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Ala-Eddine Deghmane, Sylvie Haeghebaert, Eva Hong, Améliane Jousset, Anne-Sophie Barret, et al.. Emergence of new genetic lineage, ST-9316, of Neisseria meningitidis group W in Hauts-de-France region, France 2013–2018. Journal of Infection, 2020, 80 (5), pp.519-526. 10.1016/j.jinf.2020.01.020 . pasteur-02618590

HAL Id: pasteur-02618590
https://pasteur.hal.science/pasteur-02618590

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Journal of Infection 80 (2020) 519–526

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Emergence of new genetic lineage, ST-9316, of *Neisseria meningitidis* group W in Hauts-de-France region, France 2013–2018

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ARTICLE INFO

Article history:
Accepted 23 January 2020
Available online 4 February 2020

Keywords:
Meningococcal disease
Group W
Epidemiology
Typing
Whole genome sequencing

SUMMARY

Background: The epidemiology of invasive meningococcal disease (IMD) is continuously changing in incidence, age distribution and/or the expansion of new strains of *Neisseria meningitidis*. The epidemiology of IMD due to group W (IMDW) has changed recently at a global level with the emergence of isolates belonging to the clonal complex ST-11 (CC11) derived from the South America-UK strain. A more recent change has been detected in France with the emergence of a new genotype distinct from CC11 that we aimed to analyse.

Methods: Epidemiological and microbiological surveillance data in France were used in combination with whole genome sequencing (WGS) to detect emerging phenotypes and genotypes of IMD causing strains, and their susceptibility to immunity induced by the 4CMenB vaccine. Transgenic mice expressing the human transferrin were used to analyse the virulence of emerging strain isolates by direct comparison with CC11 isolates.

Findings: Our data showed a local increase of IMDW isolates in north France since 2013. The isolates belonged to ST-9316 and few were ST-11 isolates. WGS clustered ST-9316 isolates together and were distantly separated from the isolates of the clonal complex ST-11 (CC11). Unlike cases due to W/CC11 isolates, cases due to W/ST-9316 isolates were mostly observed amongst infants under the age of 1 year but with lower mortality compared to W/CC11 cases. Genomic comparison showed that the W/ST-9316, unlike W/CC11 isolates, lacked the *hmbR* gene encoding the haemoglobin receptor that is a virulence factor involved in the acquisition of iron from haemoglobin. W/ST-9316 further showed lower virulence in mice compared to W/CC11 isolates.

Interpretation: We report the emergence of a novel sequence type (ST-9316) mostly associated with serogroup W, and exhibiting a lower virulence and a distinct age specific incidence profile than W/CC11 isolates. Surveillance requires powerful approaches combining WGS and pathophysiological analysis to adapt control measures.

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Introduction

The epidemiology of invasive meningococcal disease (IMD) is changing frequently in time and space with changes in the incidence, age distribution or group distribution which may be related the emergence and the clonal expansion of new strains of *Neisseria meningitidis* (Nm). Nm is an encapsulated bacterium and the structure of the capsule defines the 12 known groups of which six, (A, B, C, W, Y and X), are responsible for virtually all the IMD cases worldwide.[1] Molecular typing is also used to distinguish between meningococcal isolates. In particular multilocus sequence typing (MLST) catalogues the polymorphism of several metabolic genes into unique sequence type (ST). Close STs are further clustered into clonal complexes (CC). This allows the relationship amongst meningococcal isolates to be tracked. For example, in the recent years, group W isolates emerged in several regions worldwide.[2–4] These isolates belonged to ST-11 of the clonal complex (CC11) which is one of the hyperinvasive genetic lineages of Nm. NmW/CC11 first emerged globally during the pilgrimage to Mecca in 2000 that was followed by an epidemic increase of NmW/CC11

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https://doi.org/10.1016/j.jinf.2020.01.020
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in several countries of the African Sub-Saharan meningitis belt. Thereafter, these isolates decreased in this region but re-emerged again by 2010.[5,6] Another emergence was reported in South America and more recently in several European countries.[2,4] Although all isolates belonged to the same CC11, analysis based on whole genome sequencing (WGS) provided more resolution into the genetic structure of the NmW/CC11 isolates. Two major genetic sub-lineages are characterized: the first called Anglo-French-Hajj and was involved in the first Hajj-linked emergence in 2000 as well as the spread to the African sub-Saharan meningitis belt and South Africa. The second sub-lineage was called the South American-UK and was involved in the recent emergence and spread in South America and several European countries including France.[2,7] After it spreads in Europe, two groups were characterized within the South-American-UK sub-lineage: the original UK strain and the UK-2013 strain.[7–9] In France, the current vaccination strategy against IMD is composed of a compulsory vaccination (since 2018) using two doses at 5 months and 12 months of age of a conjugate vaccine against NmC with a catch-up until the age of 24. While vaccines against NmB and NmACWY are recommended for at risk population and for outbreak control.[10]

We previously described the successive waves and the epidemiology of IMDW cases associated with CC11 (IMDW/CC11) in France.[8] WGS on all isolates was implemented in 2015 by the National Reference Centre for Meningococci (NRCM) to detect and follow the emergence and expansion of Nm isolates. In this work we describe the use of WGS data to detect the emergence of NmW isolates belonging to a new genetic linage distinct from CC11. We report here the clinical, epidemiological, pathophysiological and bacteriological characteristics of cases belonging to this new genotype.

