Meningitis outbreak response in sub-Saharan Africa

WHO guideline

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Contents

Definitions and abbreviations

Definitions

Suspected case (of meningitis): Any person with sudden onset of fever (>38.5 ^{o}C rectal or >38.0 ^{o}C axillary) and one of the following signs – neck stiffness, flaccid neck, bulging fontanelle, convulsion or other meningeal signs

Confirmed case (of meningitis): Isolation or identification of the causal pathogen (*Neisseria meningitidis, Streptococcus pneumoniae, Haemophilus influenzae* type b) from the cerebrospinal fluid of a suspected or probable case by culture, polymerase chain reaction (PCR) or agglutination test

Operational threshold: Criteria that trigger specific actions to prepare for an epidemic (the alert threshold) or respond to an epidemic (the epidemic threshold) in health districts, sub-districts or populations at risk

Alert threshold: A level of incidence that triggers action to prepare for an epidemic, including strengthening surveillance, confirming cases, distributing treatment protocols and informing the authorities

Epidemic threshold: A higher level of incidence that triggers an epidemic response, including mass vaccination, antibiotic distribution and raising public awareness

Abbreviations

AFRO	WHO Regional Office for Africa
AGREE	Appraisal of Guideline, Research and Evaluation in Europe
AMSTAR	Assessment of Multiple Systematic Reviews
CERMES	Centre de Recherche Médicale et Sanitaire, Niger
CSF	cerebrospinal fluid
DECIDE	Developing and Evaluating Communication Strategies to Support Informed Decisions and Practice Based on Evidence
GAVI	Global Alliance for Vaccines and Immunization
GRADE	Grading of Recommendations Assessment, Development and Evaluation
Hib	*Haemophilus influenzae* type b
ICG	International Coordinating Group on Vaccine Provision for Epidemic Meningitis Control
IQR	interquartile range
MenAfriVac	serogroup A meningococcal conjugate vaccine
MRC	Medical Research Council, UK
Nm	*Neisseria meningitidis* (NmA, serogroup A; NmW, serogroup W, etc.)
NNV	number needed to vaccinate
PCR	polymerase chain reaction

PPV	positive predictive value
QUADAS	Quality Assessment of Diagnostic Accuracy Studies
RCT	randomized controlled trial
RDT	rapid diagnostic test
Spn	*Streptococcus pneumoniae*
ST	(multi locus) sequence type
UK	United Kingdom of Great Britain and Northern Ireland
USA	United States of America
WHO	World Health Organization

Executive summary

The meningitis belt of sub-Saharan Africa runs across the continent from Senegal to Ethiopia. This region is prone to major epidemics of meningococcal meningitis, with a high case fatality and serious sequelae that place a heavy strain on national and local health services. Until recently, most epidemics were due to *Neisseria meningitidis* serogroup A (NmA), such that the existing WHO guidelines have been directed mainly at the control of these epidemics. However, since 2010, countries in the meningitis belt have started to introduce a new serogroup A meningococcal conjugate vaccine (MenAfriVac) that is expected to confer both long-lasting individual protection and herd immunity. Following the successful roll-out of this vaccine, epidemics due to NmA are disappearing, but other meningococcal serogroups (e.g. NmW, NmX and NmC) still cause epidemics, albeit at a lower frequency and of a smaller size.

Due to these changes in the epidemiological pattern of meningitis, WHO set up a Guideline Development Group to review the evidence and recommendations for epidemic control in the meningitis belt. Four main topics were selected for review: operational thresholds for investigation and response to outbreaks, rapid diagnostic tests in outbreak management, antibiotic regimens in epidemics, and prophylaxis for household contacts of cases. This guideline does not include recommendations on vaccines that are already covered in existing WHO guidance.

The evidence was collected either through systematic searches for surveillance data (for questions on operational thresholds and antibiotic regimens) or through systematic literature reviews (for questions on rapid diagnostic tests and prophylaxis for households). The quality of the evidence was assessed – using Grading of Recommendations Assessment, Development and Evaluation (GRADE) – as "low" or "very low" for most questions. To move from evidence to recommendations, the framework from the "Developing and Evaluating Communication Strategies to Support Informed Decisions and Practice Based on Evidence" (DECIDE) project was followed, to assess the priority of the problem, quality of evidence, benefits and harms, values and preferences, resource use, equity, acceptability and feasibility before reaching a recommendation. Of the 16 recommendations developed (listed below), four were "strong" recommendations that were made in favour of an intervention, where potential benefits clearly outweighed any potential harms; the remaining 12 recommendations were "conditional".

