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Research in Complex Humanitarian Emergencies: The Médecins Sans Frontières/ Epicentre Experience

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This is the first in a series of articles on conducting research during complex humanitarian emergencies.

The United Nations (UN) defines a complex humanitarian emergency (CHE) as "a humanitarian crisis in a country, region, or society where there is total or considerable breakdown of authority resulting from internal or external conflict and which requires an international response that goes beyond the mandate or capacity of any single and/or ongoing UN country program" [1]. Such emergencies require adapted, focused, and pragmatic field responses to be organized within short time frames, often under difficult accessibility, security, and climate conditions. Over the years, operational efficiency in the field has increased thanks to research carried out during CHEs.

Early on following its inception in 1971, the international medical humanitarian organization Médecins Sans Frontières (MSF) conducted its medical missions with enthusiasm but little standardization, focusing more on individual care than on optimized public health approaches. Growing field experience, mainly acquired in refugee camps, rapidly led to the identification of ten major public health priorities for CHEs (Box 1).

Critical analysis of data collected by MSF field workers generated questions about the effectiveness of MSF's operational responses (Box 2). Recognizing the importance of epidemiological surveillance and systematic monitoring of CHE activities, MSF created its own research center, Epicentre, in 1987 with the aim of addressing those questions [2].

Twenty years later, Epicentre has developed into a large team of over 40 professionals in the headquarters in Paris, offices in Geneva and Brussels, and a field station in Mbarara, Uganda. Through partnerships with national and international institutions, universities, and research groups, Epicentre has gained recognition in the field of CHE research and, in 1995, became a World Health Organization (WHO) collaborative center for research in epidemiology and control of emerging diseases. To this day, Epicentre is dedicated to improving field operations in CHEs.

In this article, we review Epicentre's 20 years of experience conducting research during CHEs and show how such research has been critical in improving field response.

The Policy Forum allows health policy makers around the world to discuss challenges and opportunities for improving health care in their societies.

Box 1. Top Priorities to Address in Emergencies

- Rapid assessment of the health status of the population
- Mass vaccination against measles
- Water supply and implementation of sanitary measures
- Food supply and implementation of specialized nutritional rehabilitation programs
- Shelter, site planning, and non-food items
- Curative care based on the use of standardized therapeutic protocols, using essentials drugs
- Control and prevention of communicable diseases and potential epidemics
- Surveillance and alert
- Assessment of human resources and training and supervision of community health workers
- Coordination of different operational partners

Rapid Assessments and Survey Methods

Rapid assessments in CHEs, often based on population surveys, help guide emergency response by measuring mortality rates, prevalence of malnutrition, and coverage of basic needs (food, water, shelter).

Over the past 20 years, Epicentre has conducted nearly 100 mortality surveys, most of them under difficult field conditions. One illustrative example is the survey conducted in July 1994 among 800,000 Rwandan refugees in Goma, Zaïre [3]. Anyone walking along the road between Goma and Katale

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Abbreviations: ACT, artemisinin-based combination therapy; CHE, complex humanitarian emergency; MSF, Médecins Sans Frontières; RDT, rapid diagnostic test; UN, United Nations; WHO, World Health Organization

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every morning knew, by looking at the bodies piling up along the road, that the health situation was extremely severe. The survey showed that, in the first month alone, more than 10% of the population had died, 88% from diarrhea [4]. The Goma survey, like many others, highlights the role of field epidemiology in properly quantifying events, even in the most chaotic situations. The data were used for programmatic and planning purposes, and, in some instances, as advocacy material.

Survey sampling schemes used in CHEs were originally explored by the United States Centers for Disease Control and Prevention [5]. Among these schemes, cluster sampling (in which the population of interest is divided into groups, or clusters, and a random sample of these clusters is selected), initially developed by WHO for the estimation of vaccine coverage, is often the only option since it is rarely possible to survey the entire population [6]. When samples of adequate size and sufficient number of clusters are drawn, estimates are precise enough for planning purposes. Research for realistic alternatives (such as sampling based on global positioning systems) is ongoing [7].

Estimating population size, which is important for needs assessment, remains difficult [8,9]. While satellite photos could represent a quick and valuable alternative to the methods currently in use, humanitarian organizations operating on foreign soil have limited access to such pictures.

Responding to Infectious Disease Outbreaks

In a CHE, overcrowding, inadequate shelter, poor water and sanitation, collapse of health services, and the breakdown of existing infectious disease control programs can markedly increase the burden of communicable diseases and the risk of epidemics. In such a context, early detection and prompt, well-conducted outbreak investigations are essential to guide adapted responses.