Methods

Surveillance of invasive meningococcal disease in France

The French surveillance system of IMD is based on mandatory notification of cases on a standardized case definition basis as well as the typing of isolates.[11] Cases are notified to Health Regional Agencies, which are in charge of the implementation of local control measures to prevent further cases amongst close contacts (chemoprophylaxis and prophylactic vaccination for serogroups A, C, W, Y). The completed notification forms are sent and centralized at the French national public health agency (Santé publique France) for epidemiological surveillance. The clinical isolates or samples are also sent to the National Reference Centre for Meningococci (NRCM) for confirmation of group and full strain typing. Meningococcal groups are determined by agglutination of cultured isolates using specific “in house” rabbit sera and by PCR for non-cultured confirmed cases by targeting the following genes for the identification of Nm (*ctrA* and *sodC*) and for genogrouping of groups A, B, C, W, Y and X (*csaB, csb, csc, csw, csy* and *csxA*) respectively.[12,13] Epidemiological and typing data are merged by using a unique identification code. These data are used to monitor the epidemiology of IMD and to investigate clusters of increases in local incidence rates.

Genomic analysis

Meningococcal isolates were cultured on Difco™ GC (Gono-Coccal) medium base supplemented by Kellogg supplements[14] Genomic DNA is extracted with the MagNA Pure 96 system (Roche Molecular System, Pleasanton, USA). Library preparation are performed with the Nextera® XT DNA library Preparation Kit (Illumina, San Diego, USA) and WGS is processed with Illumina technology (NextSeq 500, Illumina) with paired-end strands of 150 bp and a sequencing depth of 50X. All de novo assemblies are performed with SPAdes (CAB, St. Petersburg State University, Russia). Sequences are available through the pubMLST (https://pubmlst.org/neisseria/.[15] Moreover MLST and the clonal complex (CC), porA and FetA sequencing are performed on PCR-confirmed cases.[15] For the typing purposes, the data from WGS and serogrouping are expressed as a genetic formula: G :P1.PorA-VR1,PorA-VR2:FetA:CC that define the group (G), the two variable regions (VR1 and VR2) of the outer membrane protein PorA, and of one VR of the protein FetA, as well as the CC. In this work, we used the term of group for both serogroup of cultured isolates determined by agglutination using capsule specific antisera and genogroup determined by PCR. WGS analysis was performed on the basis gene-by-gene approach of the 1605 core genome MLST loci (cgMLST) available through the pubMLST.org/neisseria platform.[15] This approach allows resolving the relationships amongst the study isolates into a distance matrix. We performed three additional genomic analyses using specific schemes available through the pubMLST.org/neisseria platform: The capsule genes as well as the regions upstream and downstream of the capsule locus on the chromosome (NEIS0001 to NEIS0044; NEIS0068 to NEIS0115 respectively).

SplitsTree4 (version 4.13.1) was used to visualise the resulting distance matrices as Neighbour-net networks.[16] The IDs of all these isolates are given in the supplementary Table to allow retrieving of WGS sequence in FASTA formats as well as the ENA accession numbers.

Epidemiological analysis

The IMD database centralized at the French public health agency and case management information transmitted by the Regional Health Agency of Hauts-de-France were used to describe the clinical and epidemiological characteristics of cases belonging to ST-9316 cluster and compare them to IMDW/CC11 cases whose incidence has constantly increased in other regions in France since 2014. The descriptive analysis was performed using Microsoft Excel. The data were presented as median age with minimum and maximum age and splitted into several age groups.

Mice infection model

The virulence of isolates belonging to the ST-9316 was compared to that of isolates belonging to the ST-11 in transgenic mice expressing the human transferrin. This model was developed in our laboratory as a relevant model allowing meningococcal growth in blood by providing the required human transferrin as an iron source.[17] This animal experiments were carried out in strict accordance with the European Union Directive 2010/63/EU (and its revision 86/609/EEC) on the protection of animals used for scientific purposes. Our laboratory has the administrative authorization for animal experimentation and the protocol was approved by the Institut Pasteur Review Board that is part of the Regional Committee of Ethics of Animal Experiments of Paris Region (Permit Number: 75–1554). All the invasive procedures were performed under anaesthesia and all possible efforts were made to minimize animal suffering.

The infection experiments were performed as previously described.[17] Briefly, 8-week-old mice were infected by intraperitoneal injection of isolates belonging to the STs (ST-11 and ST-9316). Six isolates of each ST were tested. (Table 1). Blood samples were drawn after 3 h and 24 h and the infection was followed by determining blood bacterial load by plating serial dilutions of blood on GCB plates. Mortality in mice were also followed up to 48 h infection.

An inflammatory cytokine CXCL1 also known as keratinocyte-derived chemokine, KC and has neutrophil chemotactic activity[18]

Table 1
Main clinico-epidemiological characteristics of ST-9316 and ST-11/IMDW cases identified in the Hauts-de-France region from 2013 to 2018.

