Australian Meningococcal Surveillance Programme Annual Report, 2020

Monica M Lahra, CR Robert George, Masoud Shoushtari and Tiffany R Hogan for the National Neisseria Network
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Abstract

Invasive meningococcal disease (IMD) is a notifiable disease in Australia, and both probable and laboratory-confirmed cases of IMD are reported to the National Notifiable Diseases Surveillance System (NNDSS). In 2020, there were 90 notifications of IMD, the lowest number documented since records began in the NNDSS in 1991. Of these, 97% (87/90) were laboratory-confirmed cases, with 70% (61/87) confirmed by bacterial culture and 30% (26/87) by nucleic acid amplification testing. The serogroup was determined for 85/87 laboratory-confirmed cases of IMD: serogroup B (MenB) accounted for 64% of infections (54/85); MenW for 19% (16/85); MenY for 16% (14/85); and MenC 1.2% (1/85). Fine typing was available on 60/85 (71%) of cases with serogroup determined; of the typed MenW, all were PorA antigen type P1.5,2 and sequence type 11, the hypervirulent strain reported in recent outbreaks in Australia and overseas.

The primary peaks of IMD notifications in Australia in 2020 were observed in infants less than 1 year (16/87, 18%) and in adults aged 45–64 years (14/87, 16%). MenB infections predominated in those aged less than 5 years and 15–19 years; MenW and MenY infections predominated in those aged 45 years or more.

All 61 IMD isolates were tested for antimicrobial susceptibility: none were penicillin resistant; however, 56/61 (92%) had decreased susceptibility to penicillin. All isolates were susceptible to ceftriaxone, ciprofloxacin and rifampicin.

Keywords: antibiotic resistance; disease surveillance; meningococcal disease; Neisseria meningitidis

Introduction

Australia’s National Neisseria Network (NNN) was established in 1979 as a collaborative network of reference laboratories in each state and territory that contribute to the laboratory surveillance of the pathogenic Neisseria: N. meningitidis and N. gonorrhoeae. The NNN has coordinated laboratory data from cases of invasive meningococcal disease (IMD) for the Australian Meningococcal Surveillance Programme (AMSP) since 1994, and is supported by the Australian Government Department of Health and the jurisdictions.1 The NNN laboratories supply phenotypic and genotypic data to supplement the notification data from the National Notifiable Diseases Surveillance System (NNDSS), which includes cases of probable and laboratory-confirmed IMD.

As recorded by the NNDSS, notifications of IMD in Australia peaked in 2002 at 3.5 cases per 100,000 persons,2 with the majority of disease at that time caused by MenB and MenC. In 2003 the introduction of the conjugate serogroup C meningococcal vaccine to the National Immunisation Program (NIP) was followed by significant and sustained reduction of both the number of serogroup C IMD, and the overall notifications to a nadir of 0.6 cases per 100,000 in 2013.3,4 After 2013, the IMD notification rate increased to 1.5 cases per 100,000 in 2017,2 when MenACWY immunisation programmes were
implemented across jurisdictions in targeted age groups. This was followed by a change in the NIP in 2018 substituting monovalent MenC vaccine with the quadrivalent MenACWY vaccine. IMD notifications declined to 1.1 per 100,000 in 2018, and 0.8 per 100,000 in 2019. In 2020, there were 0.3 cases per 100,000 recorded, representing a reduction in disease rate beyond expected vaccine impact and likely attributable to the impact of public health measures implemented in the coronavirus disease 2019 (COVID-19) pandemic. IMD is a rare disease in Australia, but one of public health concern, and continued monitoring of phenotypic and genotypic features of IMD strains is critical to plan and inform clinical management of cases, case clusters and outbreaks of IMD locally and nationally, and for informing and monitoring public health interventions.

Methods

Case confirmation of invasive meningococcal disease

Case confirmation is based on isolation of *N. meningitidis*, or a positive nucleic acid amplification test (NAAT) from a normally sterile site, defined as laboratory-definitive evidence of IMD according to national case definitions. Information regarding the site of infection, age and sex of the patients is collated by the NNN for the AMSP.

Invasive *N. meningitidis* infections are categorised on the basis of the site from which *N. meningitidis* was isolated, or from which meningococcal DNA was detected (blood, joint fluid, and vitreous fluid). When *N. meningitidis* is detected from both blood and cerebrospinal fluid (CSF) from the same patient, the case is classified as one of meningitis.

