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Invasive meningococcal disease on the workplaces: a systematic review

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Summary. *Background and aims of the work:* Invasive Meningococcal Disease (IMD) represents a global health threat, and occupational settings have the potential to contribute to its spreading. Therefore, here we present the available evidences on the epidemiology of IMD on the workplaces. *Methods:* The following key words were used to explore PubMed: Neisseria meningitidis, meningococcus, meningococcal, invasive meningococcal disease, epidemiology, outbreaks, profession(al), occupation(al). *Results:* We identified a total of 12 IMD cases among healthcare workers (HCW), 44 involving biological laboratory workers (BLW), 8 among school personnel, and eventually 27 from other settings, including 3 large industrial working populations. Eventual prognosis of BLW, particularly the case/fatality ratio, was dismal. As clustered in time and space, data about school cases as well as industrial cases seem to reflect community rather than occupational outbreaks. In general, we identified a common pattern for HCW and BLW, i.e. the exposure to droplets or aerosol containing N meningitidis in absence of appropriate personal protective equipment (PPE) and/or microbiological safety devices (MSD) (e.g. cabinets). Post-exposure chemoprophylaxis (PEC) was rarely reported by HCW (16.7%) workers, and never by BLW. Data regarding vaccination status were available only for a case, who had failed requested boosters. *Conclusions:* The risk for occupational transmission of IMD appears relatively low, possibly as a consequence of significant reporting bias, with the exception of HCW and BLW. Improved preventive measures should be implemented in these occupational groups, in order to improve the strict use of PPE and MSD, and the appropriate implementation of PEC. (www.actabiomedica.it)

Key words: Neisseria meningitidis, Meningitis, Meningococcal, Workplace, Vaccines

Introduction

Neisseria meningitidis (meningococcus) is a common bacterial commensal of the human upper respiratory tract and, since the latter half of twentieth century, the disappearance of many infectious competitors has presumptively increased the global prevalence of its asymptomatic carriers up to 35% reported among young-adults (1-5). For reasons that are still unclear, the carrier status can rarely but also rapidly evolve in a life-threatening invasive disease characterized by meningitis (37%-49% of cases), septicemia (18%-33% of cases), and less commonly pneumonia and arthritis, also known as invasive meningococcal disease (IMD) (2-5). Although 13 meningococcal serogroups have been identified on the basis of the capsular immunochemistry, nearly all IMD around the world are caused by only six serogroups (A, B, C, W-135, Y and X), and five of them (i.e. A, B, C, W-135, Y) may be prevented by modern and efficient conjugate vaccines (6).

Globally, IMD can occur as an endemic disease with sporadic cases or as epidemics with outbreaks, and its incidence therefore varies from less than 1 cases per 100,000 population every year (the typical incidence in many Western Countries, such as Italy) to over 1,000 cases (3, 6). With a death rate of 6% to 10% of cases, and sequelae reported in 4.4% to 11.2% of cases, IMD represents a leading cause of morbidity and mortality worldwide (3, 6-8), being a leading infectious cause of death in childhood, and the third most common cause of death in children outside infancy (7, 8).

Although usually associated with a high perceived risk among those who have had contact with a case, occupational transmission of IMD has been rarely reported, even among professionals having strict contact with cases (2, 3, 7, 9-23): in this systematic review, available evidence about occupational epidemiology of IMD will be specifically described.

Methods

Two authors independently performed a Literature search by means of the PubMed database during the month of June 2017 for the terms: *Neisseria meningitidis*, *meningococcus*, *meningococcal*, *invasive meningococcal disease*, *epidemiology*, *outbreaks*, *profession(al)*, *occupation(al)*. Only articles written in English were retrieved, without any chronological and/or geographical restrictions. Retrieved data included:

- *Settings of the case/outbreaks*: year and country where the case(s) occurred; number of cases reported; occupational settings and jobs/tasks performed by reported cases;
- *Data regarding the infection(s)*: identified serogroup(s); presumed or confirmed source(s) of infection, incubation (when multiple cases were reported, median and rage were calculated), outcome (i.e. recovery without sequelae; recovery with sequelae; death).

Workplaces were arbitrarily classified as follows:

- *healthcare settings*: all the activities whose primary purpose is to promote, restore or maintain health (24);
- *biological laboratories*: facilities within which microorganisms, their components or their derivatives are collected, handled and/or stored. Biological laboratories include clinical laboratories, diagnostic facilities, regional and national reference centers, public health laboratories, research centers (academic, pharmaceutical, environmental, etc.) and production facilities (manufacturers of vaccine, pharmaceuticals, etc.) for human, veterinary and agricultural purposes (25);
- *school*: any educational institution (including kindergarten, pre-school, first and second level schools, universities and colleges);
- *other*: all activities not included in the aforementioned definitions.

For cases occurring in healthcare and biological laboratory settings, data about biosafety and preventive measures (e.g. use of microbiological safety cabinets, MSC; use of respiratory personal protective equipment, PPE; post-exposure chemoprophylaxis, PEC; vaccination status of the reported cases, etc.) were also collected.

The results were then further screened for duplicate cases, reports regarding outbreaks occurring among military facilities, in college residences, prisons and worker hostels, in order to retain only data regarding institutional employees (i.e. School teachers, School assistants; prison personnel, etc.).

Results

The detailed research identified a total of 157 titles. After screening and assessment of eligibility, a total of 23 papers were identified as relevant to the research question. Two additional articles were identified by analyzing the reference lists of the studies identified by the above strategy. Overall, the 25 papers included in this review were in 21 cases either case reports or case series, with 4 further descriptive studies about meningococcal outbreaks associated with the occupational settings (Figure 1). As shown in Table 1, a total of 91 cases were eventually included in the analysis: of them, 19.8% died following meningococcal infection, and 2.2% recovered reporting severe sequelae such as limb amputations. The majority of cases was associated

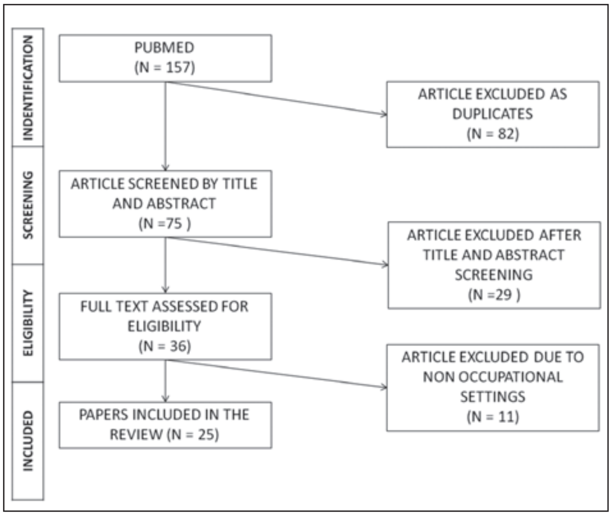

Figure 1. Flow diagram of study selection

with serogroup C (42.9%), followed by B (19.8%), and A (15.4%).

Healthcare settings. Since 1972, a total of 12 IMD cases occurring in healthcare workers (HCWs) have been described, with a median incubation of 5 days (range: 3 to 16) (7, 15, 20, 26-31). Serological data were available for 8 patients, including 4 cases (33.3%) caused by serogroup B meningococci, 3 cases (25.0%) by serogroup C, and 1 (8.3%) case by serogroup W-135. Unfortunately, patients' outcome were described only in 4 cases (33.3%), all apparently resolved without sequelae (15, 27-29) (Table 2).

