Research/Recherche

Priority during a meningitis epidemic: vaccination or treatment?*

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From November 1995 to May 1996, a meningitis epidemic occurred in northern Nigeria. More than 75 000 cases and 8440 deaths (case fatality rate (CFR), 11%) were recorded. Médecins sans Frontières, in cooperation with the Nigerian government, carried out an assistance programme (support to case management, surveillance and mass vaccination) in three states (Bauchi, Kano, Katsina) where 75% of cases occurred. Cost analysis of this assistance in Katsina State reveals that case management and mass vaccination were efficient: US$ 35 per case treated and US$ 0.64 per vaccination. There was, however, a remarkable difference in cost-effectiveness between the two strategies. The cost per death averted by improved case treatment was estimated to be US$ 396, while the cost per death averted by vaccination was estimated to be US$ 6000. In large part this difference is attributed to the late start of vaccination: more than 6 weeks after the epidemic threshold had been passed. During meningitis epidemics in countries where surveillance systems are inadequate, such as in most of sub-Saharan Africa, curative programmes should have priority.

Introduction

Northern Nigeria is part of the meningitis belt, an area that in large part consists of the Sahel (Fig. 1). In 1996 northern Nigeria was struck once again by a meningitis epidemic, the worst in 30 years, caused by *Neisseria meningitidis* serogroup A. In January and February 1996, when the news of the epidemic reached the outside world, there were already 7000 cases registered, with a case fatality rate (CFR) of >20%. An international alarm was sounded and Médecins sans Frontières (MSF) sent an exploratory team to the area by mid-February 1996. The Nigerian government was already vaccinating direct contacts of cases and conducting mass immunization in schools and military bases. The government welcomed the MSF assistance. Within 3 weeks, 40 MSF staff had arrived, and later this was increased to 90 individuals. During this epidemic, which lasted from November 1995 to May 1996, a total of 75 000 meningitis cases were registered, of which 8440 died (CFR, 11%) (*1*). MSF assistance was limited to three northern states (Bauchi, Kano, and Katsina). The population of these three states is 14 million and 75% of all the meningitis cases in the 1996 outbreak occurred there. In the course of the intervention, Nigerian health staff vaccinated 5.1 million people, 2.9 million of whom were vaccinated with the support of MSF. Furthermore, 56 700 cases of meningitis were treated, 30 000 with the support of MSF. The costs of the aid delivered by MSF totalled US$ 2.935 million.

This article describes the course of the epidemic and the assistance given by MSF in one of the three states, Katsina (population, 4.5 million) (*2*). It analyses the impact of this assistance and ends with recommendations for future interventions during meningitis epidemics in sub-Saharan Africa.

Results

Description of the epidemic and the assistance given

The course of the epidemic in Katsina (Fig. 2) showed an initial phase with a gradual increase, a second phase with a sharp increase, and a final phase with an abrupt end.

Cases (defined as individuals presenting with fever, headache, and stiff neck) were first reported in

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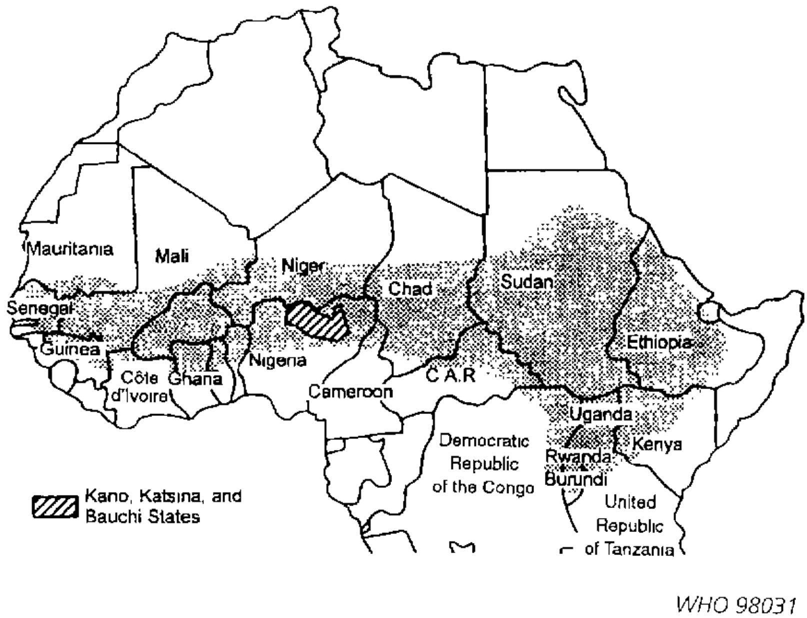
Fig. 1. **The meningitis belt in Africa** (CAR = Central African Republic).



