Clinical Manifestations of MenWY-disease

Ulrich Vogel

University of Würzburg
Institute for Hygiene and Microbiology

Reference Laboratory for Meningococci and H. Influenzae
Germany

Search term in Pubmed

Mening plus serogroup & clinical parameters (age, underl. cond., symptoms) & reasonable focus…

("neisseria meningitidis"[MeSH Terms] OR ("neisseria"[All Fields] AND "meningitidis"[All Fields]) OR "neisseria meningitidis"[All Fields]) AND

(("serogroup"[MeSH Terms] OR "serogroup"[All Fields]) AND W[All Fields]) OR (("serogroup"[MeSH Terms] OR "serogroup"[All Fields]) AND W135[All Fields]) OR (("serogroup"[MeSH Terms] OR "serogroup"[All Fields]) AND W-135[All Fields]) OR (("serogroup"[MeSH Terms] OR "serogroup"[All Fields]) AND "Y"[Journal])

AND

((clinical[All Fields] AND picture[All Fields]) OR ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "symptoms"[All Fields] OR "diagnosis"[MeSH Terms] OR "symptoms"[All Fields]) OR ("syndrome"[MeSH Terms] OR "syndrome"[All Fields]) OR ("pneumonia"[MeSH Terms] OR "pneumonia"[All Fields]) OR "clinical presentation")

NOT

("Vaccine" [TI] OR "Immunogenicity" [TI]) NOT ("diagnostic" [TI] OR "PCR" [TI] OR "assay" [TI] OR "evaluation" [TI] OR "Genomic" [Ti] OR "cluster" [TI] OR "vaccination" [TI] OR "immune response" [TI] OR "genetic diversity" [TI] OR "serum bactericidal" [TI])

Return

- Filtered by language (English) and abstract availability
  - 185 abstracts
- Exclusion criteria while reading abstracts
  - Description of clusters/outbreaks with <10 patients (except for one report of 5 cases from France with clear link to clinical manifestation)
  - Description of typing data with no evidence for clinical evaluation
  - Unrelated material
  - Case reports
- 42 items idenified
- 10 full papers were retrieved after first screening for availability (n=12 not available as full text) and suitability for research question

Full text papers

1: **Lahra MM, Enriquez RP**. Australian Meningococcal Surveillance Programme annual report, 2012. Commun Dis Intell Q Rep. 2013 Sep 30;37(3):E224-32. PubMed PMID:24890958.

2**: Faye A, Mariani-Kurkdjian P, Taha MK, Angoulvant F, Antonios M, Aubertin G, Soussan V, Bingen E, Bourrillon A**. Clinical features and outcome of pediatric Neisseria meningitidis serogroup W135 infection: a report of 5 cases. Clin Infect Dis. 2004 Jun 1;38(11):1635-7. Epub 2004 May 12. PubMed PMID: 15156454.

3: **Vienne P, Ducos-Galand M, Guiyoule A, Pires R, Giorgini D, Taha MK, Alonso JM**. The role of particular strains of Neisseria meningitidis in meningococcal arthritis, pericarditis, and pneumonia. Clin Infect Dis. 2003 Dec 15;37(12):1639-42. Epub 2003 Nov 17. PubMed PMID: 14689345.

4: **Gaschignard J, Levy C, Deghmane AE, Dubos F, Muszlak M, Cohen R, Bingen E, Faye A, Taha MK**. Invasive serogroup w meningococcal disease in children: a national survey from 2001 to 2008 in France. Pediatr Infect Dis J. 2013 Jul;32(7):798-800. doi: 10.1097/INF.0b013e31828e9e91. PubMed PMID: 23838782.

5: **Tsolia MN, Theodoridou M, Tzanakaki G, Vlachou V, Mostrou G, Stripeli F, Kalabalikis P, Pangalis A, Kafetzis D, Kremastinou J, Konstantopoulos A**. Invasive meningococcal disease in children in Greece: comparison of serogroup A disease with disease caused by other serogroups. Eur J Clin Microbiol Infect Dis. 2006 Jul;25(7):449-56. PubMed PMID: 16773393.

6: **Spanjaard L, Bol P, de Marie S, Zanen HC.** Association of meningococcal

serogroups with the course of disease in the Netherlands, 1959-83. Bull World Health Organ. 1987;65(6):861-8. PubMed PMID: 3124970; PubMed Central PMCID: PMC2491086.