	IMD W/ST-9316 ($N=15$)	IMD W/CC11 ($N=11$)
Median age (years) [min–max]	1[0–82]	53 [1–93]
<5 years	10 (67%)	1 (9%)
6–14 years	0 (–)	0 (–)
15–24 years	0 (–)	2 (18%)
25–49 years	1 (7%)	1 (9%)
≥ 50 years	4 (27%)	6 (55%)
Sex ratio M/F	0.7	0.9
Septic choc (including *purpura fulminans*) (%)	13%	73%
sequelae (%)	0%	9%
Case fatality rate (%)	1 (6.6%)	3 (33%)

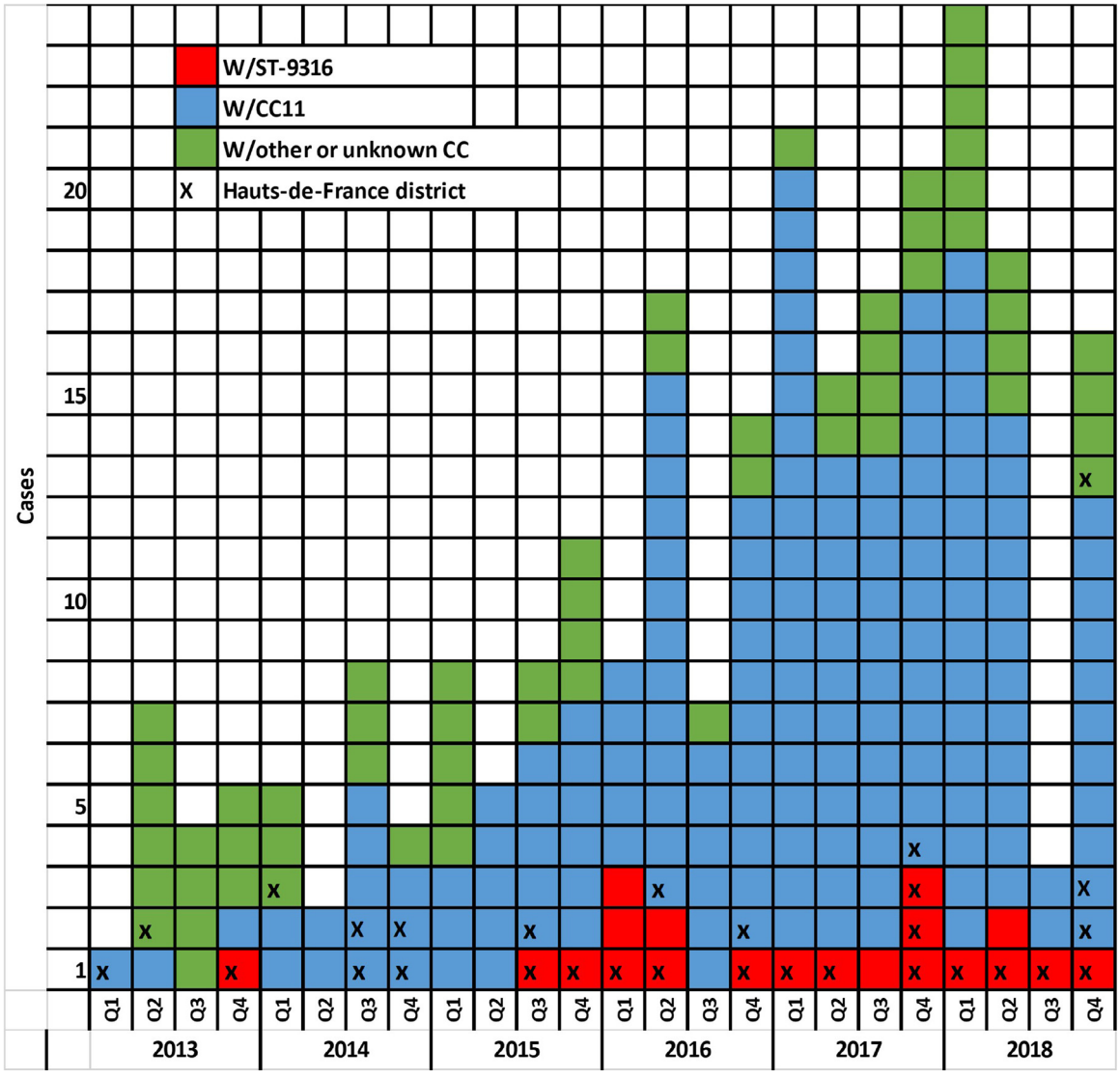


Fig. 1. Epicurve of IMDW cases by trimester of onset, France, 2013–2018.

was also followed by ELISA kit (R&D Systems Minneapolis, MN, US) according to the manufacturer's recommendations in the same blood samples that used to bacterial numerations. The results were compared using a two-tailed Mann-Whitney test for statistical analysis, with a P value of <0.05 being considered statistically significant.

Coverage of isolates by the 4CMenB vaccine

Coverage of NmW/ST-9316 isolates by the 4CMenB vaccine was explored by testing serum bactericidal activity (SBA) using sera and human complement (hSBA) and materials that were previously described.[19] Sera from two subjects and pooled sera from 10 other subjects were obtained before and after vaccination by the 4CMenB from adults who were not previously vaccinated by ACWY vaccine.