November 1995. By week 5 of 1996 (29 January–4 February) the generally accepted epidemic threshold (15 cases per 100000 population per week, averaged over 2 weeks (*3*)) was reached, and by week 11 (11–17 March) the peak of the epidemic curve had been passed. After week 15 (8–14 April) the incidence decreased rapidly. According to district, the epidemic curve varied greatly in height as well as in length. The period between passing the epidemic threshold and reaching the peak of the epidemic curve varied from 1 to 14 weeks, although several districts had curves with two peaks. The majority of peaks occurred between weeks 11–15 (11 March–14 April). The attack rate (cumulative incidence) for

Fig. 2. **Number of meningitis cases per week, Katsina State, Nigeria, November 1995 to May 1996** (epidemic threshold >15 cases per 100000 persons per week).

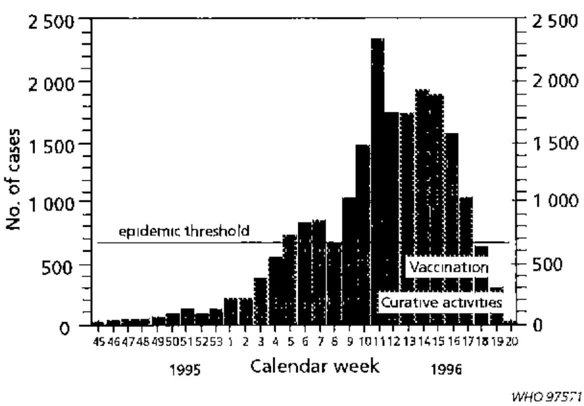


Table 1: **Meningitis cases and attack rates, by age group, Katsina State, Nigeria, November 1995 to May 1996**

Age group (years)	No of meningitis cases	Attack rate (per 100 000)
0–4	5 112 (24)[a]	650
5–14	9 990 (48)	771
15–29	3 514 (17)	269
≥30	1 627 (8)	43
Unknown	684 (3)	NA[b]
Total	20927 (100)	461

[a] Figures in parentheses are percentages
[b] NA = not available.

Katsina was 461 cases per 100 000 population, with the rate for individual districts varying from 130 to 885 per 100 000 population. Half of the 20 927 cases registered in Katsina were male, with children and young adults, especially those in the age group 5–14 years, being the most affected. Only 8% of cases were older than 30 years (Table 1).

Reported deaths from meningitis during the epidemic in Katsina are shown in Fig. 3. Before the MSF assistance, the CFR in Katsina was, on average, 17%; after the start of the intervention the CFR quickly decreased to approximately 8% (Fig 4).

The assistance had three components, curative care for meningitis patients; establishment of a surveillance system; and vaccination campaigns for part of the population. Curative care of patients was supported by providing long-acting oily chloramphenicol, syringes, and needles and by training health care staff in WHO treatment protocols. In Katsina 20 927 meningitis cases were treated in health facilities, ranging from hospital to health posts; of these, 10 117 received MSF-supported treatment

Fig. 3. **Number of meningitis deaths reported per week, Katsina State, Nigeria, November 1995 to May 1996.**

