Timely detection of meningococcal meningitis epidemics in Africa

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Summary

Background Epidemics of meningococcal disease in Africa are commonly detected too late to prevent many cases. We assessed weekly meningitis incidence as a tool to detect epidemics in time to implement mass vaccination.

Methods Meningitis incidence for 41 subdistricts in Mali was determined from cases recorded in health centres (1989–98) and from surveillance data (1996–98). For incidence thresholds of 5 to 20 cases per 100 000 inhabitants per week, we calculated sensitivity and specificity for detecting epidemics, and determined the time lapse between threshold and epidemic peak.

Findings We recorded 9084 meningitis cases. Clinic-based weekly incidence of 5 and 10 cases per 100 000 inhabitants detected all meningitis epidemics (sensitivity 100%, 95% CI 93–100), with median threshold-to-peak time of 5 and 3 weeks. Under-reporting reduced sensitivity: only surveillance thresholds of 5 or 7 cases per 100 000 inhabitants per week detected all epidemics. Crossing the lower threshold before the 10th calendar week doubled epidemic risk relative to crossing it later (relative risk 2·1, 95% CI 1·4–3·2). At 10 cases per 100 000 inhabitants per week, specificity for outbreak prediction was 88%, 95% CI 83–91). For populations under 30 000, 3 to 5 cases in one or two weeks predicted epidemics with 85% to 97% specificity.

Interpretation Low meningitis thresholds improve timely detection of epidemics. Ten cases per 100 000 inhabitants per week in one area confirm epidemic activity in a region, with few false alarms. An alert threshold of 5 cases per 100 000 inhabitants per week allows time to investigate, prepare for an epidemic, and initiate mass vaccination where appropriate. For populations under 30 000, the alert threshold is two cases in a week. High quality surveillance is essential.

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Introduction

Meningococcal meningitis caused by *Neisseria meningitidis* serogroups A and C is endemoepidemic in sub-Saharan Africa, causing tens of thousands of cases and thousands of deaths during epidemic years.[1–3] The Republic of Mali, in the heart of the meningitis belt, has had several epidemics of meningococcal disease since 1994.[3] Meningitis control relies on reactive mass vaccination with polysaccharide vaccine[4–8] and appropriate case management.[9] An emerging epidemic must be quickly distinguished from an expected rise in incidence during the dry season, and there must be time to collect and analyse data, mobilise resources, order vaccines, and implement vaccination campaigns. The time required to initiate vaccination during a meningitis epidemic was 2–5 weeks in Sudan,[10] 4–9 weeks in Burundi,[11] 6 weeks in Chad,[12] and more than 6 weeks in Nigeria.[13] It takes 1–2 weeks to complete the campaign[11] and another week to obtain immunological protection.[14] The minimum time necessary to achieve population immunity against the meningococcus is thus about 4 weeks, and every week of delay results in a 3% to 8% drop in the number of cases prevented.[6–8] Timely and accurate detection of a meningitis epidemic is therefore critical in a control strategy based on reactive mass vaccination.

A weekly incidence of 15 cases per 100 000 inhabitants, averaged over 2 consecutive weeks, was recommended as a threshold to confirm the onset of a meningitis epidemic for areas of population 30 000 to 100 000 in the African meningitis belt, and 5 per 100 000 per week was proposed to initiate vaccination when an epidemic is underway nearby.[4,5] To avoid false alarms, specificity of the threshold was given priority over sensitivity.[4,5] Experience has shown, however, that once the epidemic is detected, there is often not enough time to organise vaccination campaigns before the peak of the epidemic, resulting in a late response and a limited impact.[6–8,10–13] Furthermore, the recommendation based on data collected in health facilities[5] did not account for under-reporting of cases through surveillance. The proposed threshold, therefore, has several disadvantages: it does not detect all epidemics;[5,6,15] it does not allow time to implement mass vaccination;[6] and its effectiveness is highly dependent on the quality of surveillance.[16] Detection of epidemic meningitis in areas of fewer than 30 000 inhabitants was not addressed.

Investigators have suggested that use of lower thresholds can reduce meningitis cases and deaths without increasing the number of false alarms.[6,18] In Togo, an incidence of 7 cases per 100 000 inhabitants per week was 100% sensitive and specific, detecting and predicting all meningitis epidemics.[6] Early outbreaks run a longer course before the rains, which classically bring an end to epidemics in the meningitis belt,[17] and in Niger, low thresholds exceeded early in the dry season were excellent predictors of epidemics.[18] The aim of this work is, with data from Mali: (1) to assess the ability of meningitis incidence thresholds to detect epidemics in time to intervene effectively, according to the

epidemiological context and completeness of case-reporting, and (2) to explore prediction of meningitis epidemics in areas with less than 30 000 inhabitants. WHO has revised its recommendation for detection of meningitis epidemics in Africa,[19] in part on the basis of the data presented here.