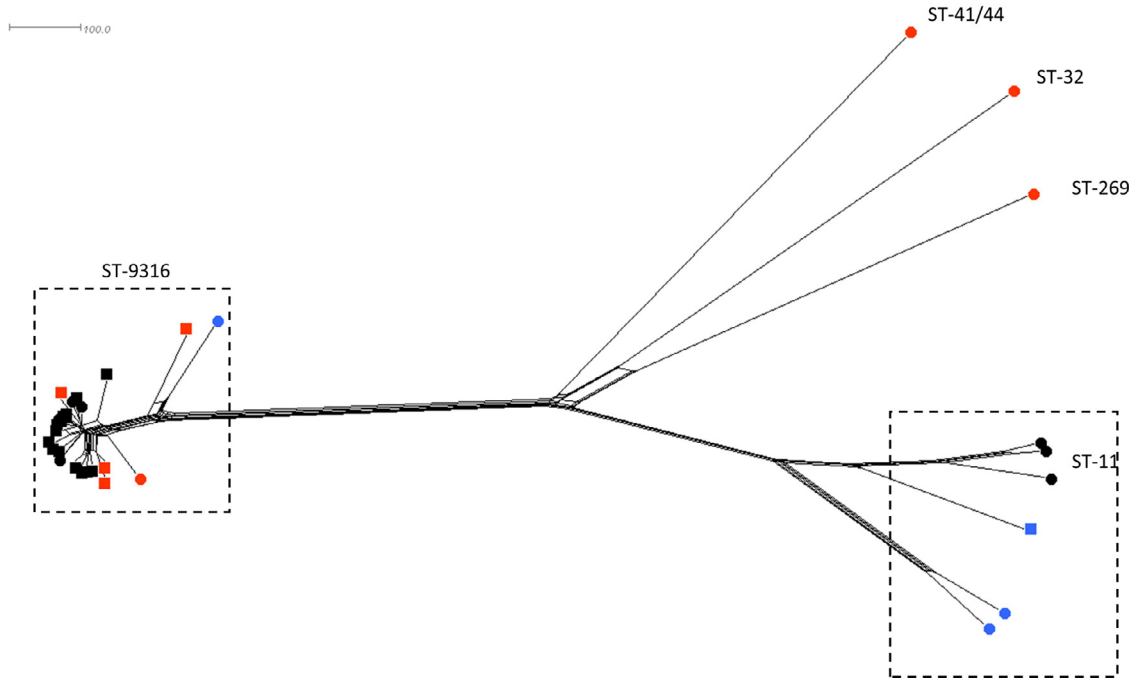


Fig. 2. A neighbour-network based on cgMLST allelic profiles of the 1605 genes of the cgMLST. The data are for 24 invasive isolates belonging to the ST-9316 with WGS data. The IDs of these isolates on the pubMLST.org/neisseria database are (group W: 41230, 41807, 41808, 42201, 43995, 49250, 50824, 50841, 51200, 51470, 52785, 56301, 56396, 56438, 56442, 58102, 61323, 61908, 84156; group B: 51194, 57622, 59519, 84153 and group C: 52778). In addition, we added isolates of ST-11 (group C: IDs 26821, 39617, 42037 and group W: ID 41857, 42758, 51648), ST-32 (group B ID 27088), ST-41/44 (group B ID 51551) and ST-269 (group B ID 39973). Isolates from the Hauts-de France are represented in square while other regions are indicated by circles. The colour of the circle indicates the group of the corresponding isolate (red, group B, bleu group C and black group W). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

These adults received 2 doses of the 4CMenB at one-month interval and blood samples were taken before the first dose and one month after the second dose. Two ST-9316 isolates and one ST-11 isolate were tested. The serogroup B strain (H44/76) was used as a positive control. The units of bactericidal titres were expressed as the reciprocal of the highest dilution that allows 50% of bacterial killing hSBA titres of at least 4 are considered to be correlated with the protection.[20]

Results

Increase of invasive meningococci belonging to a new sequent type

Between 2013 and 2018, IMD cases ($n=27$) due to an unusual sequence type, ST-9316, were identified in France by the NRCM by culture or PCR ($n=24$ and $n=3$ respectively). These isolates do not belong to a defined clonal complex amongst the currently defined CC in the pubMLST.org/neisseria database. The majority of ST-9316 isolates ($n=20$ isolates, 74%) associated with group W while only few associated with group B or group C ($n=6$ and $n=1$ respectively; 26%).

IMDW cases associated with ST-9316 (IMD/ST-9316) experienced a quasi-exponential increase and were distributed as follows: 1 case in 2013, 2 cases in 2015, 6 cases in 2016, 9 cases in 2017 and 9 in 2018. Considering only group W, the number of cases was 1 in 2013, 2 in 2015, 6 in 2016, 6 in 2017 and 5 in 2018 (Fig. 1). The index case of this cluster of IMDW/ST-9316 was identified in December 2013 in the Hauts-de-France region in a young woman of 29 years old from another European country and visiting this region. She presented a fulminant clinical presentation with septic shock syndrome and acute disseminated intravascular coagulation that led to death.

Interestingly, 19 (15 W and 4 B, 70%) of the 27 cases belonging to this ST-9316 cluster were residents of the Hauts-de-France region, located in the north part of France, but they lived in different cities. Globally, around 45–50 cases of IMD were reported per year in this region during the period 2013–2018 and were mainly due to group B and C (>75%) belonging to divers genotypes. No epidemiological links between the cases of ST-9316 were identified retrospectively when looking at the information gathered by the Regional health agency during the case management. The other 8 cases belonging to this cluster (3 in 2016, 2 in 2017 and 3 in 2018) lived in 6 different regions in France.

