country.

PO 51 - Bactericidal killing of meningococcal serogroup W strains isolated in Argentina by the sera of adolescents and infants immunized with 4-component meningococcal serogroup B (4CMenB) vaccine – updated results

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Background

As 4-component meningococcal serogroup B (4CMenB) vaccine contains immunogenic antigens present and conserved in non-serogroup B meningococci, cross-reactivity is possible.

Aim/Methods

To test the bactericidal effect of 4CMenB vaccine on meningococcal serogroup W (MenW) strains genetically representative of those isolated in Argentina to evaluate the potential impact of 4CMenB vaccine on preventing MenW disease (1).

Eleven MenW strains isolated in Argentina during 2010–2011 that were not susceptible to killing by human complement alone were tested in human complement serum bactericidal antibody (hSBA) assays (1). Three pairs of serum pools were tested, derived from: adolescents before and after 1 dose of meningococcal serogroups A, C, W and Y (MenACWY) vaccine (NCT00518180); adolescents before and after 2 doses of 4CMenB vaccine (NCT00661713); infants who had not received 4CMenB vaccine (NCT00657709) and infants after 4 doses of 4CMenB vaccine (NCT00847145) (1) .To evaluate whether the bactericidal killing of MenW strains was induced by 4CMenB vaccine, 4/11 strains were tested in competitive SBA assays in which sera were pre-incubated with 4CMenB vaccine to deplete 4CMenB vaccine antibodies (1). The subset of 11 SBA-tested MenW isolates were compared with a total of 63 MenW samples for which genetic characterization was available (these 11 plus 11 additional from 2010–2011 and 41 from 2018–2021) to evaluate their representativeness.

Results

Post-MenACWY vaccine sera elicited bactericidal titers ≥256 for all isolates (1). The post-2-dose 4CMenB vaccine adolescent and post-4-dose 4CMenB vaccine infant sera elicited titers ≥64 for 10/11 (91%) isolates (1).The 3 negative control sera pools elicited titers at or below the minimum dilution tested for all isolates (1). Bactericidal killing specificity was confirmed by the reduction of the hSBA titers of post-4CMenB vaccine sera after depletion (1). A comparison of 4CMenB vaccine antigens and clonal complex/ST of the 11 SBA-tested MenW isolates vs the complete dataset of 63 MenW samples showed that: 82% vs 92% belonged to the ST-11 clonal complex; 82% vs 90% had PorA_VR1, VR2 5,2; 82% vs 89% had fHbp variant 2 allele 22. NHBA and NadA information was available for totals of 59 and 60 strains, respectively (including 9 SBA-tested), resulting in 89% vs 90% NHBA peptide variant 29 and 89% vs 92% NadA peptide 6. This indicates that the 11 tested strains are representative.

Conclusion

These data demonstrate that 4CMenB vaccination could have an impact on MenW disease in Argentina.

PO 52 - Trends in invasive Haemophilus influenzae serotype b (Hib) disease in England; 2012/13 to 2021/22

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The Haemophilus influenzae serotype b (Hib) conjugate vaccine has been highly successful in reducing the incidence of invasive Hib disease through a combination of direct and indirect protection. Recently, several European countries have reported an increase in invasive Hib disease. We aimed to describe the epidemiology, clinical characteristics, genomic trends, and outcomes of individuals with invasive Hib disease over the past 14 years in England.

UKHSA conducts national surveillance of invasive H influenzae disease and provides a national reference laboratory for confirmation and serotyping. General practitioners are contacted to complete a clinical questionnaire for all confirmed Hib cases. Invasive Hib isolates are routinely subjected to whole genome sequencing (WGS), with multi-locus sequence typing (MLST) predicted from WGS data.

During 2012/13-2021/22, there were 6,133 invasive H. influenzae infections, of which 5,162 (84.2%) were serotyped. Most (4,305, 83.4%) were due to non-encapsulated H. influenzae, followed by Hif (531, 10.3%), Hie (167, 3.2%), Hib (107, 2.1%) and Hia (50, 1.0%). Invasive Hib disease declined from 21 cases in 2012/13 to seven in 2020/21, when COVID-19 pandemic restrictions were in place, and five in 2021/22. There were 18 (16.8%) cases in children aged <15 years, with the highest incidence in <1 year-olds (2.0/100,000; n=13).