Regarding jobs and tasks involved, a third of cases were defined among "*paramedic crew*" (20, 28, 29, 32), with two cases in nurses (20, 26) and physicians (15, 20) (16.7% for both categories), and a further case from a respiratory therapist. In 1972, Feldman reported 4 cases among workers from a "medical staff" who had performed resuscitation procedures, but no information was given about their actual qualification (30). In all cases, the contact was identified among the patients, and 10 out 12 followed close contact with airways of patients that were ultimately affected by *N meningitidis*/IMD (83.3%), either in the Emergency Room or in the ambulance. The reported interactions included airways management procedures (15, 20, 28, 30), and mouth-to-mouth resuscitation (27). In three cases, no close contacts with airways of index cases were reported, but in two of them the index cases had coughed into the face of healthcare workers (20). In the third case, the Authors reported the previous worker's involvement in the management of two community patients, but because of the very long incubation (presumptively, 16 days), and the lack of data about specific meningococcal strains of index cases, it was impossible to determine whether meningococcal infection was acquired on the workplace or in the community (29).

Table 1. Summary of papers included in the analysis

Papers eventually included in the analysis	25
Year range	1918 - 2015
Number of cases reported (n)	91
Occupational Settings (n, %)	
Healthcare	12, 13.2%
Biological laboratory	44, 48.4%
School and education	8, 8.8%
Other (industry, services, etc.)	27, 29.7%
Reporting countries (n, %)	
Argentina	1, 1.1%
Belgium	1, 1.1%
Brazil	12, 13.2%
Canada	1, 1.1%
Czech Republich	1, 1.1%
Denmark	1, 1.1%
France	4, 4.4%
Italy	1, 1.1%
New Zealand	1, 1.1%
South Africa	13, 14.3%
Sweden	1, 1.1%
United Kingdom	16, 17.6%
United States	38, 41.8%
Serogroup (n, %)	
A	14, 15.4%
B	18, 19.8%
C	39, 42.9%
W135	2, 2.2%
X	0, -
Y	0, -
N/A	18, 19.8%
Prognosis (n, %)	
Recovery, without sequelae	37, 40.7%
Recovery, with sequelae	2, 2.2%
Death	18, 19.8%
N/A	34, 37.4%

Table 2. Published studies on occupational transmission of *N meningitidis* in the healthcare settings (N/A=data not available; PPE=personal protective equipment; PEC=post-exposure chemoprophylaxis)

Author(s)	Country	Year	Patient(s)	No. of cases	Serogroup	Respiratory use of PPE reported	Source of infection	PEC	Incubation (days)	Prognosis
Feldman HA, 1972 (30)	USA	N/A	Medical staff	4	N/A	N/A	Mouth-to-mouth resuscitation	N/A	N/A	N/A
CDC, 1978 (26)	USA	1978	Nurse	1	B	NO	Patient; emergency room evaluation	YES	3	N/A
Gehanno JF et al. 1999 (15)	France	1999	Physician	1	C	NO	Patient; intubation procedures; delivery of oxygen;	NO	7	Recovered without sequelae
Gilmore A, et al. 2000 (20)	United Kingdom	1986	Physician	1	B	NO	Patient; full clinical examination; patient coughed into doctor face; daily contact thereafter.	NO	4	N/A
		1987	Paramedic crew	1	C	NO	Patient; control of airways; delivery of oxygen;	NO	7	N/A
		1996	Nurse	1	B	NO	Patient; interaction with patient who coughed and cried;	NO	5	N/A
Petsas A et al. 2008 (28)	United Kingdom	2007	Paramedic crew (Ambulance worker)	1	B	NO	Patient; control of airways; delivery of oxygen;	NO	4	Recovered without sequelae
CDC, 2010 (27)	USA	2009	Respiratory therapist	1	C	NO	Patient; intubation procedures	NO	5	Recovered without sequelae
Puleston R et al. 2012 (29)	United Kingdom	2012	Paramedic crew (Ambulance worker)	1	W135	N/A	Involved in two community cases but impossible to determine whether paramedic was a primary or a secondary case	YES	16	Recovered without sequelae
Total			Paramedic crew = 4 (33.3%) Physicians = 2 (16.7%) Nurse = 2 (16.7%) Respiratory therapist = 1 (8.3%) Medical staff (undefined) = 4 (33.3%)	12	B =4 (33.3%) C = 3 (25.0%) W135 = 1 (8.3%) N/A = 4 (33.3%)	NO = 7 (58.3%) N/A = 5 (41.7%)	Patients = 100% Airway management / resuscitation maneuvers = 10 (83.3%) Other interactions = 3 (25.0%)	NO = 6 (50.0%) YES = 2 (16.7%) N/A = 4 (33.3%)	Median: 5 days Range: 3 - 16	Recovered without sequelae = 4 (33.3%) N/A = 8 (66.7%)

Overall, no one among the aforementioned cases was apparently wearing PPE of any kind at the time of the suspected contagion, including also surgical face masks, and PEC was offered only to two cases (16.7%) (26, 29).

Laboratory settings. As shown in Table 3, a total of 44 cases of IMD were reported in biological laboratory workers (BLWs) since 1918, including one student (2.3%), with a median incubation of 4 days (range 1 to 10), 13 deaths (29.5%), and 2 cases (4.5%) where recovery was associated with significant sequelae, such as extensive upper/lower limb amputation. Apparently, none of the patient had received PEC, and a previous vaccination against meningococcus A and C was reported in only one subject (9, 13, 19, 21, 30, 31, 33-40).

Data about the supposed settings of the contagion were available for 35 out of 41 cases (85.4%), and workers had recently managed specimens of *N meningitidis* in order to perform procedures such as: plating, examining Petri solid medium plates, microscopic characterization of the samples, or serogroup identification. In nearly all cases in which data were made available (40/44, 90.2%), the contact between work-

Table 3. Published studies on occupational transmission of *N meningitidis* in the laboratory settings (N/A=data not available; PPE=personal protective equipment; PEC=post-exposure chemoprophylaxis)