Over the study period (2013–2018), 29 cases of IMDW of all subtypes were identified in the Hauts-de-France region and 230 in the rest of France. In Hauts-de-France, the incidence rate of IMDW increased from 0.05/100 000 inhabitants in 2013 to 0.12/100 000 inhabitants in 2018. In parallel, an increase in the incidence rate of IMDW in whole France was also observed from 0.04/100 000 to 0.09/100 000 in 2018.[11] This increase was mainly due to the expansion of isolates belonging to the South American/UK sublineage.[8]

In Hauts-de-France, half of IMDW cases (52%, $n=15/29$) belonged to ST-9316 versus only (2%, $n=5/230$) for the rest of the country. The other isolates belonged to the CC11 CC22 and other rare CCs. Amongst all IMDW cases, the proportion of CC11 was nearly two times lower (38%) in Hauts-de-France compared to the rest of the country (67%).

Main characteristics of W/ST-9316 IMD cases in Hauts-de-France

The male to female ratio was 0.7 for the 15 cases due to W/ST-9316, slightly lower than for cases due to NmW/CC11 (0.9) in Hauts-de-France.

The age specific incidence was different between IMDW/ST-9316 and IMDW/CC11 cases with 60% of ST-9316 cases aged less than 2 years old. The median age was lower amongst IMDW/ST-9316 cases (1 year) than for IMDW/CC11 cases (53 years) (Table 1).