Underlying comorbidity prevalence varied with age, from 53% (2/38) in <15-year-olds to 58.3% (14/24) those aged over 65 years. Pneumonia was the most common clinical presentation overall (59/106, 55.6%) except in <1 year-olds, where other clinical presentations (5/13, 38.5%) were more prevalent. There were three deaths (3/107; case fatality rate, 2.8%), with the last fatality reported in 2016/17.

WGS data from the 54 Hib isolates since 2016/17 revealed most strains (37/54, 68.5%) belonged to the ST6 lineage. The next most frequent MLSTs were 190, 206 and 95, all with only 2 isolates, indicating the majority of cases are likely caused by a single successful ST6 clone.

In England, invasive Hib disease remains rare and affecting mainly adults, with no fatalities reported since 2016/17.

PO 53 - Characterization of Haemophilus influenzae non-invasive disease in children, in Portugal: 2015-2022

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Background

Haemophilus influenzae is a Gram-negative bacterium that colonizes the human upper respiratory tract, where it can remain asymptomatic. It can also progress from colonizer to pathogen and cause acute mucosal infections, such as otitis and conjunctivitis, particularly in children. These infections are frequently associated to NTHi H. influenzae. Empirical treatment with antibiotics is of concern due to possible emergence and dissemination of resistant strains.

Aims / Methods

We aim to characterize H. influenzae isolates from two epidemiologically relevant non-invasive diseases, otitis media and conjunctivitis, in Portugal, from 2015 to 2022 and compare this data with results from invasive disease.

From January 2015 to December 2022, 134 H. influenzae isolates (78-ear-swab; 56-eye-swab) were collected in the National Reference Laboratory for Haemophilus influenzae, based at the NIH, in Lisbon. Most isolates were from children (99.5%; 132/134).

Capsular status was characterized by conventional PCR. Beta-lactamase producers were identified with nitrocefin. Antimicrobial susceptibility was determined by microdilution, according to EUCAST guidelines, for several antibiotics of interest. Genetic diversity was studied by MLST and ST assigned in PubMLST (https://pubmlst.org/organisms/haemophilus-influenzae/).

Results

Among 134 H. influenzae isolates, 99.3% were NTHi (133/134), whereas only one encapsulated isolate was found, and characterized as Hia (0.8%, 1/134). Beta- lactamase producers accounted for 6.7% (9/134). Antibiotic susceptibility results (n=113) showed that most isolates were susceptible to the antibiotics tested, with the exception of 34.5% resistance to trimethoprim-sulfamethoxazole (39/113). In the course of this study, we highlight the characterization of a beta-lactamase negative, NTHi isolate, resistant to ampicillin, cefotaxime, cefuroxime, amoxicillin-clavulanic acid, cefepime, and trimethoprim/sulfamethoxazole. This is the first time that we characterized resistance to cefotaxime in H. influenzae, in our country. The isolate, from a 67 years old man with multi-microorganisms corneal ulcer, was characterized as BLNAR group III-like, ST3 (confirmed by WGS).

High genetic diversity was observed among NTHi, as expected, with 22 different STs assigned for 31 isolates (71% 22/31), although ST12 and ST34 included three isolates each. When comparing the MLSTs results of isolates from both invasive and non-invasive diseases, we observed that 41% (9/22) of the STs were shared among both diseases: ST-12, ST-34, ST-142, ST-160, ST-262, ST-367, ST-396, ST-1034, and ST-1411.

Conclusion

This study highlights the importance of epidemiological surveillance of non-invasive H. influenzae disease with especial concern for the emergence of antibiotic resistant isolates, as is the case of a cefotaxime resistant isolate, which is described for the first time, in our country.

PO 55 - Salivary antibodies against Neisseria meningitidis serogroups A, C, W and Y in Norwegian 12-24 year olds

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Background

The incidence of invasive meningococcal disease (IMD) among Norwegian 16–19-year-olds was 1-7/100,000 in the decade before the COVID-19 pandemic, and serogroup Y (MenY) dominated. In a study from 2018-2019 in Norwegian secondary school students aged 12-24 years, 7.3% of participants were carriers of Neisseria meningitidis, with a peak (16.4%) in 18-year-olds (Watle 2020). Among capsulated carriage isolates, MenY was most common. Meningococcal vaccines are not part of the national immunization program in Norway, but the tetravalent meningococcal conjugate vaccine (MVC4) is recommended for 16–19-year-olds involved in activities that increase the risk of IMD. While serogroup-specific antibodies in serum are crucial for the protection against IMD, salivary antibodies may provide protection against acquisition and carriage of capsulated meningococci.