Author(s)	Country	Year	Patient(s)	No. of cases	Serogroup	Biosafety measures[1]	Respiratory use of PPE reported	Source of infection	PEC	Incubation (days)	Prognosis
Pike RM (33)	Denmark	1918	Laboratory technician	1	N/A	NO	NO	Manufacture of meningitis serum	NO	N/A	Died
	USA	1936	Laboratory technician	1	N/A	NO	NO	Eye contact with specimens of *N meningitidis*	NO	4	Died
Feldman HA, 1972 (30)	USA	N/A	Laboratory technicians	2	N/A	N/A	N/A	Management of specimens	N/A	N/A	Recovered without sequelae
Bhatti AR et al. 1982 (34)	Canada	1982	Laboratory technician	1	A	NO	NO	Preparing samples for negative staining for electron microscopic observation	NO	N/A	N/A
CDC, 1991 (31)	USA	1988	Laboratory technician	1	C	N/A	N/A	Management of blood from a case of meningitis C	NO	6	Died
		1988	Laboratory technician	1	B	NO	DOUBTFUL[2]	Management of isolates of meningitis B	NO	3	Died
Guibordenche M et al. 1994 (35)	France	1985	Laboratory technician	1	C	NO	NO	Agar diffusion antibiogram	NO	3	Recovered without sequelae
		1987	Laboratory technician	1	B	NO	NO	Determination of MIC on agar plates	NO	3	Recovered without sequelae
Boutet et al. 2001 (19)	United Kingdom	1992 – 1995	Laboratory technicians	5	C (n = 4) B (n = 1)	NO	NO	Management of live suspension of meningococci	N/A	3 to 7	All patients recovered
CDC, 2002 (36)	USA	2000	Laboratory technician	1	C	NO	NO	Preparation of Gram's stain; aspiration of materials	NO[3]	3	Died
		2000	Laboratory technician	1	C	YES	NO	Slide agglutination testing and recording colonial morphology	NO	14	Died
Sejvar JJ et al. 2005[4] (9)	USA	1985 - 2002	Laboratory technicians	19	A (n = 1) B (n = 9) C (n = 9)	NO = 18 YES = 1	N/A	Examining petri solid medium plates (50%), subculturing isolates (50%), serogroup identification (38%);	N/A	2 to 10 (median 4)	8 died 10 recovered 1 unknown
Athlin S et al. 2007 (37)	Sweden	2005	Laboratory technician	1	A	NO	NO	Management of specimens	NO	6	Recovered without sequelae
Kessler AT et al, 2007 (13)	USA	2006	Laboratory technician, student	1	A	NO	NO	Plating	NO	5	Recovered without sequelae
Baron J and Miller JM, 2008 (38)	USA	2002 – 2005	Laboratory technicians	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Omer H et al. 2011 (41)	France	2007	Laboratory technician	1	A	YES	YES	Management of viable bacteria; malfunctioning of a hood	NO	N/A	Recovered without sequelae
Willemarck N et al, 2012 (40)	Belgium	2000	Laboratory technician	1	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Borrow et al. 2014 (21) & Silver S 2014 (39)	New Zealand	2005	Laboratory technician	1	B	YES	YES	Meningitis strains were manipulated but contact with pathogens were initially doubtful	NO	N/A	Lost both legs, left arm and the digits of right hand
	USA	2012	Laboratory technician	1	B	NO	NO	Management of viable bacteria culture; details not available	NO	1 day	Died
	Argentina	2006	Laboratory technician	1	N/A	N/A	N/A	N/A	N/A	N/A	Lost both hands

(continued)

Table 3 ***(continued).*** Published studies on occupational transmission of *N meningitidis* in the laboratory settings (N/A=data not available; PPE=personal protective equipment; PEC=post-exposure chemoprophylaxis)

TOTAL			Laboratory technician = 43 (97.7%) Laboratory technician, student = 1 (2.3%)	44	A = 5 (11.4%) B = 14 (31.8%) C = 15 (34.1%) N/A = 10 (22.7%)	NO = 32 (72.7%) N/A = 9 (20.5%) YES = 3 (6.8%)	NO = 17 (38.6%) N/A = 24 (54.5%) YES = 2 (4.5%) DOUBTFUL = 1 (2.3%)	Management of specimens = 40 (90.9%) Accidental contact with specimens = 1 (2.3%) N/A = 3 (6.8%)	NO = 11 (25.0%) N/A = 33 (75.0%)	4 (1 to 10)	Deaths = 13 (29.5%) Recovery with sequelae = 2 (4.5%) Recovery without sequelae = 22 (50.0%) N/A = 7 (15.9%)

Notes:

[1] handling of specimens in microbiological safety cabinet;

[2] the patient had extensive rhinorrhea before performing specimens' handling, and it is therefore doubtful that she actually used respiratory PPE

[3] patients had received a non-specific antibiotic therapy following the suspicion of sore throats;

[4] two case included in CDC 2002.

ers and pathogens supposedly occurred through respiratory airways, whereas in an early report from the '30s some specimens were projected into the eye of the laboratory workers who was trying to inject an animal (33).

Data about the use of PPE and biosafety measures were not homogenously available, as reported for 20 (45.5%) and 35 (79.5%) cases, respectively. However, the majority of cases had performed procedures at risk either without PPE (38.6%), or MSC (72.7%). Interestingly enough, in one case the pathogens were appropriately handled in a safety cabinet by a laboratory worker who had been vaccinated against serogroup A and C with a polyosidic vaccine, but further investigations identified a significant malfunctioning of the MSC that ultimately allowed worker's contamination. Moreover, the patient had lacked recommended vaccination boosters in the previous five years (41). Similarly, in two further cases – one death and one recovery with severe sequelae such as extensive amputations, follow-up investigations suggested some or even severe malfunctioning in the biosafety measures (21, 39).

School settings. Whereas there is an extensive base of evidence regarding IMD outbreaks in students (23, 42-46), only two studies in English written literature have described outbreaks among school personnel (i.e. School teachers and/or School assistant) (Table 4) (8,47). Overall, 8 cases were reported, including 5 teachers (62.5%), 2 school employees (25.0%) and 1 school assistant (12.5%). In all cases, infections were caused by a serogroup C meningococcus, and presumptively found in the contact with students the original source of infection. Unfortunately, no detailed information was available regarding the incubation period, as well as the actual activities performed by workers at the time of presumptive contact, as well as workers' outcomes: only in one case Authors reported that prompt treatment eventually avoided meningococcal disease (47).

Other settings (Table 5). Three significant workplace outbreaks have been described, two of them from South America (16, 17, 48). The latter included large working populations from a food processing plant (17), and an oil refinery (16) that eventually resided in nearby factory towns. In each of South American reports, 6 meningococcal infections were reported, all from serogroup C. Data about incubation period were not available, whereas the outcome included 3 deaths and 9 recoveries without sequelae, with an estimated lethality of 25.0%.

Table 4. Published studies on occupational transmission of *N meningitidis* in the School and education settings (N/A = data not available).

Author(s)	Country	Year	Patient(s)	No. of cases	Serogroup	Source of infection	Incubation (days)	Prognosis
Woodhouse S and Hunter PR, 2001 (8)	United Kingdom	1997 – 1999	School workers of them: Teachers Employees Assistant	7 4 2 1	C	Presumptively, students	N/A	N/A
Pazdiora P et al. 2013 (47)	Czech Republich	2009	School teacher	1	C	Presumptively, students	N/A	Chemophylaxis avoided clinical disorder
Total			School teachers = 5 (62.5%) School employees = 2 (25.0%) School assistant = 1 (12.5%)	8	C = 8 (100%)	Students (presumed) = 8 (100%)	N/A = 8 (100%)	N/A = 7 (87.5%) Successful chemoprophylaxis = 1 (12.5%)

Table 5. Published studies on occupational transmission of *N meningitidis* in other than healthcare, laboratories or schools and education (N/A = data not available)

Author(s)	Country	Year	Patient(s)	No. of cases	Serogroup	Source of infection	Incubation	Prognosis
Sonnenberg P et al. 2000 (48)	South Africa	1996	Gold miners	13	A = 9 (69.2%) N/A = 4 (30.8%)	Presumptively, community outbreak; doubtful occupational spreading	6 (unknown rage)	1 Death 12 Recovered*
CDC, 2010 (27)	USA	2009	Police Officer	1	C = 1 (100%)	Unconscious subject recovered after a 911 call	2	Recovered without sequelae
Iser BPM et al, 2012 (17)	Brazil	2008	Food processing plant employees	6	C = 6 (100%)	Presumptively, community outbreak; doubtful occupational spreading	N/A	1 Death 5 Recovered without sequelae
Liphaus BL et al. 2013 (16)	Brazil	2010	Oil refinery employees	6	C = 6 (100%)	Presumptively, community outbreak; occupational spreading associated with temporary swelling in workforce due to plant management	N/A	2 Death 4 Recovered without sequelae
Stefanelli P et al. 2015 (49)	Italy	2015	Cultural Mediator	1	W = 1 (100%)	Presumptively acquired during activities performed in an immigrants' reception center.	N/A	1 Death
Total				27	A = 9 (33.3%) C = 13 (48.1%) W = 1 (3.7%) N/A = 4 (14.8%)	Community contacts (presumptive) = 25 (92.6%) Interactions with immigrants' reception center = 1 (3.7%) Other = 1 (3.7%)	6 (unknown rage)	Deaths = 5 (18.5%) Recoveries without sequelae = 10 (37.0%) Recoveries, unknown status = 12 (44.4%)

A third large report included incident cases from gold mines in South Africa (48): although the analyzed time frame spanned from 1972 to the early 2000's, reported data were fragmentary, with 588 diagnoses between 1972 and 1976, and "less than 5 cases per year" since 1978. Briefly, some further details were available only for the 1996 outbreak that included 13 subjects with 9 confirmed IMD, all from serogroup A, with one fatal case and 12 further recoveries of unknown extent, and a presumptive incubation period of 6 days.