7: **Wang JL, Liu DP, Yen JJ, Yu CJ, Liu HC, Lin CY, Chang SC.** Clinical features and outcome of sporadic serogroup W135 disease Taiwan. BMC Infect Dis. 2006 Jan 19;6:7. PubMed PMID: 16420709; PubMed Central PMCID: PMC1373656.

8: **Brooks R, Woods CW, Benjamin DK Jr, Rosenstein NE.** Increased case-fatality rate associated with outbreaks of Neisseria meningitidis infection, compared with sporadic meningococcal disease, in the United States, 1994-2002. Clin Infect Dis. 2006 Jul 1;43(1):49-54. Epub 2006 May 24. PubMed PMID: 16758417.

9: **Stephens DS, Hajjeh RA, Baughman WS, Harvey RC, Wenger JD, Farley MM**. Sporadicmeningococcal disease in adults: results of a 5-year population-based study. Ann Intern Med. 1995 Dec 15;123(12):937-40. PubMed PMID: 7486489.

10. **Bethea J, Makki S, Gray S, MacGregor V, Ladhani S.** Clinical characteristics and public health management of invasive meningococcal group W disease in the East Midlands region of England, United Kingdom, 2011 to 2013. Euro Surveill. 2016 Jun 16;21(24). doi: 10.2807/1560-7917.ES.2016.21.24.30259.

Additional papers identified by case report search

1: **Ladhani SN, Lucidarme J, Newbold LS, Gray SJ, Carr AD, Findlow J, Ramsay ME, Kaczmarski EB, Borrow R**. Invasive meningococcal capsular group Y disease, England and Wales, 2007-2009. Emerg Infect Dis. 2012 Jan;18(1):63-70. doi: 10.3201/eid1801.110901. PubMed PMID: 22261040; PubMed Central PMCID: PMC3310110.

2: **Winstead JM, McKinsey DS, Tasker S, De Groote MA, Baddour LM.** Meningococcal pneumonia: characterization and review of cases seen over the past 25 years. Clin Infect Dis. 2000 Jan;30(1):87-94. Review. PubMed PMID: 10619738.

3: **Ladhani SN, Beebeejaun K, Lucidarme J, Campbell H, Gray S, Kaczmarski E, Ramsay ME, Borrow R.** Increase in endemic Neisseria meningitidis capsular group W sequence type 11 complex associated with severe invasive disease in England and Wales. Clin Infect Dis. 2015 Feb 15;60(4):578-85. doi: 10.1093/cid/ciu881. Epub 2014 Nov 10. PubMed PMID: 25389259.

Association of meningococcal serogroups with the course of disease in the Netherlands, 1959-83

Author	Citation	Year	Population based	Study type	Period
Spanjaard	Bulletin WHO 1987	1987	NO	Association of serogroups with disease in >1,200 cases, only 33 W!	1959-1983

Highest CFR for W (18%)
Septicemia without meningitis highest in W
Most W cases in >50 yr
Case fatality of W in >50 yr >60%

Analysis of routine surveillance data

Sporadic Meningococcal Disease in Adults: Results of a 5-Year Population-Based Study

Author	Citation	Year	Population based	Study type	Period
Stephens	Ann Intern Med 1995;123:937-940	1995	Regional	Surveillance 5 yr, emphasis on adults	1988-1993, Atlanta area

5-year population-based study,
Pneumonia, sinusitis, and tracheobronchitis sources of bacteremic meningococcal disease, especially in immunocompromised patients and elderly persons.
Of 15 patients with respiratory illness 5 were caused by WY

prospective

Meningococcal Pneumonia: Characterization and Review of Cases Seen Over the Past 25 Years

Author	Citation	Year	Population based	Study type	Period
Winstead	Clinical Infectious Diseases 2000;30:87–94	2000	No	literature review	1974-1998
58 cases of pneumonia were summarized. Median age was 57.5 yr W, 19% Y, 44%					

Literature review

The Role of Particular Strains of Neisseria meningitidis in Meningococcal Arthritis, Pericarditis, and Pneumonia

Author	Citation	Year	Population based	Study type	Period
Vienne	CID 2003:37 (15 December) • 1639	2003	Yes	Lab surveillance results France	1999-2002
26 cases of arthritis, 6 cases of pericarditis, and 33 cases of pneumonia Arthritis associated with W (mostly ST-11 cc) Pneumonia mostly in patients >70yr, mostly W					