Meningococcal meningitis. Epidemics of meningococcal meningitis constitute a major and recurrent burden on public health systems in large parts of sub-Saharan Africa. An important milestone in Epicentre's research history occurred in 1988 when the production of oily chloramphenicol, the standard treatment for meningococcal meningitis, was jeopardized. MSF, with others, successfully lobbied to resume the drug's production. Epicentre conducted randomized clinical trials comparing oily chloramphenicol with ampicillin (in 1991) and later with ceftriaxone (in 2003) for the treatment of meningococcal meningitis. These studies were conducted as a reaction to nationwide epidemic responses in Niger and Mali. Time for logistic preparation was necessarily shortened, health structures were already overwhelmed by the influx of cases of meningitis, and some study sites were located in remote areas. Through the support of national authorities, the organization of MSF logistics, and the dedication of national and international staff involved, the scientific quality of the studies was ensured, ethics rules were respected, and both clinical trials were published [10,11].

Measles. Measles remains a major potential killer in CHEs. Despite the availability of a highly effective, safe, and cheap vaccine, protection of children against the disease remains suboptimal in some areas, notably those affected by long-lasting conflicts. MSF and Epicentre, with the support of WHO, recently explored the dynamics of measles outbreaks in Nigeria, Niger, and Chad to re-examine current response strategies [12,13,14]. Preliminary results indicate that the relatively slow spread and long duration of those outbreaks may, in some urban settings, leave enough time to plan for and conduct reactive mass vaccination campaigns [15]. Further analysis is needed in rural areas.

Malaria. Malaria can significantly impact public health services and morbidity and mortality during CHEs. Epicentre and MSF have conducted 43 efficacy studies in Africa and Asia from 1996 to 2004 involving more than 12,000 patients; these studies have shown the lack of efficacy of the monotherapies that are in widespread use [16]. At the same time, Epicentre/MSF conducted randomized clinical trials in Angola, Sierra Leone, and Zambia to compare the efficacy of several artemisinin-based combination therapies (ACTs) with older drugs [17,18,19]. These studies showed that ACTs were more effective than older monotherapies such as chloroquine and sulfadoxine-pyrimethamine, which helped support changes in national protocols to ACTs. Several of these trials were conducted in the malaria endemic area of Mbarara, Uganda, where a research base was set up in cooperation with the local university hospital.

Hepatitis E. In 2004, during a large hepatitis E outbreak in Darfur, Sudan, a study identified chlorinated surface water (compared with non-chlorinated water from deep drilling) as a potential risk factor for hepatitis E [20]. The methods used for the provision of safe water were considered insufficient to inactivate the hepatitis E virus from the chlorinated surface water and control this outbreak. MSF is exploring alternative methods adapted to CHEs, such as deep drilling or ultraviolet irradiation.

Micronutrient Deficiencies and Malnutrition

Pellagra. In 1989, an outbreak of pellagra (20,000 cases) erupted among Mozambican refugees in Malawi. Epicentre analysis of the outbreak, and World Food Programme log books, showed that a shortage of groundnuts (the major source of niacin) in UN rations was the cause

Box 2. Examples of Public Health Questions Generated in the Field of CHEs

- How accurate are estimates of population size provided by rapid assessments?
- What are the best indicators to measure the impact of an intervention?
- What is the validity of the various anthropometric indicators used in the field?
- Which thresholds should be used to define outbreaks of potentially epidemic diseases?
- How well do commonly used rapid diagnostic tests perform under field conditions?
- What are the risk factors of death of severely malnourished children?
- Can reactive mass vaccination campaigns help control cholera outbreaks in refugee camps?

of the outbreak. Groundnut supplies were then purchased in South Africa, and the outbreak was controlled within a few months [21]. This investigation illustrates how properly conducted studies done in close collaboration with local authorities and operational partners guided quick decision-making and successful outbreak control.

Malnutrition. A high prevalence of malnutrition is one of the most frequently encountered phenomena during CHEs. Simpler methods to measure malnutrition at the individual and community levels and better prevention and treatment protocols can reduce the burden of nutritional crises and save lives. Using data from nearly 100 MSF anthropometric surveys, Epicentre tested various measurement indices as predictors of acute malnutrition among children under five years [22,23,24]. Unfortunately, we have so far failed to identify a better tool than "weight for height," which is difficult to routinely use at primary care level. Further research is still needed in this area.