Phenotyping and genotyping of *Neisseria meningitidis*

Phenotyping is limited to the determination of the serogroup by detection of soluble polysaccharide antigens. Genotyping of both isolates and DNA extracts is performed by sequencing products derived from amplification of the *porA* gene. Multi-locus sequence typing and clonal complex assignment is also reported by the jurisdictions.

Antibiotic susceptibility testing

Meningococcal isolates were tested to determine their minimum inhibitory concentration (MIC) values for antibiotics used for treatment (ceftriaxone, penicillin), and clearance of carriage (ciprofloxacin and rifampicin). This program has historically reported penicillin testing categories as: susceptible (MIC ≤ 0.03 mg/L); less susceptible (MIC 0.06–0.5 mg/L); and resistant (MIC ≥ 1 mg/L). Additionally, to monitor across antimicrobial susceptibility testing methods, a distribution of penicillin MIC values is now reported.

Results

In 2020, there were 90 IMD cases notified to the NNDSS, of which 87 were laboratory-confirmed. Laboratory data were available to the AMSP for all 87 laboratory-confirmed cases of IMD in Australia in 2020, as shown in Figure 1. In 2020, the peak incidence for IMD occurred in summer and early autumn (1 January to 31 March) (Table 1).

In 2020 there was a decrease in notifications of IMD across jurisdictions compared with 2019. Whilst Queensland reported the highest number of cases (27 cases), this was a decrease from 58 cases in 2019; New South Wales had the second-highest number of cases (21), a decrease from 70 cases in 2019. The number of cases from each jurisdiction for 2020 is shown in Table 2.

Age distribution

The peak incidence of IMD in 2020 depicted a bimodal pattern in infants less than one year old (18%; 16/87) and in adults aged 45 to 64 years, comprising 16% (14/87) of IMD cases in 2020 (Table 3). In 2020, 29% of IMD (25/87) occurred in children less than 5 years of age. Between 2003 and 2014, the proportion of IMD
Figure 1: Number of invasive meningococcal disease cases reported to the National Notifiable Diseases Surveillance System compared with laboratory-confirmed data from the Australian Meningococcal Surveillance Programme, Australia, 1991-2020

Table 1: Laboratory-confirmed cases of invasive meningococcal disease, Australia, 2020

| IMD serogroup 2020 | 1 January – 31 March | 1 April – 30 June | 1 July – 30 September | 1 October – 31 December | 2020 total |
|-------------------|----------------------|-------------------|-----------------------|-------------------------|-------------|
| B                 | 15                   | 11                | 14                    | 14                      | 54          |
| C                 | 0                    | 0                 | 0                     | 1                       | 1           |
| Y                 | 7                    | 0                 | 3                     | 4                       | 14          |
| W                 | 7                    | 5                 | 4                     | 0                       | 16          |
| ND*               | 2                    | 0                 | 0                     | 0                       | 2           |
| **Total**         | **31**               | **16**            | **21**                | **19**                  | **87**      |

* ND: unknown / not determined.

occurring in children aged less than 5 years ranged from 28% to 36% of cases. Since 2015, in Australia the proportion of IMD in children less than 5 years of age has ranged from 21% to 27%.

Samples from laboratory-confirmed cases

In 2020, diagnosis was confirmed by a positive bacterial culture in 70% of cases of IMD (61/87); and for 30% (26/87), IMD was confirmed by NAAT testing alone (Table 4). There were 23 diagnoses of meningitis and 63 diagnoses of septicaemia (Table 4). Additionally, there was one further IMD diagnosis confirmed from a joint fluid aspirate (Table 4).
Table 2: Number of laboratory-confirmed cases of invasive meningococcal disease, Australia, 2020, by state or territory and serogroup

| State/territory             | B | C | Y | W | ND | Total |
|-----------------------------|---|---|---|---|----|-------|
| Australian Capital Territory| 0 | 0 | 0 | 1 | 0  | 1     |
| New South Wales             | 17| 0 | 2 | 2 | 0  | 21    |
| Northern Territory          | 1 | 0 | 0 | 0 | 0  | 1     |
| Queensland                  | 17| 0 | 6 | 4 | 0  | 27    |
| South Australia             | 3 | 0 | 2 | 0 | 0  | 5     |
| Tasmania                    | 3 | 0 | 0 | 0 | 0  | 3     |
| Victoria                    | 11| 0 | 1 | 4 | 2  | 18    |
| Western Australia           | 2 | 1 | 3 | 5 | 0  | 11    |
| Australia                   | 54| 1 | 14| 16| 2  | 87    |
| %                           | 62.1| 1.1| 16.1| 18.4| 2.3|       |

a ND: unknown / not determined.