Analysis of routine surveillance data

Invasive Meningococcal Capsular Group Y Disease, England and Wales, 2007–2009

Author	Citation	Year	Population based	Study type	Period
Ladhani	CID 2003:37 (15 December) • 1639	2003	Yes	Surv UK; Y increased from 34 cases in 2007 to 44 in 2008 and 65 in 2009	2007-2009
Median age 60 35% underlying conditions cc23 dominated cc 174 associated with pneumonia in older agegroups					

Analysis of enhanced surveillance data

Clinical Features and Outcome of Pediatric Neisseria meningitidis Serogroup W135 Infection: A Report of 5 Cases

Author	Citation	Year	Population based	Study type	Period
Faye	Clinical Infectious Diseases 2004; 38:1635–7	2004	No	5 ped cases	2000-2002 admitted to one hospital in Paris
4 of 5 ST-11 cc 4 of 5 cases presented with uveitis, arthritis, or pericarditis					

Retrospective case series

Clinical features and outcome of sporadic serogroup W135 disease Taiwan

Author	Citation	Year	Population based	Study type	Period
Wang	BMC Infectious Diseases 2006, 6:7 doi:10.1186/1471-2334-6-7	2006	Yes	Surveillance,	2001-2003, Taiwan
21 W with complete records W patients more likely to be between 20-54 yr old, less likely to be <9 yr old. 5/21 with pneumonia in comparison to 1/67 in Non-W					

Analysis of routine surveillance data, retrospective

Increased Case-Fatality Rate Associated with Outbreaks of Neisseria meningitidis Infection, Compared with Sporadic Meningococcal Disease, in the United States, 1994–2002

Author	Citation	Year	Population based	Study type	Period
Brooks	CID 2006:43 (1 July) • 49	2006	Yes	Surveillance, comparison outbreak and sporadic disease	1994-2004, USA

All pneumonia cases were >65r
In outbreak associated cases, 11 suffered from pneumonia.
All of those were caused by Y.

Analysis of routine surveillance data

Invasive Serogroup W Meningococcal Disease in Children: A National Survey from 2001 to 2008 in France

Author	Citation	Year	Population based	Study type	Period
Gaschig-nard	The Pediatric Infectious Disease Journal Issue: Volume 32(7), July 2013, p 798–800	2013	Yes	Surveillance	2001-2008, France

119 pediatric MenW cases were followed
54% infants,
66% meningitis
6% mortality
8% septic arthritis
2% pericarditis

Analysis of routine surveillance data

Australian Meningococcal Surveillance Programme annual report, 2012

Author	Citation	Year	Population based	Study type	Period
Lahra	CDI Vol 37 No 3 2013	2013	Yes	Surveillance	2012
7 MenW cases were followed 3 >45 yr 1 other disease type					

Analysis of routine surveillance data

Increase in Endemic Neisseria meningitidis Capsular Group W Sequence Type 11 Complex Associated With Severe Invasive Disease in England and Wales

Author	Citation	Year	Population based	Study type	Period
Ladhani	Clinical Infectious Diseases 2015;60(4):578–585	2015	Yes	Surveillance	2010-2011 to 2012-2013

Increase of MenW (cc11): 2013/4: 15%
129 MenW cases werde followed
A quarter of cases <5yr
Half of cases >45yr
12% pneumonia,
7% septic arthritis
4% epigplottitis/supraglottitis

Analysis of enhanced surveillance data

Clinical characteristics …of invasive meningococcal group W disease in the East Midlands region of England, …, 2011 to 2013

Author	Citation	Year	Population based	Study type	Period
Bethea	Euro Surveill. 2016;21(24):pii=30259.	2016	Yes	Clinical report, Midlands	2013
14 MenW cases werde followed 6 >50yr 2 deaths, 2 septic arthritis 4 breathing difficulties 4 chest pains					

Analysis of enhanced surveillance data

Case reports

("neisseria meningitidis"[TIAB] OR meningococc*[TIAB]) AND (pneumonia [TIAB] OR arthritis[TIAB] OR endocarditis[TIAB] OR endophthalmitis [TIAB] OR phlegmon [TIAB] OR abscess [TIAB] OR peritonitis [TIAB] OR pericarditis [TIAB] OR myocarditis [TIAB]) AND (serogroup [TIAB] OR capsule [TIAB] OR capsular [TIAB])

Filters:

- English
- Case report, classical article, clinical study, clinical trial, controlled clinical trial, journal article, meta-analysis, review
- Abstract availability