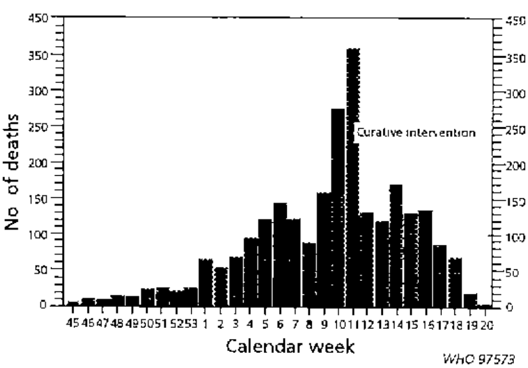
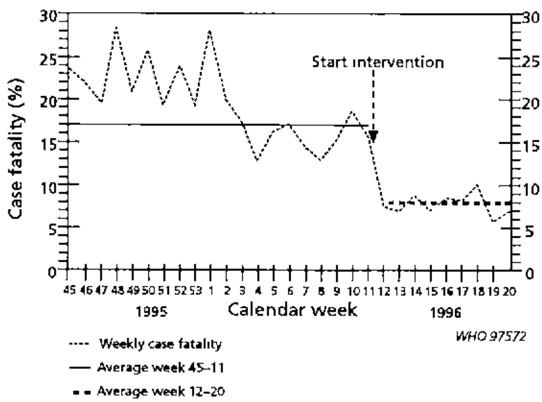


Fig. 4. **Meningitis case fatality rate, Katsina State, Nigeria, November 1995 to May 1996.**



The surveillance system was supported by an epidemiologist and by training of health care staff. Each health care facility completed a form describing the diagnosis, age, sex, treatment, and outcome of each case. The forms were gathered at the district level and a cumulative report was sent to the state capital

Vaccination (with a bivalent A + C meningococcus capsular polysaccharide vaccine) was conducted, targeting the age group 6 months to 30 years. In Katsina State an estimated 930 000 people (all ages) were vaccinated, 509 104 of whom received the vaccine with the direct support of MSF — 481 293 in the target age group (26% of the target population). The MSF-supported vaccinations were carried out in 13 of the 16 districts.

The total costs of the MSF meningitis activities in Katsina (vaccination and curative activities) were US$ 683 000. Vaccines, medicines, and materials accounted for 65% of these costs, with the rest being accounted for as follows: transport, 14%; personnel, 17%; and administration, 4%. The average cost of an expatriate MSF staff member in the field was US$ 109 per day.

Analysis of the intervention

The epidemiological data for the outbreak must be viewed with caution, as it can easily lead to erroneous conclusions about the course of the epidemic. Before the MSF intervention, financial and logistical constraints were seriously hampering the surveillance system, leading to incomplete or lack of data from many districts. In addition, only a fraction of meningitis cases were seen and registered in health care facilities, as many patients were too poor to pay for treatment and thus did not present themselves. It is therefore likely that the sharp rise in incidence after week 8 (19–25 February) was partly due to the improved surveillance and reporting, as well as the free treatment provided by MSF. In theory it is also possible that in many districts the peak of the epidemic was reached before the arrival of MSF in Katsina State.

In a setting where only the most severe cases are likely to be hospitalized, the estimate of the CFR before the intervention is probably inflated. It could be argued that because access to care improved after the MSF assistance and greater numbers of nonsevere cases are registered, the CFR would appear to fall, even without any improvement in curative services. However, not only did the CFR decrease dramatically after the start of the curative support by MSF (Fig. 4), but also the number of reported deaths from meningitis decreased dramatically (Fig. 3). This absolute reduction in reported deaths is probably an underestimate due to incomplete reporting of deaths before the intervention. Therefore, the reduction of the CFR may largely be attributed to the intervention.

Efficiency, impact, and cost-effectiveness. In terms of *efficiency*, the cost per vaccinated person was US$ 0.64 in Katsina State. The average cost of treating a meningitis case was US$ 35, with drugs accounting for more than half of this amount. However, only MSF costs are considered here; costs for the ministry of health (e.g. for the state and district health staff in the vaccination teams) are not included. As the latter costs largely consisted of national staff salaries, which on average are low compared to the costs of drugs, vaccines, materials, transport, and expatriate personnel, the results of the analysis are not greatly influenced.