Methods

Meningitis incidence

The study took place in the central Ségou region in Mali, composed of seven districts (cercles) and 41 subdistricts (arrondissements). Every meningitis case entered in the consultation registers of all health-care facilities from July 3, 1989, to June 28, 1998, was recorded. A case was defined as a person diagnosed with meningitis, as written in the register by the consulting physician or nurse on the date of presentation. Age, sex, residence, and outcome were recorded for every case. Meningitis surveillance data for every district were obtained from district and national surveillance officers for cases reported from Jan 1, 1996, to June 28, 1998. Population figures were calculated for each week from 1989 to 1998 according to annual population growth, ranging from 1·4–3·2% depending on the district, between national censuses completed in 1986 and 1998 (Direction Nationale de la Statistique et de l'Informatique du Mali).

We calculated weekly and annual meningitis incidence, expressed as cases per 100 000 inhabitants for every subdistrict, for five urban areas (two urban subdistricts and three other towns) and for the remaining rural areas, by dividing the number of new resident cases occurring per week by the weekly adjusted population of the area. Incidence was adjusted to account for missing registers (4% on average over the study period) by subtracting the population served by the dispensary for the period during which registers were unavailable. Annual meningitis incidence was the sum of weekly incidences from Aug 1, to July 31, of the next year, including a complete meningitis season (December to May).

An epidemic is usually defined as any increase of cases above the expected number, but for this analysis a fixed definition (gold standard) is required. To test the robustness of the method, four definitions were used: 70, 80, 90, and 100 meningitis cases per 100 000 inhabitants in 1 year. Results are reported mainly for an epidemic exceeding an annual incidence of 100 cases per 100 000 inhabitants, and, for clarity, distinguished from an outbreak exceeding 70 cases per 100 000 in a year. The epidemic peak was the week with the highest incidence. An early epidemic was defined as one during which weekly incidence exceeded 10 cases per 100 000 inhabitants before the tenth week of the calendar year (the first week of March, half-way through the dry season).[18] Mean weekly and annual incidence of early and late epidemics were compared with the Mann-Whitney test.

Threshold performance

Weekly meningitis incidence thresholds between 5 and 20 cases per 100 000 inhabitants, and 15 per 100 000 averaged over 2 consecutive weeks, were analysed for their ability to detect and predict epidemics within the year during which they were crossed. For subdistricts with population less than 30 000, thresholds tested were: absolute numbers of cases, ranging from 2 to 5 per week; and doubling of the number of cases over a 3-week period (example: week 1, 0–1 cases; week 2, two cases; week 3, four cases).

We calculated the number of weeks which had elapsed between the crossing of each threshold and the epidemic peak for every epidemic. Sensitivity, specificity, and positive and negative predictive values were estimated for each threshold by finding out which districts crossed, at least once, a given threshold and which ones had an epidemic during the same year.[6] Performance was assessed for 63 district-years and 369 subdistrict-years. Results are presented mainly for subdistricts, because their population size is appropriate to this analysis and the greater number of units improved precision. Performance indicators for different thresholds were compared by χ^2 and Fisher's exact tests.

Threshold performance according to epidemiological context

Three epidemic risk factors were considered: population size, where threshold specificity was tested for subdistricts