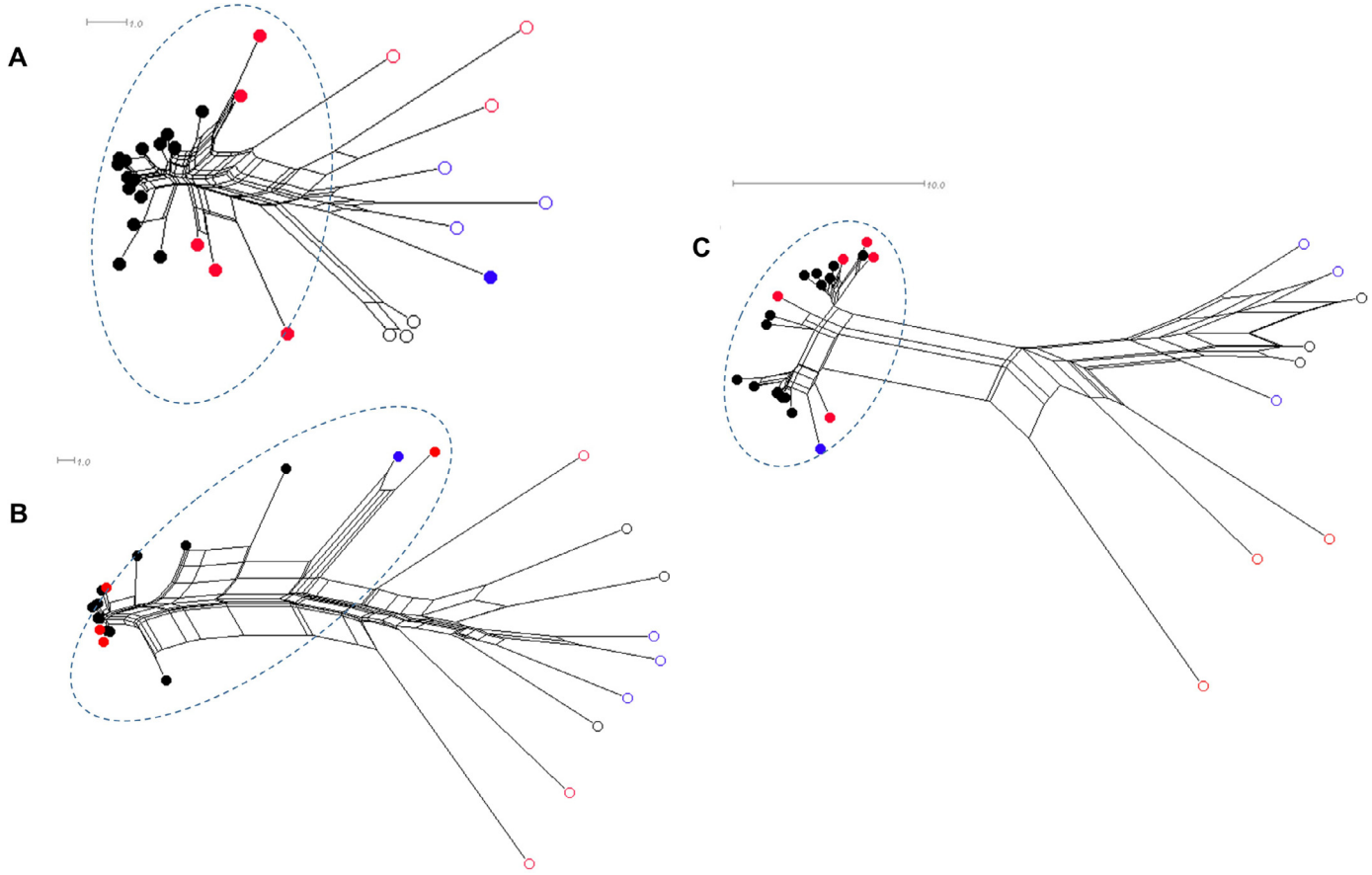


Fig. 3. A neighbour-network based on allelic profiles of the capsule genes (A), the upstream region of the capsule genes between the genes NM0001 to NM0044 (B) and the downstream region of the capsule genes between the genes NM00068 to NM0115 (C). The data are for the same isolates in Fig. 2. ST-9316 isolates are surrounded by dotted lines. Isolates of serogroup B are represented by red (filled circles represent ST-9316 and open circles represent other STs). Isolates of serogroup C are represented by blue circles (filled circles represent ST-9316 and open circles represent other STs). Isolates of serogroup W are represented by black circles (filled circles represent ST-9316 and open circles represent other STs). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Global analysis of this age distribution of cases using Mann-Whitney test suggests significant difference ($P<0.05$). However, the small number of cases per age group prevent robust analysis.

Clinically, the 10 children infected with W/ST-9316 strains all presented with meningitis while the 5 adults all developed septicaemia. Severe forms (septic shock syndrome or *purpura fulminans*) and case fatality rates were lower in W/ST-9316 cases than in W/CC11 cases (Table 1).

Genomic analysis of the ST-9316 isolates

We next analysed the WGS data by cgMLST for the 24 cultured isolates. We also added representative strains of other clonal complexes (CC11, CC32, CC41/44 and CC269) as external groups. The neighbour-network based on cgMLST tree using the allelic profiles of the 1605 loci is depicted in Fig. 2. All isolates belonging to the ST-9316 were clustered together and were highly linked. This cluster contained a single group C isolate in addition to 5 group B isolates. They were distantly separated from the other isolates, with more than 1300 alleles different compared to other STs. The close relationship between B, C and W isolates of ST-9316 suggest a common origin of these isolates. We therefore performed additional genomic analysis on the basis of genes of the capsule loci, genes that are located upstream (NEIS0001-NEIS0044) and downstream (NEIS0068 to NEIS0115) of the capsule region A. This analysis clearly suggests closer relationships of the ST-9316 group B and W isolates (Fig. 3). Moreover, most of the ST-9316 group B and W isolates shared the same alleles of the capsule transport genes (*ctrA* to *ctrF*: NEIS0055 to NEIS0058 and NEIS0066-NEISS0067). These alleles differed from those of groups W and B belonging to other genotypes (Fig. 3). These data suggest extensive recombination between ST-9316 isolates and capsule switching events between groups W and B.

The W/ST-9316 isolates shared several identical allelic profiles that are different from those of lineages of CC11 isolates. The genes corresponding to these common alleles are mainly involved in metabolic process. However, few other genes involved in interactions with host cells such as genes encoding FetA, PorA, factor H binding protein (Fhbp). Interestingly, all the W/ST-9316, unlike the W/CC11 isolates, lacked the *hmbR* gene encoding the haemoglobin receptor gene that is involved in the acquisition of iron from haemoglobin.

Comparative virulence of ST-9316 isolates

As NmW/ST-9316 isolates seem to provoke IMD with lower severity compared to NmW/cc11 isolates, we explored the virulence of these isolates in the transgenic mice expressing human transferrin. Six isolates of ST-11 from several sub-lineages (the South-American-UK strain and the Anglo-French Hajj strain) and six isolates of W/ST-9316/ ($n=6$), B/ST-9316/ ($n=3$) and C/ST-9316/ ($n=1$) were selected. After intraperitoneal injection bacteria were detectable in all mice 3 h after infection but CFU in blood of mice infected by ST-11 isolates were significantly higher after 3 h and particularly after 24 h of infection. Indeed, ST-11 isolates were able to provoke sustained bacteraemia that did not decrease after 24 h