Table 3: Laboratory-confirmed cases of invasive meningococcal disease, Australia, 2020, by age and serogroup, and the proportion of IMD attributable to MenB

| Serogroup | <1 | 1–4 | 5–9 | 10–14 | 15–19 | 20–24 | 25–44 | 45–64 | 65+ | Total |
|-----------|----|-----|-----|-------|-------|-------|-------|-------|-----|-------|
| B         | 15 | 9   | 4   | 1     | 8     | 5     | 5     | 6     | 1   | 54    |
| C         | 0  | 0   | 0   | 0     | 0     | 0     | 1     | 0     | 1   |       |
| Y         | 1  | 0   | 0   | 1     | 1     | 1     | 1     | 2     | 7   | 14    |
| W         | 0  | 0   | 1   | 1     | 0     | 1     | 3     | 6     | 4   | 16    |
| ND        | 0  | 0   | 0   | 0     | 0     | 1     | 0     | 0     | 0   | 2     |
| Total     | 16 | 9   | 5   | 3     | 10    | 8     | 10    | 14    | 12  | 87    |
| %B within age group | 94 | 100 | 80 | 33 | 80 | 63 | 50 | 43 | 8 | 62 |

Notifications and proportion of MenB, MenC, MenW and MenY IMD

Serogrouping was determined for 85/87 laboratory-confirmed cases of IMD (Tables 2 and 3), with MenB accounting for 62% of all IMD in Australia in 2020. With respect to serogroup infections by age group, as shown in Table 3, MenB IMD was the predominant serogroup in children aged 4 years and younger (24/25; 96%) and in older teenagers and adolescents (15–19 years; 8/10; 80%). MenB accounted for the majority of disease across most age groups however with only one notification in 65 years and older (1/12; 8%). By contrast MenW (13/16; 81%) and MenY (10/14; 71%) disease predominated in cases 25 years and older.

New South Wales and Queensland each reported the equal-largest number of MenB IMD notifications (17/54), each accounting for 31% of MenB IMD in 2020. New South Wales was the state with the highest proportion of MenB, with this serotype accounting for 81% of its
Table 4: Number of laboratory-confirmed cases of invasive meningococcal disease, Australia, 2020, by specimen type and method of confirmation

| Specimen       | Bacterial culture | Nucleic Acid Amplification Test | Total |
|----------------|-------------------|---------------------------------|-------|
| Blood          | 55                | 8                               | 63    |
| CSF +/- Blood  | 6                 | 17                              | 23    |
| Other          | 0                 | 1                               | 1     |
| **Total**      | **61**            | **26**                          | **87**|

a Other specimen: joint aspirate (1).

cases (17/21) (Table 2). In the years 2006–2012, the proportion of IMD cases caused by MenB was 84%–88% nationwide; in 2013–2014 it was lower (75–80%); in 2015 it was 64%, falling to 36% in 2016–2017. There was an increase in attributable proportion in 2018 to 44%, in 2019 to 50%, and the proportion has again increased to 62% of IMD cases reported (Figure 2).

There was one notification nationally of MenC IMD in 2020, from Western Australia, lower than the six cases of MenC IMD reported in Australia in 2019 (Table 3, Figure 3).

The rise in IMD notifications in Australia since 2014 was due to an increasing number of infections of both MenW and MenY, as shown in Figure 1 and Figure 2. Prior to 2015, the proportion of cases of IMD caused by MenW was low, ranging from 1.1 to 4.8% in 1997–2012, then increasing to 8.4–9.7% in 2013–2014. In 2015 it was 21%; in 2016 it was 44%; in 2017–2018 it was 36–38%; it continued to decline to 26% in 2019, as shown in Figure 2. In 2020 there were 16/87 MenW infections accounting for 18% of IMD overall. IMD caused by MenW was sporadic in children and adolescents, but was the predominant cause of IMD in the older age groups in 2020. Of all IMD infections in 2020 in those aged 45 years and older, 10/26 (38%) were MenW.