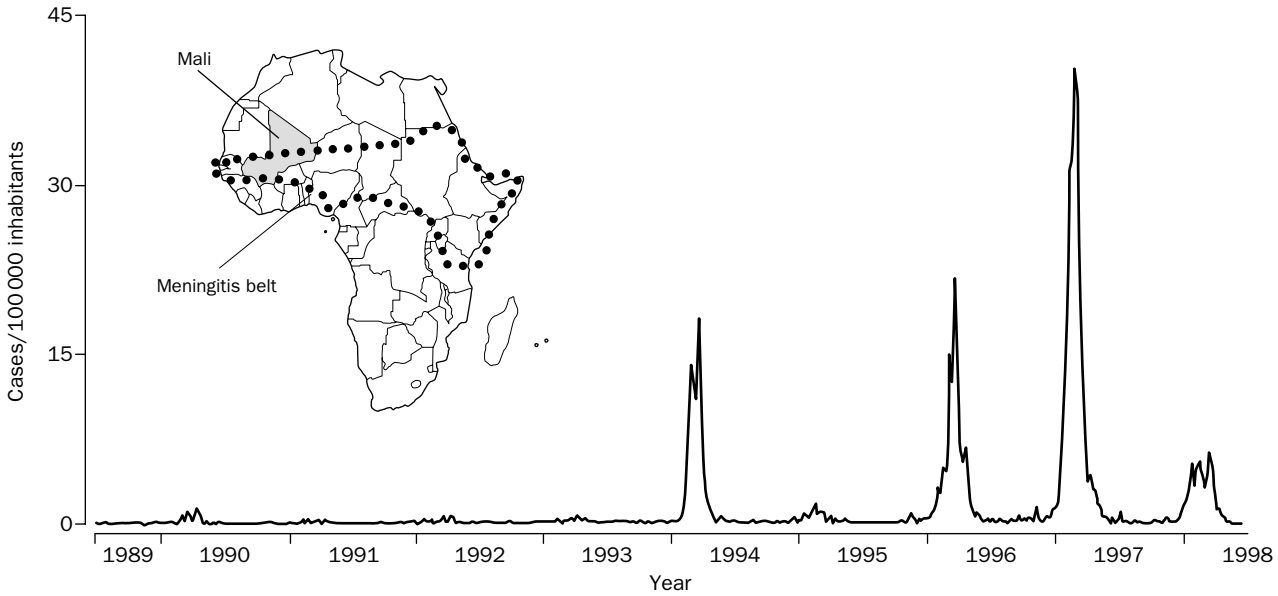

Figure 1: **Weekly incidence of meningitis in the Ségou Region, Mali, 1989–98**
Source: Health facility registers from the Ségou Region, Mali.

District	Population	Meningitis incidence* (cases/100 000 inhabitants/year)								
		1989–90	1990–91	1991–92	1992–93	1993–94	1994–95	1995–96	1996–97	1997–98
Barouelli	166 413	0	3	2	3	7	5	40	156†	52
Bla	208 480	2	2	8	2	19	8	130†	478†	22
Macina	169 025	17	4	5	18	146†	7	44	80	29
Niono	227 669	26	10	13	12	43	32	263†	285†	91
San	252 113	16	12	10	19	249†	13	93	410†	70
Ségou	489 733	15	7	7	6	86	28	104†	160†	29
Tominian	165 768	5	2	2	4	63	14	120†	304†	244†
Total Ségou Region	1679 201	11	5	6	7	96	16	118†	261†	65

*Incidence based on 8624 resident cases and rounded to the nearest unit. †Annual incidence ⩾100 cases/100 000 inhabitants/year. Source: clinic registers from the Ségou Region.

Table 1: **Annual meningitis incidence, Ségou Region, Mali, 1989–98**

grouped by their 1998 population, 30 000 to 50 000 and 50 000 to 100 000; epidemic history, where sensitivity and specificity of thresholds were compared for detection of first versus subsequent epidemics in a subdistrict during the study period; and epidemic timing, where the relative risk of an epidemic occurring during the year was calculated for a given threshold crossed before the tenth calendar week compared with the tenth week onward.

Surveillance and threshold performance

In Mali, meningitis cases are reported by radio from rural and urban health posts to district health centres, then to the regional health department, and finally to the national Division of Epidemiology. Weekly reports (daily during epidemics) include zero reporting. The number of meningitis cases reported to district and national levels was compared with the number recorded in health facility registers. Clinic-based data were excluded for weeks for which district weekly reports were missing. 1 district-year was excluded as surveillance data was unavailable. Thresholds exceeded according to district surveillance data were tested for their ability to detect district epidemics defined by clinic-based annual meningitis incidence.

Results

Descriptive epidemiology

In 1998, the Ségou region had 1679 201 inhabitants, with district populations ranging from 165 768 to 489 733. The population of the 41 subdistricts ranged from 6024 to 156 182 inhabitants: less than 30 000 for 18 (44%), 30 000 to 50 000 for 15 (37%), 50 000 to 100 000 for 7 (17%), and greater than 100 000 for 1 (2%) subdistrict.

In 9 years, 9084 meningitis diagnoses were recorded in the registers of 92 health facilities, 95% during the dry season. Of all cases, 6757 (78%) occurred during epidemics in 4 of the 9 years (figure 1).