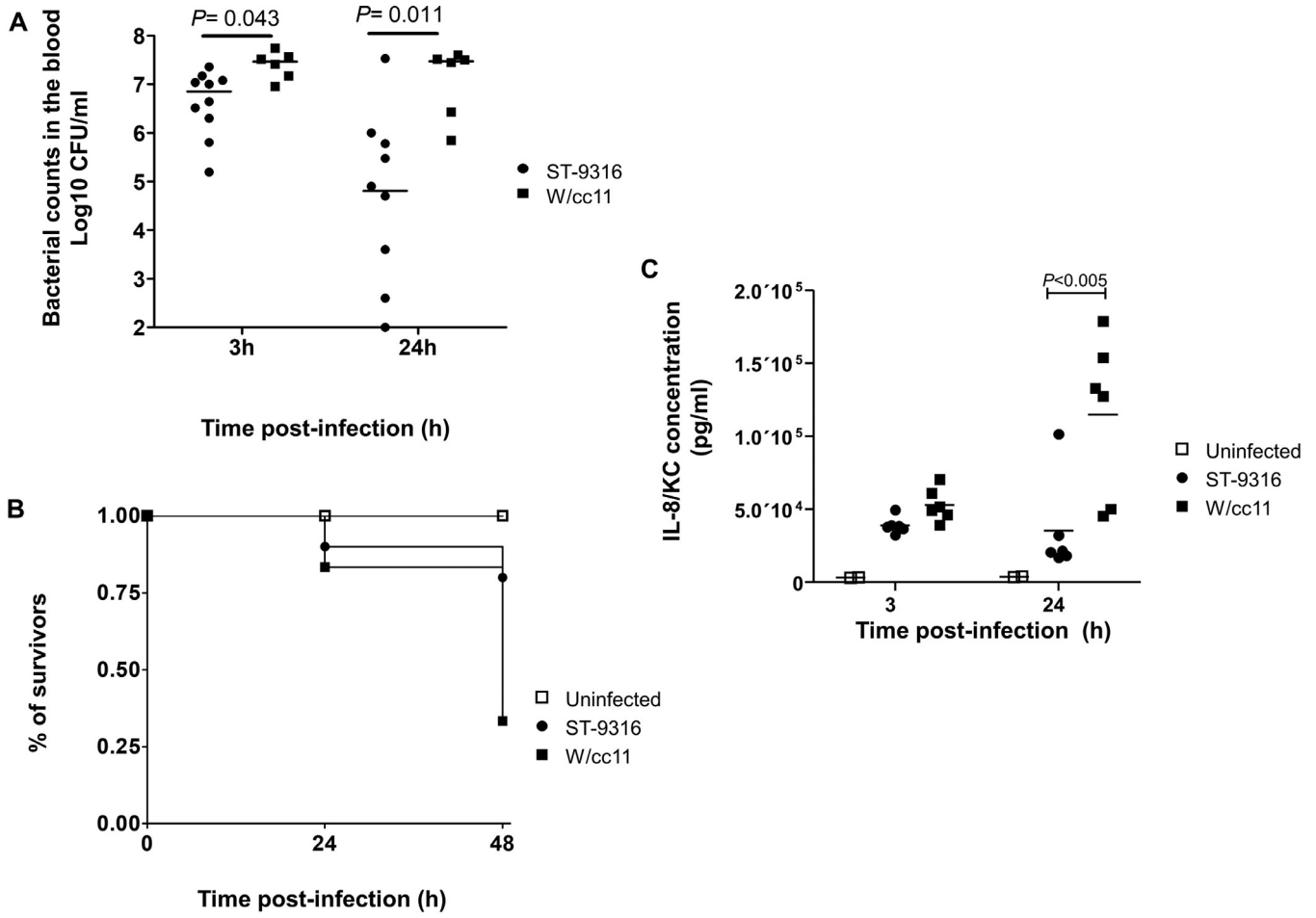


Fig. 4. Analysis of the pathogenesis of W/ST-9316 isolates compared to the W/cc11 isolates in transgenic mice expressing the human transferrin (10 mice infected by ST-9316 and 6 mice infected with W/ST-11). (A) Levels of bacteraemia in individual mice infected by and ST-9316 isolates (groups W (6 isolates), B (3 isolates) and C (1 isolate)) and W/cc11 after 3hours and 24hours of intraperitoneal infections. Data are presented as scattered points with mean for each group. (B) Survival of mice of non-infected and infected mice (ST-9316 and W/cc11 as in A) up to 48 h of intraperitoneal infection. (C) Levels the inflammatory cytokine KC in the blood of individual mice infected by and ST-9316 isolates and W/cc11 (as in A) after 3hours and 24hours of intraperitoneal infections. Data are presented as scattered points with mean for each group. A group of two non-infected mice were included as controls. Significant differences between the two groups are indicated.

Table 2
hSBA titres of 4CMenB vaccinated subjects against W/cc11 and W/ST-9316 isolate.

Strain	ST	Group	Titre before vaccination	Serum subject 1 Titre after vaccination	Serum subject 2 Titre after vaccination	Pooled sera Titre after vaccination
LNP30664	9316	B	<4	<4	<4	8
LNP30784	9316	W	<4	128	128	ND
H44/76	32	B	<4	128	128	128
LNP30813	11(UK-2013)	W	<4	128	8	ND

ND, not determined.

of infection while bacteraemia decreased drastically in mice infected with ST-9316 isolates after 24 h of infection (Fig. 4A). Moreover, mortality of mice was significantly higher at 48 h of infection in ST-11 infected mice compared to ST-9316 infected mice (67% versus 20% respectively; Fig. 4B). This lower virulence of the ST-9316 isolates correlated well with lower induction of inflammatory response. Indeed, the levels of the KC cytokine in the blood of ST-9316 infected mice were significantly lower than those of ST-11 infected mice after both 3 h and 24 h of infection (Fig. 4C).