In all three reports, Authors stated that the outbreaks were timely associated with simultaneous outbreaks spreading in the communities in which the workers actually resided, either permanently or temporarily (16, 17, 48). Interestingly, a common pattern was reported by Liphaus et al and Sonneberg et al (16, 48), as in both cases the reported outbreaks rapidly followed transient swelling of the workforce and/or its turnover, with higher rates in newcomer workers. Authors ultimately speculated that, in these large populations, crowding associated with transitory increase in the workforce may have accelerated the diffusion of pathological strains, suggesting that the contacts occurred rather in the original communities of the workers or in their temporary residing places (hostels, etc.) than in the workplaces.

Another case of occupational transmission of IMD disease was described in an American policeman from a crew of 4 police officers that had a contact with the index case, a man aged 36 years found unconscious at home. In the following hours, contagious occurred also in the healthcare workers caring for the index case, and have been detailed previously (27). Although the worker had no significant interaction with airways of index case, he ultimately developed clinical symptoms in the following 2 days: after hospitalization, he fully recovered without sequelae.

Eventually, a case of fatal IMD was recently reported by Stefanelli et al. in a cultural mediator working in an immigrants' reception center (49). The worker did not have any exposure outside the workplace and did not travel outside Italy in the previous year: as the involved serogroup was of North-African origin (W/ST-11), Authors suggested an occupational exposure.

Discussion

Even though occupational settings can potentially contribute to a rapid spread of meningococcal infection among unvaccinated workers (11, 20, 23, 44), we identified relatively few reports detailing IMD in which occupational risk factors actually induced exposure and following contagion of patients. More specifically, available reports underscore that only some professionals, such biological laboratory and healthcare workers, habitually face a significantly increased risk for work-related IMD, as during their duties they may be deliberately but also unconsciously exposed to cases of IMD (7, 9, 20). In case of higher endemic rates, as in '90s in the United Kingdom, also occupational settings characterized by close social interaction of workers with high risk groups may be associated with an increased spreading of IMD (8, 50): this is apparently the case of school employees. In cases of outbreaks or larger epidemics, high rates of IMD may be found also in other working populations, but the actual contribution of the occupational environment to the spreading of meningococcal infection still remains more doubtful.

However, some remarks should be addressed. First at all, it should be stressed that available evidence is based on relatively few reports, mainly from relatively few geographical areas (i.e. United States and United Kingdom), and the epidemiology of IMD is significantly heterogeneous (2, 3, 51, 52). Moreover, as conjugate vaccines are able to interfere with the carrier status of *N meningitidis* also in the healthy population, new vaccine schedules have eventually put in motion significant changes in global epidemiology of IMD (2-5, 11, 18, 23, 43, 44, 51, 53-68).

School data in particular are substantially drawn from reports collected in the Cheshire (United Kingdom) in the late '90s, that is before immunization campaigns against meningococcus C had been put in place (8, 46, 50, 51, 69). Moreover, available data should suggest an even more critical assessment, as 3 out of the 7 reported cases of occupational meningococcal disease transmission actually involved either School assistants or School employees, whose actual interaction with high risk groups represented by students and children may be reasonably questioned (8, 47). In other words, despite some Authors have documented very high attack rates for educational workforce (8, 46, 50), available evidence suggests that occupational contagion of school employees is possible but eventually unlikely. Even though guidelines about PEC on the school settings have been recently issued (52, 70-72), these figures were somehow unexpected for several reasons.

Firstly, the carrier status for *N meningitidis* still peaks in school-age subjects, and not coincidentally even large outbreaks have been and are still repetitively reported in pre-schools, schools, and colleges.

Moreover, global diffusion of new vaccines in younger age groups is too recent and too heterogeneous to have *per se* significantly reduced the exposure risk in occupationally exposed adults to such extent (2, 6, 11, 22, 23, 44, 45, 54, 56, 61, 73-76).

Eventually, schools environments are well-known potential outbreak centres for infectious diseases because of the frequent and prolonged personal contact among students, faculty and staff, their interface with the community, and nonetheless their large population (77-81). In fact, school employees represent a significant occupational group: recent estimates suggest that in Italy alone around 1 million people (i.e. 1.7% of total population and 2.6% of adults 18-67 years-old) are employed either as school teachers (STs) or school assistants (SAs). However, this very same remark offers a possible explanation for the low reporting of IMD in the school settings. In other words, is possible that available data may have been significantly flawed by reporting bias, with cases accounted as community-acquired rather than as work-related ones (82), with subsequent underestimation of actual rates of occupational IMD.

Data regarding occupational transmission of meningococcal disease in HCWs are similarly tantalizing. Analysis of available data shows a common pattern in nearly all reported cases, as unprotected, close contact exposures to the airways of patients affected by IMD were ultimately identified, either during mouth-to-mouth ventilation or airway management (15, 20, 26-31, 83). In this regard, also the use of the oxygen face mask during emergency procedures on IMD patients apparently increases the risk for disease transmission, even without close contact with index cases, as turbulent fluxes of aerosols may spread infectious droplets at larger distances (14). However, not only such exposures are quite a daily experience for a large number of professionals, in particular for ambulance paramedic and for healthcare workers (i.e. physicians, nurses, etc.) from emergency departments (83-85), but also a large share of IMD usually requires extensive airway management, including intubation procedures, and nowadays only few secondary IMD cases among HCWs have been globally reported.

Some explanations of such figures have been otherwise suggested (83). First at all, all available reports underscore that involved HCWs did not wear PPE at time of the presumed contact, even for close interactions (15, 20, 26-31). As *N meningitidis* is only transmitted from person to person, and dies quickly outside the host, successful transmission of meningococcal infection is unlikely beyond a distance of one meter, and may be successfully impaired by wearing simple respiratory PPE (3, 11, 15, 20, 44, 54, 58, 83-88).

Such remarks may explain as absolutely few cases of secondary IMD have been accounted also in personnel that may share some exposure to ambulance workers, such as policemen (27), and a reasonable inference it that our data eventually reflect the incidence in subjects who failed to apply even basic preventive measures. Moreover, scant information is available regarding PEC and the immunization status of involved HCWs. Actually, not only efficacy of PEC has been repetitively proven, but specific recommendations have been issued for all HCWs whose mouth or nose is directly exposed to infectious respiratory droplets within a distance of less than 1 meter from a probable or confirmed case of IMD (72, 83). Despite the high risk perception usually associated with IMD (89-92), HCWs may fail to adhere to these recommendations, in particular as they may did not perform any airway management procedure on the index patient, being then unconscious of his/her actual state at the time of the exposures, as it was reported in some of the aforementioned cases (20, 29). Nonetheless, antibiotics may cause adverse reactions in some patients (93), and some workers may deliberately avoid chemoprophylaxis in more doubtful cases. In other words, the limited number of secondary cases in healthcare workers may be interpreted as combined failure of PPE use and PEC.