An analysis of the *impact of the vaccination* campaign requires an estimate of the number of cases of meningitis prevented, calculated by comparing the number of cases that occurred with a projection of the number of cases that *would* have occurred had there been no vaccination. For Katsina we calculated the number of cases prevented by the MSF vaccination campaign using the method described by Pinner et al. (*5*). The estimate is based on the fact that cases occur among nonimmunized persons and the assumption that vaccination protects only those who are vaccinated and does not prevent meningococcal carriage or transmission. The group of nonimmune persons consists of unvaccinated individuals and vaccinated persons with incomplete seroconversion. The overall attack rate in the nonimmune population was calculated using the registered weekly attack rates per district, the weekly vaccination coverage per district, and the efficacy of the vaccine (estimated at 85%). If the attack rate among the nonimmune population is projected to the entire population, an estimate can be made of the number of meningitis cases that would have occurred had no vaccinations been given. The difference between this estimate and the number of cases can be attributed to the vaccination campaign. Weekly attack rates in both the vaccinated and nonvaccinated populations were estimated using the following equations (*5*):

Weekly overall attack rate = (vaccinated population attack rate × proportion vaccinated) + (nonvaccinated population attack rate × proportion nonvaccinated)

Vaccinated population attack rate = 0.15 × nonvaccinated population attack rate

Application of the equations to the 13 districts in Katsina where MSF assisted indicates that the total number of meningitis cases prevented by the MSF-supported vaccinations was 700 (*4*). This is a reduction of only 3.3% of the 20927 total registered number of cases; with an average CFR among treated patients in Katsina of 8%, this is equivalent to only 54 averted deaths. The MSF assistance to the vaccination campaign cost US$ 326000, and the cost per death averted by vaccination is therefore about US$ 6000. Therefore the *cost-effectiveness of the MSF vaccination* intervention was low.

It could be argued that vaccination offers protection for future epidemics and that the campaigns had an important indirect effect. Unfortunately, the future protective effect of such vaccination campaigns is quite limited, since meningitis vaccine provides protection for only 3–5 years in persons aged >4 years and for <1 year in under-4-year-olds (*3*). Only if a large epidemic were to occur within 3–5 years of a vaccination campaign would part of the population be sufficiently protected.

To calculate the *impact of the MSF-supported curative activities*, we used two methods to estimate the number of deaths prevented.

- Before MSF assistance the average meningitis CFR was 17% in Katsina; after the supply of free drugs and provision of training to the Nigerian health facilities, the CFR fell to 8%. The number of deaths prevented by MSF intervention can be calculated by taking the product of the number of treated cases and the difference in the CFR = 10 117 × (0.17 − 0.08) = 910.

• The CFR in untreated patients is at least 50% (range, 50–80%, (*3*, *6*)). The total number of prevented deaths can then be estimated as $10\,117 \times (0.50 - 0.08) = 4249$.

Since at the time of the arrival of MSF in the country the Nigerian health authorities were experiencing an acute shortage of antibiotics and oily chloramphenicol was completely unavailable, the second of these two estimates is not unrealistic. The total cost of the curative activities of MSF in Katsina was US$ 357000. Depending on which estimate is used, the cost of treatment per death prevented was US$ 396 (first calculation above) or US$ 83 (second calculation above). Again, only MSF costs are considered here; those for the ministry of health (e.g. for the state and district health staff in the health facilities) are not available.

Vaccination strategies. Determining the appropriate vaccination strategy is a problem. Priorities have to be set and there is always insufficient time and material to vaccinate everyone. How can we determine when, where, and whom to vaccinate? When to vaccinate is fairly clear. To be effective, a mass vaccination campaign must be conducted as early as possible in the epidemic, within 4–6 weeks after passing the threshold (*7*). A simulation model used for the 1995 meningitis epidemic in Niger (*8*) shows that if the vaccination campaign starts as soon as the epidemic threshold is passed, the number of prevented cases is five times greater than if the campaign begins at the peak of the epidemic.