Aims and methods

We measured the level of meningococcal antibodies in saliva collected in the 2018-2019 study. Saliva samples were analyzed for meningococcal A, C, W and Y polysaccharide (PS)-specific IgA using a bead-based multiplex immunoassay (Bårnes 2015). Antibody levels were linked to data on meningococcal carriage, vaccination status and risk factors for carriage (questionnaire data) and analyzed by linear regression of log transformed concentrations.

Results

Saliva samples were collected from 1367 participants. Among the 1356 participants with known vaccination status (99.2%), mean age was 16 years (range 12-24 years), 71% were from upper secondary schools, 61% were females and 206 (17%) were vaccinated with MCV4. Preliminary results indicated that PS-IgA geometric mean concentrations (GMCs) were higher among vaccinated than among unvaccinated individuals, $p < 0.001$.

Among the 1150 unvaccinated individuals, the PS-IgA GMCs were 17.4, 7.4, 9.7 and 20.1 ng/mL for serogroups A, C, W and Y, respectively. PS-IgA levels were higher among upper than lower secondary school students for all four serogroups ($p < 0.001$). PS-IgA levels against MenY were higher among males than females ($p=0.006$), and higher in carriers of MenY ($n=19$) compared to non-carriers ($p=0.001$). Such differences were not observed for serogroups A, C or W. In multivariable analyses, attending upper secondary school or being a carrier of MenY were associated with higher MenY PS-IgA antibody levels.

Conclusion

The students had low levels of IgA antibodies in saliva against meningococci. Carriage of MenY may contribute to induction of salivary IgA antibodies against this serogroup. Further analyses will be conducted to look at meningococcal IgG antibody levels in saliva and the relationship between antibody levels in serum and saliva.

References

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PO 57 - Interlaboratory Comparison of the Meningococcal Antigen Surface Expression (MEASURE) Assay for Quantitating Surface Expression of Factor H Binding Protein

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Background

Bactericidal antibodies protect against invasive meningococcal disease (IMD). As a surrogate of protection against IMD, antibody-dependent complement-mediated killing of bacteria is measured in serum bactericidal activity assays using human complement (hSBA). However, hSBA is not suitable for testing large numbers of isolates because of the volume of sera and complement required. The surface protein factor H binding protein (FHbp) is a virulence factor and a component antigen of two vaccines licensed for meningococcal serogroup B (NmB) disease. As sequencing has identified hundreds of FHbp variants, performing hSBA assays to evaluate breadth of vaccine coverage is challenging. Since FHbp levels impact killing in hSBAs, the MEningococcal Antigen SURface Expression (MEASURE) assay was developed to quantitate surface expression of FHbp and used to predict susceptibility to antibody elicited in response to FHbp vaccine antigens.

Aims

To ensure that the MEASURE assay is robust and generates valid, reproducible results when performed in different laboratories.

Materials and Methods

FHbp surface expression is determined by flow cytometry using a broadly cross-reactive monoclonal antibody. Expression is considered positive with an FHbp-specific mean fluorescence intensity (MFI) of ≥100 that is over 3 times the MFI measured using a non-specific isotype control antibody. Pfizer transferred the validated MEASURE assay to laboratories at the UKHSA and CDC that support global meningococcal surveillance. FHbp sequence diversity and inclusion of low (n=7), medium (n=25), and high (n=10) FHbp-expression guided selection of

42 NmB test strains. Aliquots from a master cell bank for each strain were shared, and common reagent lots and equipment used. Laboratories recorded assay results in duplicate and a comprehensive statistical analysis of the composite primary data from the 3 laboratories was performed.

Results

Of the 42 pairwise comparisons, there was no disagreement between assay results from the CDC and UKHSA. Only 1 of 42 pairwise comparisons differed when comparing results from Pfizer to the CDC or UKHSA (97.6% agreement). Intermediate precision of the assay was ≤20.2% total RSD at each of the 3 laboratories.

Conclusion

The MEASURE assay provides robust quantification of meningococcal FHbp expression that can be transferred to other labs with consistent reliability and precision.