Of all patients, 8624 (95%) reported residence in the Ségou Region. The male to female ratio was 1·2. Ages ranged from 1 month to 84 years (mean 11·8 years, median 9 years). Case distribution was similar during epidemics and dry season endemic peaks. The proportion of cases under 1 year of age was 5·3% in the dry season and 18·9% the rest of the year ($p<0·0001$), and the proportion aged 5 to 30 was 69% and 49%, respectively ($p<0·0001$). Of the 3062 patients admitted to hospital, 380 died (case fatality ratio 12·4%).

Meningitis epidemics occurred in 63 (17%) of 369 subdistrict-years, affecting 10 (24%) of 41 subdistricts in 1994, 15 in 1996, 30 in 1997, and 8 in 1998. Incidence per 100 000 inhabitants peaked at 216 cases in 1 week (mean 1·2, median 0) and 1121 cases in a year. Of the 63 epidemics, 27 (43%) were early, accounting for 48% of epidemic meningitis cases. Early epidemics had, on average, higher peak weekly (76 *vs* 52 cases per 100 000 inhabitants per week; $p=0·045$) and annual incidence (375 *vs* 198 cases per 100 000 inhabitants per year; $p=0·045$) than late epidemics. Annual incidence between 70 and 100 cases per 100 000 occurred in 17 subdistricts. Of 13 such outbreaks (1989 to 1997), 9 (69%) were followed by epidemics the next year.

Annual meningitis incidence in districts ranged from 0 to 32 cases per 100 000 inhabitants in non-epidemic years (mean 8·9, median 7·5) and up to 478 per 100 000 in epidemic years (table 1).

5 towns with 11·4% of the population had 1467 (17%) of the resident meningitis cases, and 1169 (17%) of epidemic cases. From 1989 to 1996, annual incidence was more than twice as high in urban than in rural areas (figure 2). In 1997 and 1998, rural incidence exceeded urban incidence.

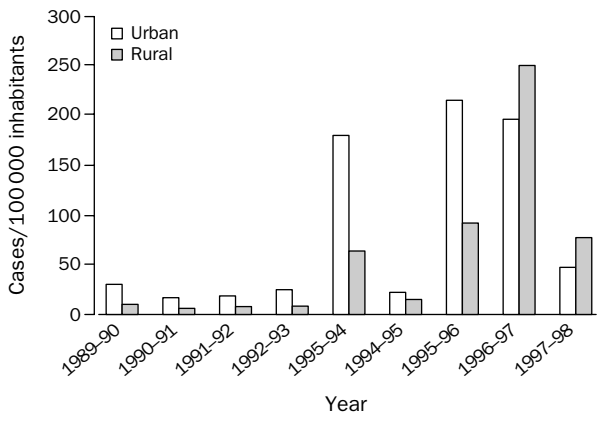

Figure 2: **Annual meningitis incidence in 5 urban and 39 rural areas, Ségou Region, Mali, 1989–98**

Urban areas (1998 population): two urban subdistricts, Ségou Commune (90 898) and San Commune (41 529), and three towns, Niono (25 552), Markala (18 355), and Bla (15 213). Rural areas: 39 rural subdistricts, excluding population of towns.

Incidence threshold (cases/100 000 inhabitants/week)	Time from threshold to peak (weeks)		Epidemics* for which time=0 (n)
	Mean	Median (range)	
5	8·5	5 (0–35)	1
7	6·6	4 (0–35)	4
10	4·2	3 (0–35)	7
15†	3·6	2 (0–33)	11
20‡	2·1	1 (0–18)	24
15×2§‡	2·1	1 (0–18)	22¶

*Epidemics detected the same week as the peak; †n=62 epidemics, as 1 was not detected; ‡n=60 epidemics, 3 not detected; §15 cases/100 000 inhabitants/week, averaged over two weeks; ¶n=19 at peak, 3 after the peak. 1998 population of Ségou Region: 1679 201 inhabitants.

Table 2: **Time elapsed between crossing the incidence threshold and reaching the peak for 63 meningitis epidemics in 41 subdistricts, Mali 1989–98**

Incidence threshold (cases per 100 000 inhabitants/week)	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value % (95% CI)	Negative predictive value % (95% CI)
5	100 (93–100)	68 (63–73)	39 (32–47)	100 (98–100)
7	100 (93–100)	75 (70–80)	45 (37–54)	100 (98–100)
10	100 (93–100)	83 (78–87)	55 (45–64)	100 (98–100)
15	98 (90–100)	90 (86–93)	67 (57–77)	100 (98–100)
20	92 (82–97)	95 (92–97)	81 (69–89)	98 (96–99)
15×2*	95 (86–99)	97 (94–99)	87 (76–94)	99 (97–100)

Data from 352 units of observation (41 subdistricts×9 years). Epidemic defined as ≥100 cases/100 000 inhabitants/year. 1998 population of Ségou region: 1679201.
*15 cases/100 000 inhabitants/week, averaged over 2 consecutive weeks.