On the contrary, it is reasonable that vaccination status had only a limited effect on the reported data. Despite polysaccharide vaccines became available in the 1970s, only sporadically specific recommendations have been issued promoting vaccination of HCWs, even for personnel potentially exposed to IMD cases such as professionals from emergency departments or laboratories, ambulance workers, pediatricians (83, 94, 95). Also the recently issued Italian National Vaccine Prevention Plan 2017-2019 did not include any specific recommendation regarding meningococcal vaccination in healthcare settings (96-98).

More extensive evidence details IMD cases acquired in the biological laboratories, as such reports have appeared in the literature for many years, being previously summarized (9, 21). Collectively, available data suggest that BLWs would be at a significantly higher risk both for contracting IMD and for developing a more severe disease, with a relatively high prevalence of severe sequelae in surviving cases.

Such results may be somehow explained. Firstly, even though immunization data are not homogenously available in all cases, only one among the 41 reported cases was vaccinated, but failed to perform period boosters, and such results are consistent with reports suggesting low rates for meningococcal vaccination in BLWs (9, 19, 21). This is particularly frustrating, as most of available recommendations and guidelines are aimed to improve vaccination rates for all meningococcal serogroups (83, 94-98), and conjugate vaccines have been proven as efficient in eliciting a sustained immune response in BLWs (12).

Second, a large share of reported cases occurred in BLWs who did not use MSC when manipulating microbiological specimens and/or viable cultures (9, 13, 19, 34-37), and even when appropriate biosafety measures were apparently applied, follow-up investigations have sometimes identified violations and/or malfunctioning that increased the extent of exposures (19, 21, 39, 41). Such reports are somewhat worrisome, as malfunctioning MSC may give to the laboratory personnel a false sense of security, with potential detrimental effect especially when BLWs are asked to manage specimens from more aggressive strains, with subsequent higher risk for a more severe disease in case of infection.

In BLWs, unnoticed or underestimate exposures are even more worrisome, as some Authors have reported a diffuse lack of accurate training on the early signs and symptoms of IMD: their management may be therefore affected by significant delays in diagnosis and treatment, with only late access to appropriate PEC, and these remarks may collectively explain their often dismal prognosis. Actually, none of cases we analyzed had apparently received any PEC (9, 19, 21, 39, 41).

The evidences we collected regarding work-related secondary cases in occupational sectors other than healthcare, laboratory and schools are even more conflicting. Some workplaces may expose workers to significant crowding in enclosed spaces, with subsequent increased risk for prolonged close contact (e.g. hotel industry, large industrial plants, activities associated with the reception of mass gathering, etc.), and subsequent transmission of the pathogens. Similarly, some reports have identified bars, restaurants, discotheques as environments at high risk for meningococcal contagion, in particular in age groups characterized by higher carrier status (1, 4, 57, 73, 99-104). Again, there are some hints that airborne factors that may potentially damage the epithelium of the upper airways (e.g. active and passive smoking, dusts, irritating vapors, etc.) may contribute to the early phases of meningococcal invasion of the bloodstream, in turn increasing the risk for developing IMD (16, 17, 48). However, our research identified only three work-related outbreaks in the industrial sectors (16, 17, 48), and all the aforementioned reports require a cautious assessment.

First at all, South American reports included large populations that resided in nearby communities that may be defined as "factory town": working populations and communities were therefore largely coincident, and even large community outbreaks occurred simultaneously or nearly simultaneously with reported occupational IMD cases, whose contagion may therefore be accounted to community rather than to the occupational settings (16, 17). Second, the Authors also pointed out that the outbreaks were at least partially consequent temporary swelling of the working population: as most of temporary workers shared recoveries and hostels, again it is possible that a significant share of cases were rather from the community than secondary to workplace exposures (16, 48). In this regard, Sonnenberg et al were able to identify an interesting historical trend, with a significant reduction in incident cases following extensive interventions aimed to improve the quality of temporary dwelling sites for the workforce (48).

The single case reported from the migration reception center deserve some further reflection. Despite the ever increasing flow of migrants from high-risk countries, and the significant number of workers involved in migrants' reception, no other cases have to date been reported (49). Before accepting a relatively low risk for such occupational settings, it is possible that the reported case eventually represents an early warning, suggesting the importance of adopting more stringent public health measures. First at all, interventions on migrants' reception centers are required in order to improve housing conditions and allowing access to health services even in irregular situations (105-108). Eventually, as the staff of migrants' reception centers eventually interact with people from high risk countries where vaccination campaigns are usually enforced (2-7, 49), it is reasonable suggesting the active offer of meningococcal vaccines also for this occupational group (92, 105).

Conclusions

In conclusion, despite several occupational settings have the potential to expose workers to an increased risk for *N meningitidis* infections and ultimately IMD, available reports suggest that only in HCWs and BLWs increased preventive measures may found some base of evidence. Such interventions should include educative interventions aimed to improve knowledge of IMD, and in particular its risk factors and the recommendations for PEC. Both HCWs and BLWs must be made aware that PPE must be regularly worn, in particular when managing the airways of unconscious patients not apparently involved in major trauma, or during the handling of viable biological specimens from even suspected IMD cases. Again, BLWs should avoid to manage biological specimens without appropriate biosafety measures.

Data regarding vaccination policies appear more conflicting: whereas higher incidence and lethality of IMD in BLWs stress the importance for improve their vaccination rates, the cost-effectiveness in HCWs seems doubtful. However, in cases of increased IMD rates in the reference population, vaccination campaigns may found some rationale not only in BLWs and then in HCWs, but also for certain occupational groups such as school personnel and staff of reception centers.

Note: This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors. Ethics approval was not required for this narrative review.