A similar pattern and trend was seen in the number and proportion of IMD caused by MenY in 2020 (n = 14; 16% of total IMD). Prior to 2015, the proportion of cases of IMD caused by MenY ranged from 1.3 to 4.6% in the period 1997–2010; then 6.2–11% in 2011–2014. In 2015 the proportion rose to 13%, increasing to 17% in 2016 and again to 20% in 2017. The proportion was lower in 2018 (16%) and in 2019 increased to 21% (Figure 2). Nine of the 14 MenY IMD (64%) reported in 2020 were in those aged 45 years and older.

Of the 14 cases of IMD caused by MenY in 2020, Queensland reported the largest number (6/14 notifications in 2020). MenY was reported in all jurisdictions excepting the Australian Capital Territory, the Northern Territory, and Tasmania (Table 2). MenY IMD was reported in all age groups in 2020, excepting those aged 1 to 9 years (Table 3, Figure 3).

Genotyping

In 2020, genotyping was possible for 69% of IMD laboratory confirmed cases (60/87); results are shown in Figure 4, Figure 5, and Table 5. There were 33/60 MenB typed; the predominant \( \text{porA} \) types in 2020 were P1.7,16-26 (7 cases; 21%) and P1.22,14 (6 cases; 18%). The \( \text{porA} \) type P1.7-2,4, the predominant type in previous years, only accounted for 4/33 (12%) of MenB cases able to be typed in 2020 (Figure 4). There was one MenC IMD in 2020 from Western Australia, of the \( \text{porA} \) type P1.5,2 (Table 5). For serogroup W IMD with typing information available (13/16 cases, 81%), all were of the single genotype P1.5,2 (Figures 5 and Table 5). The \( \text{porA} \) type P1.5,2 has been the predominant genotype in recent years, from the clonal complex 11, the...
same strain type as the hypervirulent serogroup W strain also reported in the United Kingdom and South America since 2009 (Table 6). For MenY IMD, of the 13 cases with typing information available, the predominant genotype was P1.5-1,10-1 (8/13 able to be typed; 62%), as has been reported since 2014, when the increase in serogroup Y IMD was first noted in Australia (Figure 5).

Antibiotic susceptibility testing

Isolates of *N. meningitidis* are tested against both treatment (ceftriaxone and penicillin) and clearance antibiotics (rifampicin and ciprofloxacin). In 2020, seventy percent of laboratory-confirmed IMD (61/87) had *N. meningitidis* cultured, permitting antimicrobial susceptibility testing (AST) to be performed by the NNN laboratories. Ceftriaxone susceptibility testing was performed on all 61 isolates and all were susceptible in 2020. With regards to penicillin, the distribution of penicillin MIC values is shown in Table 7. Eight percent of IMD isolates (5/61) were fully susceptible to penicillin (MIC ≤ 0.03 mg/L); and 92% (56/61) less susceptible to penicillin (MIC 0.064–0.5 mg/L). Of the isolates tested, 8/61 (13%) had a penicillin MIC of 0.5 mg/L, which is close to the MIC breakpoint for resistance; 7/8 (88%) of these were MenW. In recent years, MenW has demonstrated higher penicillin MIC values and higher proportions of resistance. In 2020, none of the 61 IMD isolates tested were resistant to penicillin (MIC ≥ 1 mg/L). The proportion of penicillin resistance in all IMD isolates has gradually declined since 2016 at 5.8%, to 5.1% in 2017, then to 1.4% in 2018 and 0.6% in 2019 as shown in Figure 6. Regarding the clearance antibiotics for IMD, all 61 isolates were susceptible to ciprofloxacin and rifampicin.
Figure 3: Number of serogroups B, C, Y and W cases of laboratory-confirmed invasive meningococcal disease, Australia, 2020, by age

Figure 4: Number of \textit{porA} genotypes for MenB in laboratory-confirmed cases of invasive meningococcal disease Australia, 2020
Figure 5: Number of *porA* genotypes for MenW and MenY IMD in laboratory-confirmed cases of invasive meningococcal disease, Australia, 2020

Discussion

In 2020, 97% of IMD notifications in Australia (87/90) were laboratory confirmed, a similar proportion to previous years. Notably in 2020, there was an overall decrease in notifications of IMD by 57% when compared with 2019, coincident with widespread public health initiatives designed to reduce COVID-19 transmission. These included social and personal distancing, hand hygiene and cough etiquette, use of masks, restrictions to travel and access to aged care and hospitals. Notifications of influenza were also reduced, of relevance as antecedent infection is a risk factor for IMD.