Table 3: **Performance of weekly meningitis incidence thresholds for detecting and predicting meningitis epidemics, Ségou Region, Mali, 1989–98**

Threshold performance

The mean time elapsed in subdistricts between epidemic threshold and peak ranged from 2·1 weeks for a 2-week average of 15 cases per 100 000 inhabitants per week, to 8·5 weeks for 5 per 100 000 in 1 week (table 2). At 5 and 10 per 100 000 per week, half the epidemics were detected 5 and 3 weeks before the peak, respectively. At 15 per 100 000 averaged over 2 weeks, 25 (40%) of 63 epidemics were detected at (n=19) or after (n=3) the peak, or not at all (n=3).

Exceeding a 2-week average of 15 cases per 100 000 inhabitants per week yielded 95% sensitivity for epidemic detection in a particular year, or 60% if epidemics crossing the threshold at or after the peak were regarded as undetected. Specificity was 97% and decreased at lower thresholds (table 3). No threshold had perfect specificity. Thresholds of 11 or fewer cases per 100 000 inhabitants per week detected all epidemics. At 10 cases per 100 000 inhabitants per week, sensitivity was 100% (89% if epidemics detected at the peak were not considered); specificity was 83% overall (55% in epidemic and 97% in non-epidemic years); in epidemic years, the positive predictive value was 58% for epidemics and 73% for outbreaks.

Threshold performance was similar for detection of outbreaks. At 11 cases per 100 000 inhabitants per week or less, sensitivity remained at 100%. Higher thresholds had sensitivity 3–12% lower for detection of outbreaks than for the standard epidemic definition. For all thresholds, specificity was 5% higher for predicting outbreaks than for epidemics.

Table 4 shows, for every year, the number of times each threshold was crossed in the 41 subdistricts. For example, weekly incidence exceeded 10 cases per 100 000 inhabitants 115 times, 108 (94%) during an epidemic year. Of the 52 false-positive results, 45 (87%) occurred during an epidemic year, and 17 (33%) when incidence was between 70 and 100 cases per 100 000 inhabitants. In 369 district-years, weekly incidence exceeded 10 per 100 000 in the absence of an epidemic, 7 times (1·9%), 3 of which were in subdistricts of less than 30 000 people.

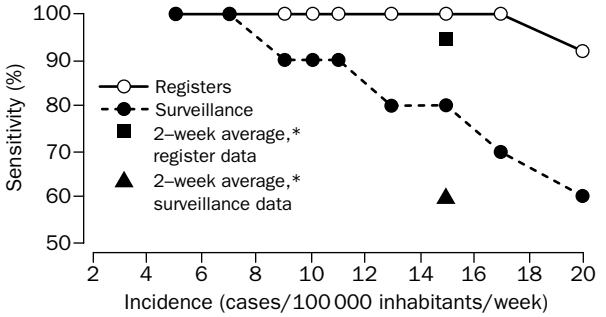

Figure 3: **Sensitivity of incidence thresholds for detection of meningitis epidemics, according to source of data in seven districts, Ségou Region, Mali, 1989–98**
*An incidence of 15 cases per 100 000 inhabitants per week, averaged over 2 weeks.

Threshold performance according to epidemiological context

With increasing population size, there was a tendency for meningitis incidence thresholds to be more specific, but this findng was not significant. For example, at 10 cases per 100 000 inhabitants per week, specificity was 81% for 30 000 to 50 000 people and 90% for 50 000 to 100 000 people (p>0·05).

From 1989, 4–7 years elapsed before the first meningitis epidemic in a subdistrict (four subdistricts had no epidemic); 282 pre-epidemic and 87 subsequent subdistrict-years were analysed. Weekly thresholds of 11 or fewer cases per 100 000 inhabitants detected all first and subsequent epidemics (sensitivity 100%). Sensitivity of higher thresholds was 100% for first and 96% for subsequent epidemics. For all thresholds, specificity was higher for predicting first compared with subsequent epidemics. At 5, 10, and 15 weekly cases per 100 000 inhabitants, specificity was 73%, 87%, and 92% for first and 51%, 67%, and 82% for subsequent epidemics, respectively (p<0·05).