Recommendations
Operational thresholds
(i) Timeliness of response. It is recommended that vaccination campaigns be implemented as soon as possible, and within 4 weeks of crossing the epidemic threshold (Strong recommendation; low-quality evidence) *(ii) Population size for use in calculating operational thresholds*. The recommended population denominators are <30 000 and 30 000–100 000. Where district populations are >100 000, assessment of incidence is recommended in administrative zones of 30 000–100 000 (No change [a]) (Conditional recommendation; low-quality evidence) *(iii) Alert threshold for populations of 30 000–100 000*. The recommended alert threshold is 3 cases/100 000 people in a week (Strong recommendation; low-quality evidence) *(iv) Alert threshold for populations <30 000*. The recommended alert threshold is either two cases in 1 week or a higher incidence than in a non-epidemic year (No change [a]) (Conditional recommendation; expert opinion) *(v) Epidemic threshold for populations of 30 000–100 000*. The recommended epidemic threshold is 10 cases/100 000 people in a week (Conditional recommendation; low-quality evidence) *(vi) Epidemic threshold for populations <30 000*. The recommended epidemic threshold is five cases in 1 week, or a doubling of incidence in a 3-week period (No change [a]) (Conditional recommendation; expert opinion) *(vii) Vaccination in populations adjacent to epidemic areas*. Vaccination is recommended if the population is considered to be at risk (Conditional recommendation; expert opinion) *(viii) Special situations such as mass gatherings, refugees, displaced persons, or closed institutions such as schools or barracks.* An immediate response, including mass vaccination, is recommended when two cases of meningococcal disease are confirmed in 1 week (No change [a]) (Conditional recommendation; expert opinion)
Rapid diagnostic tests
(i) Rapid diagnostic tests (latex agglutination or immunochromatography dipsticks) are recommended for use in the investigation of meningitis outbreaks (Conditional recommendation; low-quality evidence) (ii) If rapid diagnostic tests are positive for a vaccine preventable serogroup, verification of serogroup by polymerase chain reaction (PCR) or culture is recommended before a decision is taken to initiate a vaccine response (Strong recommendation; expert opinion)
Antibiotic regimens in epidemics
(i) For treatment of suspected bacterial meningitis in children aged under 2 months, a 7-day course of ceftriaxone is recommended (No change [a]) (Conditional recommendation; expert opinion) (ii) For treatment of suspected bacterial meningitis in adults and in children aged 2 months and over, a 5-day course of ceftriaxone is recommended (Conditional recommendation; very low quality evidence)
Prophylaxis for household contacts
(i) Antibiotics are recommended as a prophylactic measure for household contacts of all ages in non-epidemic periods, but not during epidemics (No change [a]) (Conditional recommendation; very low quality evidence) (ii) Ciprofloxacin is the preferred prophylactic agent, with ceftriaxone as an alternative when ciprofloxacin is contraindicated (Conditional recommendation; very low quality evidence) (iii) Rifampicin is not recommended for use as a prophylactic agent (Strong recommendation; low-quality evidence) (iv) Vaccination is not recommended for household contacts(No change [a]) (Conditional recommendation; low-quality evidence)

[a] No change from previous WHO guidelines

Background

Epidemiology

For over 100 years, major epidemics of meningococcal disease have occurred every few years within the African meningitis belt, which runs across the continent from Senegal to Ethiopia (Lapeyssonie, 1963). These epidemics are very disruptive, requiring the establishment of emergency treatment centres, and placing a severe strain on routine health services. The reason for the susceptibility of this region of Africa to major epidemics of meningococcal disease is at least in part related to its climatic features, with outbreaks occurring mainly in the hot, dry season (Sultan et al., 2005). Most epidemics have been due to *Neisseria meningitidis* serogroup A (NmA), and some have been due to serogroups W, X and C, but there has been a conspicuous absence of outbreaks due to serogroups B and Y. The hypervirulent clonal complexes ST-5 (mainly serogroup A) and ST-11 (mainly serogroup W) have accounted for most epidemics in this region. NmW, in particular, has been responsible for several epidemics in the past 10 years (e.g. in Burkina Faso, Ghana and Niger), but the dynamic of these NmW outbreaks appears to differ from those due to NmA. Based on district-level data from 2002 to 2012 in Burkina Faso, Chad, Niger and Nigeria, and defining an epidemic as crossing a weekly threshold of 10 cases/100 000 population, there were fewer NmW epidemics (36) than NmA epidemics (177) during this period. On average, NmW epidemics were 78% the size of NmA epidemics, with median cumulative attack rates of 109/100 000 (interquartile range [IQR] 79–134) for NmW and of 139/100 000 (IQR 99–230) for NmA.

Since 2010, countries in the extended meningitis belt (Figure 1) have started to progressively introduce a new serogroup A meningococcal conjugate vaccine (MenAfriVac) through mass campaigns (WHO, 2013). This preventive measure is expected to confer both long-lasting individual protection and herd immunity (Kristiansen et al., 2013; Novak et al., 2012; Sow et al., 2011). With the support of the Global Alliance for Vaccines and Immunization (GAVI), all but one country in the meningitis belt have, since 2000, introduced *Haemophilus influenzae* type b (Hib) vaccines, and many have already introduced *Streptococcus pneumoniae* (Spn) conjugate vaccines; hence, the incidence of bacterial meningitis due to non-meningococcal pathogens is also evolving.