In Australia in 2016–2017, increased notifications of MenW and MenY IMD prompted time-limited, jurisdictional MenACWY vaccination programs for target age groups. In July 2018, the NIP replaced MenC vaccine at 12 months of age with a quadrivalent ACWY vaccine. There followed a decrease in both notifications and proportion of MenW and MenY disease, accompanied by a gradual increase in the proportion of disease caused by MenB (from 44 to 50% in 2018–2019 to 62% in 2020). Prior to the introduction of the MenC vaccine in 2003 in Australia, the proportion of MenB IMD was 84–88% in the years 2006–2012 then declining. Notifications of IMD subsequently increased with the emergence of MenW and MenY disease since 2014 in Australia.

With regards to serogroup infections by age group: MenB accounted for majority of disease in all age groups (range 50–100%) excepting the age groups of 10–14 years and 45 years and older, where in the latter age group MenW and MenY were in the majority. A recombinant multi-component meningococcal B vaccine has been available in Australia since 2014, although this vaccine is not currently on the NIP. MenW caused 18% (16/87) of IMD in Australia, a decrease from 26% in 2019, and of these MenW IMD cases, 13/16 (81%) occurred in those aged 25 years and older. In 2020, MenY accounted for 16% of IMD nationally (14/87), and was reported sporadically across age groups; however, 9/14 MenY IMD cases (64%) were reported...
Table 5: Distribution of porA genotype laboratory-confirmed cases of invasive meningococcal disease, Australia, 2020, by state or territory

| 2020 AMSP | GENOTYPE | NSW | QLD | VIC | SA | WA | ACT | TAS | NT |
|----------|---------|-----|-----|-----|----|----|-----|-----|-----|
| GENGROUP |         |     |     |     |    |    |     |     |     |
| W        | P1.5,2  | 0   | 4   | 4   | 0  | 5  | 0   | 0   | 0   |
| C        | P1.5,2  | 0   | 0   | 0   | 0  | 1  | 0   | 0   | 0   |
| Y        | P1.5-1  | 0   | 0   | 0   | 1  | 0  | 0   | 0   | 0   |
| Y        | P1.5-1,10-1 | 2 | 3   | 1   | 1  | 1  | 0   | 0   | 0   |
| Y        | P1.5-1,10-8 | 0 | 1   | 0   | 0  | 0  | 0   | 0   | 0   |
| Y        | P1.5-2,10-4 | 0 | 1   | 0   | 0  | 1  | 0   | 0   | 0   |
| B        | P1.7,13 | 0   | 1   | 0   | 0  | 0  | 0   | 0   | 0   |
| B        | P1.7,16-26 | 0 | 3   | 3   | 0  | 1  | 0   | 0   | 0   |
| B        | P1.7-1,11 | 0 | 0   | 1   | 0  | 0  | 0   | 0   | 0   |
| B        | P1.7-2,4  | 1   | 1   | 1   | 1  | 1  | 0   | 0   | 0   |
| B        | P1.7-2,30-1 | 0 | 1   | 0   | 0  | 0  | 0   | 0   | 0   |
| B        | P1.7-12,14 | 0 | 2   | 0   | 0  | 0  | 0   | 0   | 0   |
| B        | P1.12-1,13-1 | 0 | 0   | 1   | 0  | 0  | 0   | 0   | 0   |
| B        | P1.12-1,16 | 0   | 1   | 0   | 0  | 0  | 0   | 0   | 0   |
| B        | P1.17,16-3 | 0   | 1   | 0   | 0  | 0  | 0   | 0   | 0   |
| B        | P1.18-1,3  | 0   | 0   | 1   | 0  | 0  | 0   | 0   | 0   |
| B        | P1.38-1,34 | 0   | 1   | 0   | 0  | 0  | 0   | 0   | 0   |
| B        | P1.18-1,34-5 | 0 | 0   | 1   | 0  | 0  | 0   | 0   | 0   |
| B        | P1.18-4,10-1 | 0 | 1   | 0   | 0  | 0  | 0   | 0   | 0   |
| Y        | P1.18-4,25 | 0   | 0   | 0   | 0  | 1  | 0   | 0   | 0   |
| B        | P1.19,15  | 0   | 1   | 0   | 0  | 0  | 0   | 0   | 0   |
| B        | P1.19-1,26 | 0   | 1   | 0   | 0  | 0  | 0   | 0   | 0   |
| B        | P1.21-7,16 | 0   | 0   | 0   | 0  | 0  | 0   | 1   | 0   |
| B        | P1.22,9   | 0   | 0   | 1   | 0  | 0  | 0   | 0   | 0   |
| B        | P1.22,14  | 0   | 3   | 1   | 0  | 0  | 0   | 2   | 0   |