The epidemic risk for the year was higher when thresholds were crossed before, rather than after, the tenth calendar week. At 5, 10, and 15 cases per 100 000 inhabitants per week, the relative risks were 2·1 (95% CI 1·4–3·2), 1·4 (1·02–1·9), and 1·4 (1·06–1·8), respectively.

Small populations

For 18 subdistricts with fewer than 30 000 residents, absolute numbers of 2 to 5 cases per week had 100% sensitivity for detection of epidemics. Specificity for 2, 3, 4, and 5 cases per week was 78%, 85%, 91%, and 94%, respectively. The mean threshold-to-peak time was 7·0 (median 4·5), 4·4 (2), 3·3 (2), and 2·8 (2) weeks, respectively. Doubling of the number of cases from one week to the next, starting with at least one case, resulted in 18% sensitivity and 99% specificity. With zero cases as the starting point (example: 0, 1, 2 cases), sensitivity rose to 54% whereas specificity was 97%. For these two

Incidence threshold (cases per 100 000 inhabitants per week)*	Number of subdistricts crossing incidence thresholds									
	Total* (n=63)	1989–90 (n=0)	1990–91 (n=0)	1991–92 (n=0)	1992–93 (n=0)	1993–94 (n=10)	1994–95 (n=0)	1995–96 (n=15)	1996–97 (n=30)	1997–98 (n=8)
15×2†	74	0	0	0	1	13	0	19	33	8
15	91	1	0	0	1	14	1	25	35	14
10	115	2‡	0	0	1‡	20	4‡	30	39	19
5	160	9	2	3	5	30	9	34	40	28

*n=number of subdistricts with epidemic activity, defined as ≥100 cases/100 000 inhabitants/year; †≥15×2=15 cases/100 000 inhabitants/week, averaged over 2 weeks; ‡Four of seven of these subdistricts had <30 000 inhabitants.

Table 4: **Annual occurrence of epidemic meningitis and crossing of weekly incidence thresholds in 41 subdistricts**

case-doubling scenarios, the threshold was crossed far too late (at or after the peak), 40% and 26% of the time, respectively.

Surveillance

From January, 1996, to June, 1998, 6117 meningitis cases were recorded in health facility registers, whereas 4737 (77%) cases were reported to district health centres and 4131 (68%) to the national Division of Epidemiology. Figure 3 shows the ability of incidence thresholds to detect district-level epidemics with clinic-based and surveillance case data. With surveillance data, thresholds for 5 or 7 cases per 100 000 inhabitants per week detected all epidemics (sensitivity 100%), but sensitivity fell rapidly as the threshold was raised. At 10 and 15 cases per 100 000 per week, sensitivity was 90% and 80%, respectively. A 2-week average of 15 cases per 100 000 inhabitants per week had 60% sensitivity (95% CI 27–86).

Discussion

Our findings show that a meningitis incidence threshold of 10 cases per 100 000 inhabitants in just 1 week can reliably be used to confirm an epidemic in time to respond, whereas higher thresholds are much less effective. To be effective, strategies to control epidemic meningococcal disease must allow for early detection and confirmation of epidemic activity in a region, and rapid implementation of mass vaccination in affected districts.[20] Detection thresholds must be sensitive enough to detect all epidemics, timely enough to allow mobilisation of resources, and specific enough to avoid unnecessary vaccination campaigns. To facilitate rapid action, we propose a two-tier strategy: an alert threshold of 5 cases per 100 000 inhabitants per week, to sound an early warning and launch an investigation when the number of meningitis cases first begins to rise; and an epidemic threshold of 10 cases per 100 000 inhabitants per week, which when exceeded in one zone of population 30 000 to 100 000 confirms the emergence of epidemic activity in a larger area, such as a region.[4–7] Finally, we propose thresholds for areas with fewer than 30 000 people.

Our results from Mali confirm certain high-risk situations for epidemic meningitis in Africa. Outbreaks beginning early in the dry season increased the risk and scale of an epidemic.[18] Low population immunity to the meningococcus also increased risk, as low meningitis incidence was a better epidemic predictor after an extended non-epidemic period than following a previous epidemic. Urban zones were at far greater risk early in the epidemic wave than were rural areas[5] and urban risk remained high despite previous epidemics. This result may be partly explained by migration of susceptible individuals into urban areas.[12] The effect of vaccination campaigns on subsequent epidemic risk could not be directly assessed but immunisation efforts in Ségou in 1997 might help explain reduced epidemic activity in 1998.