Although the proportion of prevented meningitis cases as a result of MSF support to the vaccination campaign for the entire Katsina State was calculated to be 3.3% per district, this proportion varied from 2% to 17%. Analysis at the district level shows that the timing of the vaccination campaign relative to the threshold (time elapsed between the threshold and the start of the campaign) is more important than the timing relative to the peak of the epidemic (before, during, or after the peak incidence) (Table 2). This arises because in most cases the epidemic curve is asymmetrical with the peak occurring late in the epidemic. Most meningitis cases occur before the peak incidence. Thus, the earlier that vaccination starts after passing the epidemic threshold, the greater will be the effect on the number of cases prevented.

In Katsina, where vaccination was carried out in 13 of the total 26 districts, only two did so before the peak and only two were within 6 weeks of passing the epidemic threshold. These data speak for themselves. It should be borne in mind, however, that in retrospect it is simple to determine that vaccination

Table 2: **Effectiveness of Médecins sans Frontières' vaccination activities, according to time of vaccination, Katsina, Nigeria**

Time of vaccination	Average % of prevented cases	No. of districts
Before peak incidence	5	2
At peak incidence	9	3
After peak incidence	5	8
<8 weeks after passing threshold[a]	12	3
8–12 weeks after passing threshold	6	6
>12 weeks after passing threshold	3	4

[a] >15 Cases per 100000 per week.

was carried out too late to be effective. During an epidemic ad hoc decisions (to mass vaccinate or not) are needed while the progression of the epidemic and position on the epidemic curve are unclear.

The following priorities were used to determine where to vaccinate:

— those districts where the epidemic threshold of 15 cases per 100000 had been surpassed within the previous 6 weeks;

— those districts where the alert threshold of 5 cases per 100000 had been surpassed within the previous 8 weeks if an epidemic had been declared in a neighbouring district; and

— villages with more than 10000 inhabitants in the chosen districts.

As is the case in previous studies (*9*), our epidemiological data did not reveal a clear relationship between the size of villages and the attack rate. The epidemic foci were not uniformly distributed among the villages in the affected areas and research was needed to locate where most cases were occurring in Katsina State.

Finally, vaccination should be restricted to the population most affected by the epidemic: those aged 6 months to 30 years. In reality this is not always possible since during a meningitis epidemic everyone demands to be vaccinated.

It has been suggested that in high-risk countries meningitis vaccination should be included in the Expanded Programme on Immunization (EPI) as the cheapest and most efficient solution. In general, EPI attains high vaccination coverage. The short duration of protection afforded by meningitis vaccine, however, requires revaccination every 3 years until 30 years of age in order to maintain effective immunity among the population. In young children, for whom seroconversion is low and the duration of protection is <1 year, an even higher vaccination frequency would be required (*10*).

Conclusions

It is tempting to attribute the end of the epidemic to the coordinated effort of MSF and the Nigerian government (treatment with chloramphenicol, surveillance, training and mass vaccination). We calculated that the impact of the mass vaccination campaign was marginal. In most districts the epidemic had progressed too far or was even in decline when vaccination commenced, and only 3.3% of cases were prevented by vaccination. Other factors such as the onset of the rainy season and herd immunity (the number of people who develop a natural immunity after contact with the disease) probably played a crucial role in ending the epidemic (*11*).

In view of the rapidity of the epidemic and the relatively late access that MSF had to the affected areas, it would have been better not to vaccinate from a cost-effectiveness perspective. In practice, however, this option is not realistic since pressure to vaccinate is great from governmental and international organizations. Also, vaccination is often a precondition for gaining access to implement curative activities. Therefore, a strict, more selective vaccination strategy is an effective option: vaccinate only in those districts where it is clear that it will still have a significant protective effect. Mass vaccination against meningitis is effective only if it is conducted within 4–6 weeks after passing the epidemic threshold (>15 cases per 100000 population per week). A functioning early warning and surveillance system is an absolute precondition for this. Only on the basis of timely and reliable information is it possible to develop effective vaccination strategies. Surveillance must occur at the level of the small administrative unit (*3*), since the epidemic threshold at the level of large administrative units (population >100000) will occur too late. In most African countries in the meningitis belt surveillance systems function poorly or not at all because of the increasing financial and logistic constraints that these countries face. In Nigeria MSF has started a cooperative programme with the ministry of health to strengthen local capacity for early recognition of epidemics (not only meningitis but also cholera, measles, yellow fever, etc.).