References

1. Gioia CAC, de Lemos APS, Gorla MCO, Mendoza-Sassi RA, Ballester T, Groll Von A, et al. Detection of Neisseria meningitidis in asymptomatic carriers in a university hospital from Brazil. Rev Argent Microbiol 2015; 47: 322-327.
2. Strifler L, Morris SK, Dang V, Tu HA, Minhas RS, Jamieson FB, et al. The Health Burden of Invasive Meningococcal Disease: A Systematic Review. J Pediatric Infect Dis Soc 2016; 5: 417-443.
3. Stephens DS, Greenwood B, Brandtzaeg P. Epidemic meningitis, meningococcaemia, and Neisseria meningitidis. Lancet 2007; 369: 2196-2210.
4. Chatelet du IP, Deghmane AE, Antona D, Hong E, Fonteneau L, Taha MK, et al. Characteristics and changes in invasive meningococcal disease epidemiology in France, 2006-2015. J Infect 2017; 74: 564-574.
5. Stefanelli P, Fazio C, Neri A, Di Taranto A, Labonia M, De Robertis AL, et al. Twenty years of surveillance of Invasive Meningococcal Diseases in Puglia, Italy. Ann Ist Super Sanità 2015; 51: 366-370.
6. Bosis S, Mayer A, Esposito S. Meningococcal disease in childhood: epidemiology, clinical features and prevention. J Prev Med Hyg 2015; 56: E121-4.
7. Pollard AJ, Begg N. Meningococcal disease and healthcare workers. BMJ 1999; 319: 1147-11478.
8. Woodhouse S, Hunter PR. Risk of Invasive Meningococcal Disease among School Workers in Cheshire, United Kingdom. Clin Infect Dis 2001; 32: 1795-1797.
9. Sejvar JJ, Johnson D, Popovic T, Miller JM, Downes F, Somsel P, et al. Assessing the Risk of Laboratory-Acquired Meningococcal Disease. J Clin Microbiol 2005; 43: 4811-4814.
10. Rim K-T, Lim C-H. Biologically Hazardous Agents at Work and Efforts to Protect Workers' Health: A Review of Recent Reports. Saf Health Work 2014; 5: 43-52.
11. Harrison LH, Trotter CL, Ramsay ME. Global epidemiology of meningococcal disease. Vaccine 2009; 27S2: B51-B63.
12. Hong E, Terrade A, Taha M-K. Immunogenicity and safety among laboratory workers vaccinated with Bexsero® vaccine. Hum Vaccin Immunother 2016; 13: 645-648.
13. Kessler Tkeshelashvili A, Stephens DS, Somani J. Laboratory-Acquired Serogroup A Meningococcal Meningitis. J Occup Health 2007; 49: 399-401.
14. Fusco FM, Puro V. Meningococcal disease in an ambulance worker. Euro Surveill 2008; 13: pii=8061.
15. Gehanno J-F, Kohen-Couderc L, Lemeland J-F, Leroy J. Nosocomial Meningococcemia in a Physician. Infect Control Hosp Epidemiol 1999; 20: 564-5.
16. Liphaus BL, Cappeletti-Gonçalves-Okai MI, Silva-Delemos AP, Gorla MC, Rodriguez-Fernandes M, Pacola MR, et al. Outbreak of Neisseria meningitidis C in a Brazilian oil refinery involving an adjacent community. Enferm Infecc Microbiol Clín 2013; 31: 88-92.
17. Iser BPM, Lima HCAV, De Moraes C, De Almeida RPA, Watanabe LT, Alves SLA, et al. Outbreak of Neisseria men-

ingitidis C in workers at a large food-processing plant in Brazil: challenges of controlling disease spread to the larger community. Epidemiol Infect 2012; 140: 906-15.
18. Li J, Li Y, Shao Z, Li L, Yin Z, Ning G, et al. Prevalence of meningococcal meningitis in China from 2005 to 2010. Vaccine 2015; 33: 1092-1097.
19. Boutet R, Stuart JM, Kaczmarski EB, Gray SJ, Jones DM, Andrews N. Risk of laboratory-acquired meningococcal disease. J Hosp Infect 2001; 49: 282-284.
20. Gilmore A, Stuart J, Andrews N. Risk of secondary meningococcal disease in health-care workers. Lancet 2000; 356: 1654-1655.
21. Borrow R, Findlow J, Gray S, Taylor S, Kaczmarski E. Safe laboratory handling of Neisseria meningitidis. J Infect 2014; 68: 305-12.
22. Pelton SI. The Global Evolution of Meningococcal Epidemiology Following the Introduction of Meningococcal Vaccines. J Adolesc Health 2016; 59S1: S3-S11.
23. Borrow R, Alarcón P, Carlos J, Caugant DA, Christensen H, Debbag R, et al. The Global Meningococcal Initiative: global epidemiology, the impact of vaccines on meningococcal disease and the importance of herd protection. Expert Rev Vaccines 2017; 16: 313-28.
24. World Health Organization. The World Health Report, 2000. World Health Organization. Geneva; 2000: 1-215.
25. World Health Oganization. Biorisk management - Laboratory Biosecurity Guidance. World Health Organization. Geneva; 2006: 1-41.
26. Centers for Disease Control and Prevention. Nosocomial Meningococcemia - Wisconsin. MMWR Morb Mortal Wkly Rep 1978; 27: 358-363.
27. Centers for Disease Control and Prevention. Occupational Transmission of Neisseria meningitidis - California, 2009. MMWR 2010; 59: 1480-1484.
28. Petsas A, Sharma A, Aghadiuno O, Abid M, Paranthaman K. A secondary case of meningococcal disease in an ambulance worker, Berkshire, November 2007. Euro Surveill 2008; 13: pii=8020.
29. Puleston R, Beck C, Tahir M, Bardhan M, Charlemagne P, Alves C, et al. An unusual transmission event of Neisseria meningitidis serogroup W135 type 2a in a healthcare setting, England, 2012. Euro Surveill. 2012; 17: pii=20308.
30. Feldman HA. Meningococcal infections. Adv Intern Med 1972; 18: 117-140.
31. Centers for Disease Control and Prevention. Epidemiological Notes and Reports. Laboratory Acquired Meningococcemia --- California and Massachusetts. MMWR 1991; 40: 46-57, 55
32. Petsas A, Abid M. Author's reply: meningococcal disease in an ambulance worker. Euro Surveill. 2008; 13: pii=8062.
33. Pike RM. Laboratory-Associated Infections: incidence, fatalities, causes, and prevention. Ann Rev Microbiol 1979; 33: 41-66.
34. Bhatti AR, DiNinno VL, Ashton FE, White LA. A laboratory-acquired infection with Neisseria meningitidis. J Infect 1982; 4: 247-252.
35. Guibourdenche M, Darchis J-P, Boisivon A, Collatz E, Riou J-Y. Enzyme electrophoresis, Sero- and Subtyping, and Outer Membrane Protein Characterization of Two Neisseria meningitidis Strains Involved in Laboratory-Acquired Infections. J Clin Microbiol. 1994; 32: 701-704.
36. Centers for Disease Control and Prevention. Laboratory-Acquired Meningococcal Disease - United States, 2000. MMWR 2002; 51: 141-144.
37. Athlin S, Vikerfors T, Fredlund H, Olcén P. Atypical clinical presentation of laboratory-acquired meningococcal disease. Scand J Infect Dis 2009; 39: 911-913.
38. Baron EJ, Miller JM. Bacterial and fungal infections among diagnostic laboratory workers: evaluating the risks. Diagn Microbiol Infect Dis 2008; 60: 241-246.
39. Silver S. Laboratory-acquired lethal infections by potential bioweapons pathogens including Ebola in 2014. FEMS Microbiol Lett 2014; 362: 1-6.
40. Willemarck N, Van Vaerenbergh B, Descamps E, Brosius B, Dai Do Thi C, Leunda A, et al. Laboratory-Acquired Infections in Belgium (2007-2012). Institut Scientifique de Santé Publique Wetenschappelijk Instituut Volksgezondheid. Brussels; 2012; 1-49.
41. Omer H, Rose G, Jolley KA, Frapy E, Zahar J-R, Maiden MCJ, et al. Genotypic and Phenotypic Modifications of Neisseria meningitidis after an Accidental Human Passage. PLoS ONE 2011; 6: e17145.
42. MacDougall DM, Langley JM, Li L, Ye L, MacKinnon-Cameron D, Top KA, et al. Knowledge, attitudes, beliefs, and behaviors of university students, faculty, and staff during a meningococcal serogroup B outbreak vaccination program. Vaccine 2017; 35: 2520-2530.
43. Sridhar S, MD BG, Head C, Plotkin SA, Safadi MA, Saha S, et al. Global incidence of serogroup B invasive meningococcal disease: a systematic review. Lancet Infect Dis 2015; 15: 1334-1346.
44. Gabutti G, Stefanati A, Kuhdari P. Epidemiology of Neisseria meningitidis infections: case distribution by age and relevance of carriage. J Prev Med Hyg 2015; 56: E116-E120.
45. Basta NE, Mahmoud AAF, Wolfson J, Ploss A, Heller BL, Hanna S, et al. Immunogenicity of a Meningococcal B Vaccine during a University Outbreak. N Eng J Med 2016; 375: 220-228.
46. Davison KL. Clusters of meningococcal disease in school and preschool settings in England and Wales: what is the risk? Arch Dis Child 2004; 89: 256-60.
47. Pazdiora P, Morávková I, Bergerová T, Štruncová V, Křížová P, Musílek M, et al. Cluster of three cases of invasive meningococcal disease in a preschool facility in West Bohemia, the Czech Republic. Folia Microbiol 2012; 58: 123-126.
48. Sonnenberg P, Silber E, Ho KC, Koornhof H. Meningococcal disease in South African goldmines - Epidemiology and strategies for control. S Afr Med J 2000; 90: 513-7.
49. Stefanelli P, Fazio C, Neri A, Rezza G, Severoni S, Vacca P et al. Imported and Indigenous cases of Invasive Meningococococcal Disease W:P1.5,2:F1-1: ST-11 in migrants' re-