PO 58 - MATS estimated 4CMenB coverage during the period 2009 to 2019 in the Republic of Ireland

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Introduction

Neisseria meningitidis is a common cause of bacterial meningitis and sepsis in children and young adults worldwide. The CMenB vaccine contains subcapsular antigens which can induce immunity against strains of N. meningitidis, regardless of serogroup1. The meningococcal antigen typing system (MATS) estimates the potential coverage of CMenB against panels of invasive MenB strains.

Aims/Methods

We estimated MATS coverage against a panel of 122 invasive MenB strains isolated in the Republic of Ireland (RoI) between 2013 and 2019, extending MATS coverage from a previous 2009 to 2013 report.

Sequence data characterising the multilocus sequence typing (MLST) alleles and the major CMenB antigen peptides were extracted from isolate genome sequence data, hosted in the Bacterial Isolate Sequencing database (BIGSdb; www.pubmlst.org/organisms/neisseria-spp/).

Results

MATS data indicated that 4CMenB may induce protective immunity against 69% (95% coverage interval [CI95%], 54% to 90%) of circulating MenB strains in RoI. The most important peptides contributing to coverage were fHbp (49.2%) and NHBA (48.4%), then PorA p1.4 (18.9%) and NadA (0.8%). Estimated coverage was highest against the most prevalent disease-causing lineage cc41/44. While coverage varied between years, no significant temporal trends were observed. 4CMenB strain coverage was also estimated by genetic MATS (gMATS) and predicted to be 77% (LL-UL: 66-88%).

Conclusion

This dataset allows for a comparison of strain coverage against invasive MenB strains isolated either side of the introduction of 4CMenB (December 2016) into the routine national infant immunization program. The proportion of strains covered by more than one antigen decreased over time, while the overall MATS coverage estimate remained consistent.

PO 62 - Epidemiology of invasive meningococcal disease in Portugal from 2012 to 2022

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Introduction

Surveillance of invasive meningococcal disease (IMD) is essential to monitor changes in disease epidemiology, and for more effective infection control.

Aims

This work aims to analyse both the epidemiology of IMD and the genetic diversity of Neisseria meningitidis strains during the last 11 years (2012-2022) in Portugal.

Methods

Clinical samples from suspected cases of IMD and N. meningitidis isolates were sent for confirmation and strain characterization to the National Reference Laboratory for Neisseria meningitidis at the Portuguese National Institute of Health. Epidemiological analysis included demographic and epidemiological data. All identified invasive N. meningitidis isolates were characterized by WGS and sequences were submitted to the PubMLST/Neisseria database.

Results

During 2012-2022, 549 cases of IMD were reported in Portugal, 516 with the criteria of confirmed case. The average annual incidence rate of IMD was 0.48 cases per 100,000 population. A decrease of the annual incidence rate was observed, ranging from 0.72 per 100,000

population in 2012 to 0.15 cases per 100,000 population in 2022. The highest incidence rate was seen in children under 12 months (mean 14.62/100,000) and decreased markedly in the 1-4 years age group (mean 3.55/100,000). Serogroups were identified in 87% of all confirmed cases recorded. Serogroup B was the most frequent (66.3%), followed by serogroups Y (9.1%), C (4.8%), and W (4.7%). A total of 341 invasive isolates (66.1% from all IMD confirmed cases) was characterized by WGS. Twenty meningococcal clonal complexes (cc) were identified, with serogroup B cc41/44 (25.6%), cc213 (17.10%) and cc162 (8.5%), serogroup Y cc23 (65.8%), serogroup W cc11 (79.2%) and serogroup C cc11 (76.5%) the most prevalent ones. Most clonal complexes were recurrently identified over time with a similar distribution in the many Portuguese geographical regions.

Conclusions

Although the incidence of meningococcal disease has decreased over the past 11 years in Portugal, MenB meningococci are still an important cause of meningitis and septicaemia. While serogroup C IMD was rare and restricted to adults, serogroup Y IMD affected all age groups. On the other hand, serogroup W cc11 IMD has increased since 2017, initially in adults and later in children under 4 years of age. Our results underline the need for continuous surveillance of N. meningitidis infections susceptible to changes in their pattern, in order to promptly adapt IMD control strategies in Portugal.