Treatment of meningitis patients in the present study was effective: at least 900 deaths were prevented in Katsina, a mortality reduction of at least 36%. During meningitis epidemics in countries where surveillance systems are inadequate, such as in most of sub-Saharan Africa, curative care programmes should have priority.

Acknowledgements

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Résumé

Quelle priorité pendant une épidémie de méningite: vaccination ou traitement?

De novembre 1995 à mai 1996, une épidémie de méningite a frappé le nord du Nigéria. Plus de 75000 cas et 8440 décès ont été enregistrés (taux de létalité: 11%). Médecins sans Frontières (MSF), en coopération avec le gouvernement nigérian, a réalisé un programme d'assistance (aide à la prise en charge des cas, surveillance, vaccination de masse) dans trois Etats du nord du pays (Bauchi, Kano, Katsina) où sont survenus 75% des cas. Cet article décrit l'évolution de l'épidémie et l'assistance fournie par MSF dans l'Etat de Katsina (4.5 millions d'habitants).

La semaine 5 de l'année 1996, le seuil épidémique de 15 cas pour 100000 habitants par semaine (moyenne sur deux semaines) a été atteint, et la semaine 11 le pic de l'épidémie était dépassé. Au total, 20927 cas ont été enregistrés; seuls 8% d'entre eux avaient plus de 30 ans. Le taux d'atteinte était de 461 cas pour 100000 Avant l'assistance de MSF le taux de létalité était de 17%; après le début de l'intervention il est rapidement tombé à 8%.

Environ 930000 personnes ont été vaccinées (dont 509104 avec le soutien direct de MSF) par des équipes de personnels de santé de l'Etat et du district; 10117 malades ont reçu un traitement avec le soutien de MSF. Le coût total des activités de MSF consacrées à la méningite (vaccination et traitement) dans l'Etat de Katsina a été de USD 683000. La prise en charge des cas et la vaccination de masse ont été efficientes: USD 0,64 par vaccination et USD 35 par cas traité. Le nombre total de cas de méningite évités grâce aux vaccinations effectuées avec le soutien de MSF a été évalué à 700 (soit une réduction de 3,3% seulement), avec un nombre de décès évités estimé à 54. Compte tenu du coût de l'assistance de MSF à la campagne de vaccination (USD 326000), on estime à environ USD 6000 le coût par décès évité.

Le coût total des activités de MSF en matière de traitement a été de USD 357000. Selon le mode de calcul, le nombre de décès évités a été estimé

soit à 900 soit à 4280 et le coût du traitement par décès évité, à USD 396 ou USD 83.

L' analyse au niveau du district montre que la chronologie de la campagne de vaccination par rapport au seuil épidémique (temps écoulé entre le franchissement du seuil et le début de la campagne) est plus importante que par rapport au pic de l'épidémie. Une fois le seuil épidémique passé, plus la vaccination est pratiquée tôt, plus l'effet sur le nombre de cas évités sera sensible

Dans la plupart des districts étudiés, l'épidémie était déjà trop avancée ou avait même commencé à décliner lorsque la vaccination a commencé. Une stratégie vaccinale plus sélective est donc une option efficace: il ne faut vacciner que dans les districts où il est certain que la vaccination aura encore un effet protecteur significatif. La vaccination de masse n'est efficace que si elle est pratiquée 4 à 6 semaines après le franchissement du seuil épidémique. Pour déterminer ce moment, il est absolument indispensable de disposer d'un système opérationnel de surveillance et d'alerte précoce.