ception centers. Italy, June-November 2014. Adv Exp Med Biol 2016; 897: 81-3.
50. De Wals P, Deshaies P, De Serres G, Duval B, Goulet L, Pouliot B, et al. Risk and prevention of meningococcal disease among education workers: A review. Can J Infect Dis 2004; 15: 89-93.
51. Whittaker R, Dias JG, Ramliden M, Ködmön C, Economopoulou A, Beer N, et al. The epidemiology of invasive meningococcal disease in EU/EEA countries, 2004 - 2014. Vaccine 2017 Apr 11; 35(16): 2034-2041.
52. Vygen S, Hellenbrand W, Stefanoff P, Hanquet G, Heuberger S, Stuart J. European public health policies for managing contacts of invasive meningococcal disease cases better harmonised in 2013 than in 2007. Euro Surveill 2016 Feb 4; 21(5): 30125-9.
53. Boccia D, Andrews N, Samuelsson S, Heuberger S, Perrocheau A, Stuart JM. Effectiveness of different policies in preventing meningococcal disease clusters following a single case in day-care and pre-school settings in Europe. Epidemiol Infect 2006; 134: 872–6.
54. Caugant DA, Maiden MCJ. Meningococcal carriage and disease - Population biology and evolution. Vaccine 2009; 27: B64-B70.
55. Christensen H, Hickman M, Edmunds WJ, Trotter CL. Introducing vaccination against serogroup B meningococcal disease: An economic and mathematical modelling study of potential impact. Vaccine 2013; 31: 2638-2646.
56. Christensen H, May M, Bowen L, Hickman M, Trotter CL. Meningococcal carriage by age: a systematic review and meta-analysis. Lancet Infect Dis 2010; 10: 853-861.
57. Delbos V, Lemée L, Bénichou J, Berthelot G, Taha MK, Caron F, et al. Meningococcal carriage during a clonal meningococcal B outbreak in France. Eur J Clin Microbiol Infect Dis 2013; 32: 1451-1459.
58. Dellicour S, Greenwood B. Systematic review: Impact of meningococcal vaccination on pharyngeal carriage of meningococci. Trop Med Int Health 2007; 12: 1409-1421.
59. Gryniewicz O, Kolbusz J, Rosinska M, Zielinski A, Stefanoff P. Epidemiology of meningococcal meningitis and changes in the surveillance system in Poland, 1970-2006. Euro Surveill 2007; 12: E7-8.
60. Harrison LH. Epidemiological Profile of Meningococcal Disease in the United States. Clin Infect Dis 2010; 50: S37-S44.
61. Lopez Castelblanco R, Lee M, Hasbun R. Epidemiology of bacterial meningitis in the USA from 1997 to 2010: a population-based observational study. Lancet Infect Dis 2014; 14: 813-819.
62. Perrocheau A, Taha M-K, Lévy-Bruhl D. Epidemiology of invasive meningococcal disease in France in 2003. Euro Surveill 2005; 10: 238-241.
63. Polkowska A, Toropainen M, Ollgren J, Lyytikäinen O, Nuorti JP. Bacterial meningitis in Finland, 1995–2014: a population-based observational study. BMJ Open 2017; 7: e015080-10.
64. Sáfadi MAP, Carvalhanas TRMP, Paula de Lemos A, Gorla MCO, Salgado M, Fukasawa LO, et al. Carriage Rate and Effects of Vaccination after Outbreaks of Serogroup C Meningococcal Disease, Brazil, 2010. Emerg Infect Dis 2014; 20: 806-811.
65. Soeters HM, Whaley M, Alexander-Scott N, Kanadanian KV, MacNeil JR, Martin SW, et al. Meningococcal Carriage Evaluation in Response to a Serogroup B Meningococcal Disease Outbreak and Mass Vaccination Campaign at a College - Rhode Island, 2015–2016. Clin Infect Dis 2017; 64: 1115-1122.
66. Stahl JP, Cohen R, Denis F, Gaudelus J, Lery T, Lepetit H, et al. Vaccination against meningococcus C. vaccinal coverage in the French target population. Med Mal Infect 2013; 43: 75-80.
67. Vescio F, Busani L, Mughini Gras L, Fazio C, Neri A, Avellis L, et al. Climate, demographic factors and geographical variations in the incidence of invasive meningococcal disease in Italy. Epidemiol Infect 2015; 143: 1742-1750.
68. Veronesi L, Virdis R, Bizzoco S, Colucci ME, Affanni P, Paganuzzi F, et al. Vaccination status and prevalence of enteric viruses in internationally adopted children. The case of Parma, Italy. Acta Biomed 2011; 82: 208-213.
69. McGill F, Heyderman RS, Michael BD, Defres S, Beeching NJ, Borrow R, et al. The UK joint specialist societies guideline on the diagnosis and management of acute meningitis and meningococcal sepsis in immunocompetent adults. J Infect 2016; 72: 405-38.
70. European Centre for Disease Prevention and Control (ECDC). Public health management of sporadic cases of invasive meningococcal disease and their contacts. ECDC, Stockholm; 2010: 1-50.
71. Health Protection Agency, Public Health Medicine Environmental Group, Stuart JM, Evans MR, Monk PN, Barker M, et al. Managing meningococcal disease (septicaemia or meningitis) in higher education institutions. Universities UK. London; 2004; 1-30.
72. Centers for Disease Control and Prevention. Prevention and Control of Meningococcal Disease: recommendations of the Advisory Commitee on Immunization Practices. MMWR Morb Mortal Wkly Rep 2013; 62: 1-28.
73. Delisle E, Larrieu S, Simoes J, Laylle N, De Pommerol M, Taha M-K, et al. Community outbreak of group B meningococcal disease in southwest France – December 2008 to September 2009. Euro Surveill 2010; 15: pii=19665.
74. MacNeil JR, Rubin L, Folaranmi T, Ortega-Sanchez IR, Patel M, Martin SW. Use of Serogroup B Meningococcal Vaccines in Adolescents and Young Adults: Recommendations of the Advisory Committee on Immunization Practices, 2015. MMWR Morb Mortal Wkly Rep 2015; 64: 1171-1176.
75. Nolan T, O'Ryan M, Wassil J, Abitbol V, Dull P. Vaccination with a multicomponent meningococcal B vaccine in prevention of disease in adolescents and young adults. Vaccine 2015; 33: 4437-4445.
76. Rodriguez P, Alvarez I, Torres MT, Diaz J, Bertoglia MP, Carcamo M, et al. Meningococcal carriage prevalence in