In terms of treatment at community level, building on work by André Briend and Steve Collins [25,26], Epicentre compared malnutrition treatment strategies based on home-based care versus therapeutic feeding centers in Maradi, Niger from 2002–2003 [27]. Results showed similar and satisfactory weight gains but lower defaulting and death rates with the home-based care approach. MSF has implemented strategies to address large numbers of cases of malnutrition, such as in Niger, with data collected and analysed by Epicentre. In 2005, nearly 60,000 children with malnutrition in the Maradi region of Niger were treated with a ready-to-use therapeutic food (Plumpy'nut), resulting in recovery rates of about 90% and death rates of less than 5% [28].

Improving Diagnostic Tools

Diagnostic tools adapted to field conditions can serve two purposes—diagnosis of individuals and confirmation of an outbreak. Few rapid diagnostic tests (RDTs) are designed for use in CHEs, and little is known about their performance in such a context. However, the use of RDTs can potentially improve the capacity of case detection and the efficacy of treatments. Epicentre has tested the performance of several RDT kits, which are now used in the field.

Malaria RDTs must be reliable, cheap, and user-friendly, particularly if used in CHEs. In addition, the performance of the test is maximized if the local epidemiology of the disease and the immunity of the population are taken into account. MSF/Epicentre has tested several commercially available malaria RDTs under field conditions. Beyond the classical evaluation of the sensitivity and specificity of the tests, our studies focused on practical considerations such as ease of use, shelf life, and storing conditions [29,30]. This approach, although usually neglected by researchers, is critical to maintaining field-oriented research in response to questions raised by the humanitarian community.

Other RDTs, adapted to the specific conditions of CHEs, are crucially needed [31]. In 2003, Epicentre conducted a randomized clinical trial assessing the sensitivity and specificity of a latex agglutination RDT (Pastorex) for *Neisseria meningitidis* serogroup A during a meningitis epidemic in Niger [32]. Results from 484 samples showed 88% sensitivity and 93% specificity, suggesting that this RDT could be a favorable alternative to current diagnostic tests. Other promising tools such as a dipstick for diagnosis of *Shigella flexneri* and *Shigella* spp. [33] and a one-step RDT for cholera [34] need to be evaluated in field conditions.

Lessons Learned

Finding pragmatic and efficacious answers to public health questions generated by the field has led Epicentre research activities over the last 20 years. Such an intimate and continuous link between field operations and applied research is unusual in the world of humanitarian response to CHEs. The nonstop interaction between field actors and researchers has been key in developing an original research agenda and conducting successful projects, which help improve the quality and effectiveness of the operational response. This, in turn, enhances the capacity of the scientific community and of aid agencies to cope with increasingly complex humanitarian crises.

Since the creation of Epicentre in 1987, a number of operational and clinical research projects have been conducted. Constraints faced in CHEs, too often underestimated, make research projects particularly challenging. Conditions of their success include rigorous technical and logistic support, close collaboration with local authorities, and fully mobilized national and international staff.

The role of epidemiologists extends beyond their traditional scientific research functions to a broader range of responsibilities, including exchanges with field workers to help generate research ideas and reconciliation of rigorous methods with local constraints. External ethical review, written informed consent, and involvement of the local community are some of the systematic mechanisms that helped Epicentre carry out research projects that respect the principles of ethical human subjects research.

The results of the research conducted by MSF/Epicentre and others over the last two decades have shown the limitations of current therapeutic and preventive resources for most of the diseases prevalent in developing countries. The Drugs for Neglected Diseases Initiative (DNDi), initially promoted and funded by MSF in 2003, focuses on developing new drugs or formulations for patients suffering from the world's most neglected diseases [35]. Today, 22 DNDi research and development projects are under way, with the goal of developing six to eight new treatments in the next ten years [36]. Some projects have been implemented within MSF CHE programs, with Epicentre providing research and data analysis support.

Next Steps

Looking towards the future, Epicentre continues to address unanswered questions in the field epidemiology of CHEs. Among these, the aim is to continue to improve the control of infectious diseases and patient management, including easy-to-use and cheap alternative therapeutic regimens and preventive strategies. Conducting high-quality research in CHEs means testing new techniques in remote areas, while taking into consideration all usual aspects of logistics and ethics. Improved survey methods and surveillance systems are continuing challenges for the future. Some under-

researched areas should be further explored. The ultimate goal remains to address questions aimed at significantly improving the health status of affected populations. ■

Supporting Information

Text S1.

Additional studies by Epicentre/MSF on rapid assessments and survey methods (list 1), nutrition (list 2), infectious disease control (list 3), and epidemics, malaria, and diagnostic tools (list 4)

Found at doi:10.1371/journal.pmed.0050089.sd001 (58 KB DOC)

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