Le traitement des malades a été efficace: au moins 900 décès ont été évités dans l'Etat de Katsina, soit une réduction de la mortalité d'au moins 36%. Pendant les épidémies de méningite dans les pays où les systèmes de surveillance sont insuffisants, comme c'est le cas dans la plupart des pays d'Afrique subsaharienne.

References

1. Cerebrospinal meningitis in Africa. *Weekly epidemiological record*, 1996, **71**(42): 318–319.
2. **Farese P, Procupet Blaustein A, Margets J.** *Meningitis epidemic in Nigeria, 1996. Evaluation of the MSF operation in North Nigeria from February to May 1996.* Brussels, Association Européene pour le Développement et la Santé, 1996 (unpublished document).
3. *Control of epidemic meningococcal disease. WHO practical guidelines.* Lyon, Fondation Mérieux, 1995
4. **Bastos JA, Carriere C.** *Meningitis epidemic, Nigeria 1996. MSF emergency programme. Activity report.* Paris, Médecins sans Frontières, 1996 (unpublished document).
5. **Pinner RW et al.** Epidemic meningococcal disease in Nairobi, Kenya, 1989. *Journal of infectious diseases*, 1992, **166**: 359–364
6. *Conduite a tenir en cas d'épidémie de méningite à méningocoque* Paris, Médecins sans Frontières, 1993
7. **Varaine F et al.** Meningitis outbreaks and vaccination strategy. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1997, **91**: 3–7
8. **Ritmeijer K.** [Medecins sans Frontières and the meningitis epidemic in Niger in 1995: vaccinate or treat?] *Nederlands tijdschrift voor geneeskunde*, 1996, **140** 1613–1616 (in Dutch).
9. **Moore PS et al.** Detection of meningitis in Africa a population-based analysis. *International journal of epidemiology*, 1992, **12**: 155–162.
10. **Reingold AL et al.** Age-specific differences in duration of clinical protection after vaccination with meningococcal polysaccharide A vaccine *Lancet*, 1985, **2**: 114–118.
11. **Moore PS.** Meningococcal meningitis in Sub-Saharan Africa a model for the epidemic process *Clinical infectious diseases*, 1992, **14**: 515–525

WHO Global Database on Child Growth and Malnutrition

The book presents and interprets the vast amount of data contained in the WHO Global Database on Child Growth and Malnutrition. The data, which indicate the growth and nutritional status of children under the age of five, have been collected by WHO since 1986 as part of its efforts to monitor global progress in combatting childhood malnutrition and to identify those groups in need of priority interventions.

Information is derived from population-based nutrition surveys of representative samples collected and assessed according to standardized procedures. The database currently reflects over 1700 nutritional studies and covers 84% of the world's total population of under-fives and 95% of this age group living in the developing world.

The book has two parts. Part one explains the importance of global nutritional surveillance and describes the origins and development of the database. Against this background, subsequent chapters summarize global, regional, and national situations and trends for key indicators of child growth and nutritional status. Numerous tables and selected maps are used to indicate the country-specific prevalence and geographical distribution of underweight, stunting, wasting, and overweight for boys, girls, and the two sexes combined in developing countries and developed countries; to classify countries according to very high, high, medium and low prevalence for each indicator; and to estimate global and regional trends over time. While noting important achievements in overcoming malnutrition among under-fives, the analysis concludes that global progress is entirely inadequate to reach the goal, set for the year 2000, of a 50% reduction in 1990 prevalence levels of moderate and severe malnutrition. Part one concludes with chapters describing the methods used in data collection and their standardized presentation, and offering guidance in the interpretation of the statistical tables.

Part two contains over 600 pages of data tables and references. Data on the nutritional status of under-fives in 173 countries are presented, disaggregated by rural and urban areas, by regions, and by sex and age group. Survey data indicate the percentage of children wasted, stunted, and under- and overweight. Each country data table is followed by relevant survey references and additional information useful in interpreting the data.

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