university students, 18-24 years of age in Santiago, Chile. Vaccine 2014; 32: 5677-5680.
77. Mikolajczyk RT, Akmatov MK, Rastin S, Kretzschmar M. Social contacts of school children and the transmission of respiratory-spread pathogens. Epidemiol Infect 2008; 136: 813-822.
78. Macintosh J, Luthy KE, Beckstrand RL, Eden LM, Orton J. Vaccination perceptions of school employees in a rural school district. Vaccine 2014; 32: 4766-4771.
79. Ha C, Rios LM, Pannaraj PS. Knowledge, Attitudes, and Practices of School Personnel Regarding Influenza, Vaccinations, and School Outbreaks. J Sch Health 2013; 83: 554-561.
80. Luthy KE, Thompson KE, Beckstrand RL, Macintosh JLB, Eden LM. Perception of safety, importance, and effectiveness of vaccinations among urban school employees in Utah. J Am Assoc Nurse Pract 2015; 27: 313-320.
81. Luthy KE, Houle K, Beckstrand RL, Macintosh J, Lakin RG. Vaccination Perceptions and Barriers of School Employees: A Pilot Study. J Sch Nurs 2013; 29: 284-293.
82. Azzari C, Nieddu F, Moriondo M, Indolfi G, Canessa C, Ricci S, et al. Underestimation of Invasive Meningococcal Disease in Italy. Emerg Infect Dis 2016; 22: 469-475.
83. Stuart JM, Gilmore AB, Ross A, Patterson W, Kroll JS, Kaczmarski EB, et al. Preventing secondary meningococcal disease in health care workers: recommendations of a working group of the PHLS Meningococcus Forum. Commun Dis Public Health 2001; 4: 102-105.
84. Dorevitch S, Forst L. The Occupational Hazards of EmergencyPhysicians. Am J Emerg Med 2000; 18: 300-311.
85. Committee HICPA. Part II. Recommendations for prevention of infections in health care personnel. Am J Inf Control 1998; 26: 328-335.
86. Kepenekli Kadayifci E, Güneşer Merdan D, Soysal A, Karaaslan A, Atıcı S, Durmaz R, et al. Prevalence of Neisseria meningitidis carriage: a small-scale survey in Istanbul, Turkey. J Infect Dev Ctries 2016; 10: 413-417.
87. Neri A, Pezzotti P, Fazio C, Vacca P, D'Ancona FP, Caporali MG, et al. Epidemiological and Molecular Characterization of Invasive Meningococcal Disease in Italy, 2008/09-2012/13. PLoS ONE 2015; 10: e0139376-12.
88. Stephens DS. Biology and pathogenesis of the evolutionarily successful, obligate human bacterium Neisseria meningitidis. Vaccine 2009; 27S: B71-7.
89. de Waure C, Quaranta G, Ianuale C, Panatto D, Amicizia D, Apprato L, et al. Knowledge, attitudes and behaviors of the Italian population towards Neisseria meningitidis, Streptococcus pneumoniae and HPV diseases and vaccinations: A cross-sectional multicentre study. Public Health 2016; 141: 136-42.
90. Dinelli MIS, Neves Fraga Moreira das T, Regina Cruz Paulino E, Pereira da Rocha MC, Bracale Graciani F, de Moraes-Pinto MI. Immune status and risk perception of acquisition of vaccine preventable diseases among health care workers. Am J Infect Control 2009; 37: 858-60.
91. Faure E, Cortot C, Gosset D, Cordonnier A, Deruelle P, Guery B. Vaccinal status of healthcare students in Lille. Med Mal Infect 2013; 43: 114–117.
92. Riccò M, Cattani S, Casagranda F, Gualerzi G, Signorelli C. Knowledge, attitudes, beliefs and practices of occupational physicians towards vaccinations of health care workers: A cross sectional pilot study in North-Eastern Italy. Int J Occup Med Environ Health 2017 ; 30: 775-790.
93. Giovannetti F. Anaphylaxis following unnecessary meningococcal chemoprophylaxis of a healthcare worker. Euro Surveill 2009; 14: pii=19207.
94. Maltezou HC, Wicker S, Borg M, Heininger U, Puro V, Theodoridou M, et al. Vaccination policies for health-care workers in acute health-care facilities in Europe. Vaccine 2011; 29: 9557-9562.
95. Maltezou HC, Poland GA. Vaccination policies for health-care workers in Europe. Vaccine 2014; 32: 4876-4880.
96. Bonanni P, Ferro A, Guerra R, Iannazzo S, Odone A, Pompa MG, et al. Vaccine coverage in Italy and assessment of the 2012- 2014 National Immunization Prevention Plan. Epidemiol Prev 2015; 39: 145-158.
97. Biasio LR, Corsello G, Costantino C, Fara GM, Giammanco G, Signorelli C, et al. Communication about vaccination: A shared responsibility. Hum Vaccin Immunother 2016; 12: 2984-2987.
98. Signorelli C, Odone A, Bonanni P, Russo F. New Italian immunisation plan is built on scientific evidence: Carlo Signorelli and colleagues reply to news article by Michael Day. BMJ 2015; 351; h6775.
99. Deghmane AE, Parent du Chatelet I, Szatanik M, Hong E, Ruckly C, Giorgini D, et al. Emergence of New Virulent Neisseria meningitidisSerogroup C Sequence Type 11 Isolates in France. J Infect Dis. 2010; 202: 247–250.
100. Memish ZA, Al-Tawfiq JA, Almasri M, Azhar EI, Yasir M, Al-Saeed MS, et al. Neisseria meningitidis nasopharyngeal carriage during the Hajj: A cohort study evaluating the need for ciprofloxacin prophylaxis. Vaccine 2017; 35: 2473-2478.
101. Memish ZA, Goubeaud A, Bröker M, Malerczyk C, Shibl AM. Invasive meningococcal disease and travel. J Infect Public Health 2010; 3: 143-151.
102. Lucidarme J, Scott KJ, Ure R, Smith A, Lindsay D, Stenmark B, et al. An international invasive meningococcal disease outbreak due to a novel and rapidly expanding serogroup W strain, Scotland and Sweden, July to August 2015. Euro Surveill 2016; 21: pii=30395.
103. Honish L, Soskolne CL, Senthilselvan A, Houston S. Modifiable Risk Factors for Invasive Meningococcal Disease During an Edmonton, Alberta Outbreak, 1999-2002. Rev Can Sante Pub 2008; 99: 46-51.
104. Mayoral Cortés JM, Torres Butrón E, Garcia Fernandez M, Herrardor Ortiz Z, Huarte Osakar S, Santos Luque R, et al. Community cluster of meningococcal disease by Neisseria meningitidis serogroup C in Andalusia, Spain, March to May 2011. Euro Surveill 2012; 17: pii=20261.
105. Signorelli C, Riccò M, Odone A.The Italian National Health Service expenditure on workplace prevention and

safety (2006-2013): a national-level analysis. Ann Ig 2016; 28: 313-318.
106. Manzoli L, Sotgiu G, Magnavita N, Durando P; National Working Group on Occupational Hygiene of the Italian Society of Hygiene, Preventive Medicine and Public Health (SItI). Evidence-based approach for continuous improvement of occupational health. Epidemiol Prev 2015; 39: S81-S85.
107. Odone A, Riccò M, Morandi M, Borrini BM, Pasquarella C, Signorelli C. Epidemiology of tuberculosis in a low-incidence Italian region with high immigration rates: differences between not Italy-born and Italy-born TB cases. BMC Public Health 2011; 11: 376.
108. Signorelli C, Riccò M. The health-environment interaction in Italy. Ig Sanita Pubbl 2012; 68: 374-380. Italian.

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