A meningitis incidence of 5 cases per 100 000 inhabitants in 1 week was 100% sensitive even with surveillance data, making the number a good alert threshold. It was also the only threshold to consistently detect epidemics well before the peak, leaving time in most cases to implement mass vaccination. The threshold of 10 cases per 100 000 inhabitants in 1 week detected most epidemics before the peak and was specific enough for false alarms in the absence of epidemic activity to be uncommon. Most (87%) false positives occurred in years with epidemics throughout the region, when vaccination is in any case recommended in zones with 5 or more cases per 100 000 per week.[4–7,20] Furthermore, ability of low thresholds to predict an epidemic improved early in the meningitis season, in the absence of a recent epidemic and in areas of population greater than 50 000. An epidemic was arbitrarily defined as an annual incidence of at least 100 cases per 100 000 inhabitants to enable comparison with other studies,[5,6,15] but threshold specificity was higher for predicting smaller, clinically important outbreaks.[11,21]

In sparsely populated areas, small changes in the number of cases could cause major incidence fluctuations, and poor access to laboratory services might make bacterial identification difficult. A meningitis epidemic must therefore not be declared too hastily on the basis of a few cases, and an indicator with high specificity is needed. To ensure reliability, use of weekly incidence should be reserved for areas of 30 000 to 100 000 people. For any population under 30 000, two meningitis cases in 1 week, or any increase over the number expected, should raise the alarm, whereas 3 or 4 cases over one or two weeks should be the minimum required to declare an epidemic. When an epidemic is underway nearby, fewer cases should suffice to initiate mass vaccination.[19]

Our primary estimates of threshold performance are based on meningitis cases seen and recorded in health facilities, but actual performance will vary with surveillance quality and will therefore be site-specific. Under reporting significantly reduced threshold sensitivity in our study; with surveillance data, the previously recommended threshold detected at most 60% of epidemics. However, at lower surveillance thresholds sensitivity approached or equalled values obtained with clinic-based data. Timeliness could not be assessed, but since late reporting would delay any rise in meningitis cases, our study over-estimates the sensitivity of all surveillance-based thresholds and the time available for intervention.

From 1989 to 1998, meningitis epidemiology in the Ségou Region was typical of the African meningitis belt, characterised by seasonal increases in the number of cases and a wave of epidemics with attack rates as high as 1·2% of the population. The Mali epidemics were due to group A *Neisseria meningitidis* clone III-1,[22,23] the strain responsible for most epidemics in Africa since 1988.[2,23] Although clinically ascertained meningitis could not be confirmed, the likelihood of a correct diagnosis during epidemics is high.[24] Cases may have been missed, particularly in rural areas with poorer access to health care, but in view of the large variations in incidence during short periods, such under-reporting is unlikely to affect our conclusions. Specificity of incidence thresholds was higher in Mali than in Burkina Faso (1979–84),[5] possibly because of the greater virulence of clone III-1,[23] and higher still in Togo (1990–97).[6] Sensitivity was highly consistent in all three studies, and the time from threshold to peak incidence was much the same in Mali and Togo. The robustness of these findings, despite differences in location, time span, and meningococcal strain, adds to their credibility, making it reasonable to generalise some conclusions to parts of Africa with similar demographic and geoclimatic characteristics.

WHO guidelines revised

In view of field experience and new evidence, a meeting was held in June, 2000, to revise WHO guidelines for

detection of meningococcal meningitis epidemics in Africa.[19,25] After comprehensive review of operational research, including our present work, a consensus was reached. The WHO now recommends for areas of population greater than 30 000: an alert threshold of 5 cases per 100 000 inhabitants per week; and an epidemic threshold of 10 per 100 000 in 1 week when epidemic risk is high, or 15 per 100 000 per week otherwise.[19]

The epidemic threshold is used only once in a region to confirm an epidemic. For small populations, thresholds are defined by absolute numbers of cases. Once epidemic meningitis is confirmed, weekly incidence should be used to determine vaccination priorities, including immunising in areas that have crossed the alert threshold.[4–7,19,20]

These new guidelines are justified by the evidence and the need for operational effectiveness. In most circumstances in sub-Saharan Africa, 10 cases per 100 000 inhabitants in 1 week would be an appropriate simple-to-calculate epidemic threshold. However, if 100% sensitivity is desired in real time, for example in the case of known delay or incompleteness of case reporting, a lower epidemic threshold could be used, such as 5 or 7 cases per 100 000 inhabitants per week. Conversely, where meningitis surveillance is timely and complete and high-risk criteria are not met, a higher epidemic threshold, such as 15 cases per 100 000 inhabitants in 1 week, might be considered to reduce the risk of false alarms. In deciding vaccination strategy, epidemic risk factors should be assessed, including season, recent epidemics or vaccination, population density, and patterns of migration. Awareness of meningitis incidence in neighbouring countries can also improve response time.[7] The quality and timeliness of meningitis surveillance should be reinforced early in every dry season and meningitis outbreak investigations should always include a rapid assessment of the surveillance system.