PO 67 - The epidemiological situation of IMD in Slovakia in 2022.

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Introduction

IMD are still life threatening conditions despite advances in medicine. In 2022 the IMD death rate reached 44% which is the highest in Slovakia so far.

Aims

To describe and inform about the epidemiological situation of IMD and carriage in Slovakia in 2022. Clonal analysis of strains isolated from IMD in Slovakia during the years 2008 - 2022.

Material and methods

In the NRC for meningococci, there are confirmed and characterized the isolates and clinical specimens from IMD by classical and molecular methods (rtPCR, MLST, WGS). Information from the active surveillance of IMD in Slovakia can be found in the infectious diseases data (EPIS database) and in the NRC for Meningococci.

Results

Within the surveillance program, 31 cases of invasive meningococcal disease (IMD) were reported in Slovakia in 2022. In NRC for Meningococci we confirmed 28 ones. IMDs have showed the highest incidence at infants and 1-4 years old children. The serogroup B prevailed in 68%, serogroup W135/Y 4% and in 28% the group was not determined. Serogroup B occurred in invasive diseases of children from 0 to 9 years of age, in the adult population it occurred in one case in a patient over 50 years of age. In one case (77-year-old female patient), we failed to genomically differentiate serogroup Y from W, and therefore we present it as W/Y according to latex agglutination. The highest morbidity was observed in Sabinov region 14,9/100 000). Diseases were represented by the same percentage in men and women 50% = 50%. Clinically it was meningitis in 44 % cases, in other cases sepsis or meningitis with sepsis and WF syndrome. 13 out of 31 diseases were fatal. 7 deaths were at 0-4 years old children (5xB, 2xNG). Next 2 deaths were at teenegers (2xNG). 4 deaths involved adults (1xB, 3xNG). In 2022 the highest death rate in Slovakia was registered so far (44%). In the years 2008 - 2022 we determined that the most common hypervirulent clonal complexes involved in IMD were :11, 32, 41/44, 18, 213, 35, 865 and 23. There was proven the highest representation of serogroup B (50 %) in carriers in the years 2020-2022. Others: NG 24 %, C 4 %, D 0.8 %, Y 6.5 %, W135 4.5 %, E 5 %, X 1.7 %, H 0.5 %, Z 3 %.

Conclusion

Advanced molecular methods are essential for high quality surveillance of IMD in Slovakia.

PO 71 - Invasive Meningococcal Disease in Sweden 2019-2022

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Invasive meningococcal disease (IMD) is notifiable in Sweden. The reporting system comprises of mandatory notification of cases and mandatory laboratory notification of samples to the Public Health Agency of Sweden, Stockholm. All samples should be sent to the National Reference Laboratory (NRL) for Neisseria meningitidis in Örebro for further typing and surveillance.

Compiled data representing all reported cases of IMD in Sweden during 2019 to 2022 resulted in 127 cases of IMD, where of 52% (n=66) were reported in 2019, 22% (n=28) in 2020, 8% (n=10) in 2021 and 18% (n=23) in 2022. Indicative of decrease in meningococcal disease, as well as for other invasive respiratory infections, noted during the COVID-19 pandemic. The year 2021, demonstrated an all-time low incidence of IMD in Sweden (10 cases, corresponding to an incidence of 0.1 per 100 000 population and year), which is the lowest reported number of meningococcal disease during the last century.

Of the 127 reported cases of IMD, samples from 109 were sent to the NRL, where 100 were culture- and nine were PCR-confirmed. The group distribution was 36% MenW (n=39), 34% MenY (n=37), 21% MenB (n=23) and 9% MenC (n=10). Among the patients 48% were females and 52% males, aged from 1 month to 94 years with median age of 32 years (mean 41 years). The

incidence was highest among infants (<1 year), teenagers (age group 15-19), young adults (age group 20-24) and elderly (age group >80). The case fatality rate was 14% in 2019, 4% in 2020, 10% in 2021 and 9% in 2022. The majority of IMD episodes were sporadic, however two IMD cases in 2019 had an epidemiological linkage.

To conclude, the incidence of IMD in Sweden is low and decreased further during the COVID-19 pandemic to a record low incidence in 2021. However, the number has now started to rise again and the coming years will elucidate what this sudden interruption, the COVID-19 pandemic, will lead to in terms of disease burden, group and age distribution.