in those aged 45 years and older. The primary peak of IMD notifications was observed in infants less than 5 years (25/87; 29%), with this peak due primarily to MenB (96%).

With regards to prevailing IMD serogroups and genotypes, the number of IMD cases caused by MenB in 2020 was less than in 2019, although the proportion was higher (54/87, 62%, in 2020, compared with 101/202, 50%, in 2019). New South Wales and Queensland reported the largest equal numbers of MenB notifications, however, South Australia continues to report the highest proportion of MenB, with the exception of Tasmania where all three IMD notifications in 2020 were MenB. The predominant MenB genotype in Australia is P1.7,16-26 (7/33), followed by genotype P1.22,14 (6/33), marking a
change from recent years; the previous dominant MenB genotype, P1.7-2,4, now accounts for 4/33 of MenB IMD.

The predominant circulating strain of MenW continues to be genotype P1.5,2 sequence type (ST) 11. This same MenW strain previously emerged in the United Kingdom (UK) and South America in 2009,\(^8,9\) and spread to account for 25% of IMD in the UK in 2014–2015 and 59% of all cases in Chile in 2012. MenW ST11 is hypervirulent and associated with atypical clinical presentations, more severe disease, and a higher case fatality rate.\(^9\) The initial increase in MenW overseas and in Australia was seen in older adults, but was subsequently reported in all age groups, particularly in adolescents and infants.\(^12\) The predominant MenY genotype since 2014 continues to be P1.5-1,10-1; whereas previously MenY genotype distribution had been more heterogeneous.\(^13\)

Antimicrobial susceptibility testing of IMD isolates in 2020 demonstrated no penicillin resistance in clinical isolates. The incidence of penicillin resistance in \textit{N. meningitidis} in Australia was less than 1% annually of IMD isolates tested in 1996–2014, rising to 3.4% in 2015; 5.8% in 2016; and 5.1% in 2017; and decreasing to 0.6% in 2019. The majority of penicillin-resistant meningococcal isolates are MenW.

However, the proportion of IMD isolates less susceptible to penicillin has been increasing from 62–75% in 1996–2006; 67–79% in 2007–2009; 78–88% in 2010–2015; 90–94% in 2016–2019; and 92% in 2020. All IMD isolates tested in 2020 were susceptible to ceftriaxone, ciprofloxacin and rifampicin.

There has been an ongoing decrease in IMD notifications from 1.5 cases per 100,000 in 2017; to 1.1 per 100,000 in 2018; 0.8 cases per 100,000 in 2019; and 0.3 cases per 100,000 in 2020. The year 2020 has also seen a decrease in the proportion of isolates attributable to MenW and MenY. This was coincident both with widespread public health initiatives designed to reduce COVID-19 transmission and following changes in the NIP. The NNN is continuing to lead further investigations with the Australian Government Department of Health and is closely monitoring the phenotypic and genotypic features of \textit{N. meningitidis} causing IMD.
Figure 6: Proportion of penicillin-susceptible, less susceptible and resistant invasive meningococcal disease isolates, Australia, by year

in Australia. Additional investigations by the NNN, including whole genome sequencing of IMD isolates, are in progress to enhance IMD surveillance in Australia. The AMSP data are used for informing treatment guidelines and disease prevention strategies; and to monitor the effect of interventions.

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