The new WHO recommendation for detecting meningococcal meningitis epidemics in Africa is action oriented, to promote epidemic preparedness and improve response time, and is context specific, to limit false alarms. Decisions must be timely, and surveillance quality remains critical. During a meningitis epidemic, reactive mass vaccination with meningococcal polysaccharide vaccine can prevent at most two-thirds of cases,[6–8] but it is the best strategy currently available, more effective and less costly than routine vaccination.[8] Preventive mass immunisation with polysaccharide vaccine would not be feasible or effective.[26,27] Even with high coverage, polysaccharide vaccine cannot prevent epidemics because of its moderate efficacy,[26,28] short duration of protection,[28] questionable effectiveness of multiple doses in children[29] and absence of herd immunity in vaccinated African populations.[30,31]

Meningococcal A and C conjugate vaccines may further meningitis control in Africa when they become available.[32] However, since high levels of vaccination coverage are unlikely to be achieved everywhere,[27] epidemics will continue to occur and the threshold strategy will remain relevant. Further research on the roles of population density and vaccination in the epidemiology of meningococcal disease may help further refine guidelines. In the meantime, in the face of devastating epidemics we must use the tools available to respond as quickly as possible.

Contributors

Rosamund Lewis designed the study, supervised its implementation and analysis, and prepared the paper. Nicolas Nathan collected the data, did the analysis, and helped to write the paper. Lamine Diarra participated in protocol design, supervised data collection, and reviewed the paper. François Bélanger participated in protocol design and data analysis. Christophe Paquet supervised part of the analysis and reviewed the paper.

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Clinical picture: Oesophageal varix bleed

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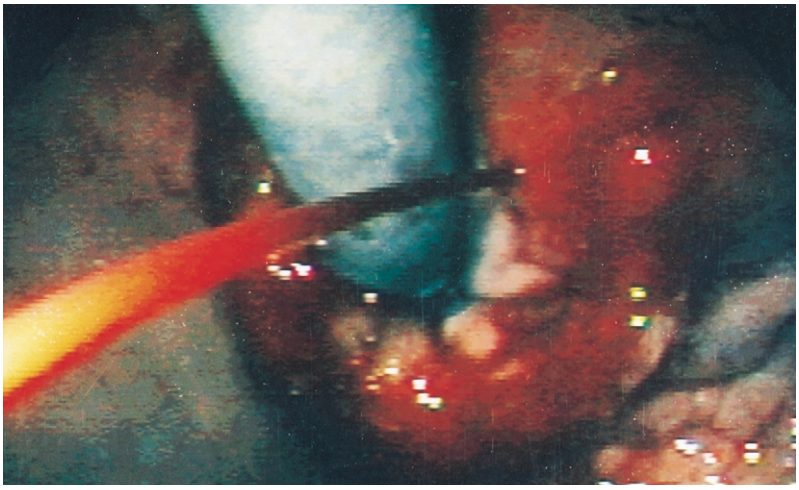

A 47-year-old man with cirrhosis secondary to alcohol abuse and hepatitis C virus infection presented with upper gastrointestinal bleeding. Upper endoscopy revealed varices at the gastro-oesophageal junction. During sclerotherapy, a varix began to bleed near to, but not in, the area of sclerosant injection. The variceal pressure was so high that blood gushed out in a horizontal stream (figure). A Blakemore tube was inserted and intravenous octreotide started. The patient was sent to interventional radiology for an emergency transjugular intrahepatic portosystemic stent (TIPS). Hepatic venography demonstrated a patent hepatic vein, and the portosystemic gradient was high at 19 mm Hg. After stenting, pressure fell to 5 mm Hg. Risk factors for oesophageal variceal bleeding include the presence of the "red spot" sign during endoscopy, a portal pressure gradient of greater than 12 mm Hg, and poor hepatocellular function.

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