- 95 articles
- 32 contained useful and retrievable information
- The search furthermore identified important papers not found in the initial search for population based studies

Publication year	Country	Serogroup	Clinical condition	Case number	Age	Age category	DOI	PMID
2016	Germany	C	endophtalmitis	1		child	10.1093/jpids/piw012	27000867
2016	USA	C	arthritis	1	1	toddler	10.1097/MD.0000000000002745	26844522
2015	Germany	C	arthritis	1	19	adult	10.1007/s00113-014-2716-y	25648871
2013	Spain	B	pericarditis, purulent	1	0	infant	10.5546/aap.2013.e144	24196773
2013	Japan	W	immunoreactive complications: pericarditis, polyarthritis, tenosynovitis	1	44	adult		24047748
2012	UK	Y	pneumonia	1		elderly	10.1136/bcr.11.2011.5095	
2011	Spain	Y	pneumonia	1	94	elderly	0.1016/j.rmedc.2011.11.005	26057210
2011	Germany	C (latex)	pericarditis, purulent	1			10.1007/s00108-010-2742-y	20978733
2009	Australia	W	arthritis, hip			infant	10.1111/j.1440-1754.2009.01607.x	20416000
2009		X	arthritis	1	38	adult	10.1097/SMJ.0b013e31819ba3c0	19279530
2008	Spain	B	arthritis, knee	1	73	elderly	10.1016/S1699-258X(08)71815-1	21794512
2007	France	C	pericarditis, purulent	1	55	adult	10.1016/j.annfar.2007.02.001	17337156
2006	Brazil	C	pericarditis, purulent	1	20	adult	10.1080/00365540500279934	16449011
2006	Brazil	C	pericarditis, purulent	1	5	child	10.1016/j.ijcard.2005.09.042	16324757
2004	The Netherlands	C	pericarditis, purulent; pneumonia	1	37	adult		15255084
2004	UK	C	pericarditis, purulent	1		child		15014314
2004	France	C	pericarditis, purulent	1	0	infant		14766892
2001	France	W	arthritis	4		adult		11721491
2001	Germany	B	Secondary immunologically-caused myocarditis, pericarditis and exudative pleuritis	1				11315579
2000	Spain	C	pericarditis, purulent	1	15	adolescent		11084013
2000	Austria	W	arthritis	1		child		10947226
1998	UK	W	pneumonia, sinusitis	1	>90	elderly		9854302
1998	Germany	B	peritonitis, ambulant peritoneal dialysis	1	41	adult		9721963
1990	Nigeria	W	arthritis	1		child		2109513
1989	Spain	C	arthritis, pericarditis, purulent	1				2623251
1989	France	A	arthritis	1				2498830
1982	USA	W	pneumonia	2		adults	10.1164/arrd.1982.125.2.255	6802047
1981		W	pneumonia	1				6784688
1980		W	arthritis	1	1	toddler		6767281
1979		Y	pneumonia	1				464460
1975		Y	pneumonia, arthritis	1				805852
1975		Y	pneumonia	3				164144

Analysis of the number of case reports

Clinical condition	∑	A	B	C	W	X	Y
arthritis	10	1	1	2	5	1	
arthritis, pericarditis, purulent	1			1			
endophtalmitis	1			1			
immunoreactive complications: pericarditis, polyarthritis, tenosynovitis	1				1		
pericarditis, purulent	8		1	7			
pericarditis, purulent; pneumonia	1			1			
peritonitis, ambulant peritoneal dialysis	1		1				
pneumonia	6				2		4
pneumonia, arthritis	1						1
pneumonia, sinusitis	1				1		
Secondary immunologically-caused myocarditis, pericarditis and exudative pleuritis	1		1				

Summary: what is known, what needs to be studied

- W and Y disease appear to more frequently occur in the **elderly**
- W and Y appear to be more frequently associated with **pneumonia** and **arthritis** than other serogroups
- Pericarditis seems to be more a matter of serogroup C

- **Limitations**
  - Only few prospective studies
  - Papers very heterogenous
  - Accuracy of clinical records maybe questionned in many studies
  - The role of clonal complexes has been insufficiently studied

- **Research needs**
  - Population based and prospective studies are needed
  - Clinical information must be validated
  - International studies are needed due to differential distribution of clonal complexes
  - WGC should be included to study contribution of strain attributes beyond the capsule