Coverage of NmW isolates by the 4CMenB vaccine

NmW isolates are expected to be covered by the plain or conjugated polysaccharide capsule vaccines containing component against the serogroup W capsule. Furthermore, the protein-based vaccine, 4CMenB vaccine that targets isolates of serogroup B, can be effective against serogroup W/CC11 isolate as these isolates produce vaccine-matching proteins.[21] The majority of W/ST-9316 cases were amongst infants under the age of 1 year where vaccine targeting Nm serogroup B (such as the 4CMenB) can be used. We therefore were interested in testing whether this protein-based vaccine covers the NmW of the ST-9316 isolates. For this purpose, we explored the coverage of NmW isolates by the 4CMenB by hSBA assays and using pooled sera from vaccinated before and after vaccination (see Materials and Methods). hSBA titre using sera before vaccination was lower than the threshold[4] that is correlated with protection. The titre against the W/ST-9316 and the B/ST-9316 isolates increased to 128 and 8 in sera obtained 1

month after the second dose of the 4CMenB respectively. This titre against the W/ST-9316 isolate was similar to hSBA titres against the strain H44/76 and a W/CC11 isolates (Table 2). These data suggest that the isolates W/ST-9316 are expected to be covered by the 4CMenB vaccine. Accordingly, all the ST-9316 isolates associated with groups B, C and W harboured the same peptides of fHbp, NHBA, NadA (321, 243 and 21 respectively). These isolates are predicted to be covered by the 4CMenB by at least the NHBA peptide on the basis of the genetic Meningococcal Antigen Typing System, MATS (gMATS).[22]

Discussion

This work describes an emerging cluster of IMDW/ST-9316 cases that were genetically linked and geographically clustered in the Haut-de-France region in France. The increase of IMDW/ST-9316 cases that was concomitant to that observed in the whole country but mostly due to isolates of group W/CC11.[8] The ST-9316 isolates are genetically quite different from CC11.

The systematic sequencing of invasive meningococcal isolates for surveillance purpose allowed the identification of this new "genetic cluster" of IMD cases belonging to the ST-9316. The vast majority of cases were clustered in the Hauts-de-France region. The index case was most likely imported and was detected in 2013 in a person visiting Hauts-de-France but who lived in another European country.

The isolates of the ST-9316 that are reported to the pubMLST.org/neisseria database (accessed on the 14th November 2019) are of groups B, C and W and were mainly from France and Poland in addition to few isolates from the Czech republic, Germany, Ireland and the UK. The earliest isolates were of group B and were detected in 2010 in Poland. In France, this sequence type is dominated by group W with geographical localization in the north of France. However, ST-9316 group B isolates seem to be highly related to those of group W and the genomic analysis suggest several events of capsule switching between these two groups. The data may suggest intensive circulation of these isolates. The limited vaccination amongst close contacts may have selected W to B switching but this hypothesis remains to be explored. A generalized vaccination can be advocated to prevent the circulation of these isolates.

We also observed in our study that clinico-epidemiological characteristics of NmW/ST-9316 cases were different from those of NmW/CC11 cases and mainly occurred in young children.

The proportion of severe clinical forms and the case fatality rate were also lower than for CC11 supporting the hypothesis of less pathogenicity or virulence amongst ST-9316 strains. These data were further supported by data from the experimental infection in mice with significant lower bacteraemia and lower mortality in ST-9316 infected mice as well as lower inflammatory response. Indeed, the genomic comparison revealed several differences between these isolates that mostly involved metabolic enzymes that may impact on the competition of the isolates with other bacterial species for the colonization of the ecological niche, the nasopharynx (metabolic fitness).[23] In addition, few other genes involved in virulence differed from those of the CC11 hyperinvasive isolates. These genes, such as Fhbp, are involved in meningococcal survival in the blood.[24] Of interest, the absence of *hmbR* gene in the NmW/ST-9316 isolates: this gene has been recently shown to contribute to different virulence profile between carriage and invasive of meningococci.[25] These differences may be correlated with the lower severity of infections by W/ST-9316 isolates.

Changing meningococcal epidemiology may therefore occur rapidly with varying situation across the country. The concomitant increase in ST-9316 in Hauts de France while CC11 strains increased in the rest of France needs further exploration to be explained. Such a situation highlights the need for extensive and integrated surveillance using WGS to detect rapidly the spread of a new isolate. Capsular-based vaccination against group W isolates should cover most of ST-9316 isolates. Moreover, these NmW/ST-9316 isolates are also expected to be covered by the 4CMenB that may be used in infant <1 year to control IMDB disease on the basis of expressing at least one matching peptide (NHBA) with the 4CMenB vaccine. This information would be interesting in future evaluation of possible vaccination strategies against IMD in infants, considering vaccination using the 4CMenB or the ACWY vaccines.

In Hauts de France, the situation did not require to implement specific preventive measures for the population, beyond the prophylactic vaccination for close contacts of cases, given that no clear geographical clustering of cases nor epidemiological link were identified between IMDW/ST-9316 cases. However, the situation is closely monitored to detect any rise in the disease in a specific population group or in a geographical area.

Declaration of Competing Interest

The authors declare that there is no conflict of interest.

Acknowledgments

This work was supported by the Institut Pasteur, and Santé Publique France. We would like to acknowledge the persons who contributed to this investigation, in the Regional Health Agency and in the regional office of the French public health agency in Hauts-de-France region. We also thank the team in charge of the surveillance of IMD at the French national public health agency (Denise Antona, Christine Campese, Daniel Lévy-Bruhl, Catherine Maine, Yann Savitch). We also thank the team of the NRCM (Myriam Aouiti-Trabelsi, Sara Chehboub, Mélanie Denizon, Michaël Falguières, and Aude Terrade). This publication made use of the Neisseria Multi Locus Sequence Typing website (https://pubmlst.org/neisseria/) developed by Keith Jolley and sited at the University of Oxford.[15] We also acknowledge the PIBNET-P2M platform at the Institut Pasteur.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2020.01.020.

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