

CLINICAL CASE REPORT

Injections that kill: nosocomial bacteraemia and degedege in Tanzania

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Submitted: 18 February 2010; **Revised:** 7 July 2010; **Published:** 20 September 2010

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Rural and Remote Health 10: 1391. (Online), 2010

Available from: <http://www.rrh.org.au>

A B S T R A C T

Context: In Tanzania and some other African rural settings, a traditional proscription of injections for the treatment of cerebral malaria (*degedege*) stems from parents' fear that injections will kill a child with fever and convulsions. The re-use of injection equipment in rural clinics is associated with bacterial contamination even where sterilization is practiced to prevent HIV transmission. A secondary infection with bacterial sepsis is indistinguishable from non-responsive malaria on clinical examination, and may be a significantly under-reported adverse event in rural Tanzania. In a prospective survey of patients whose venous catheter was culture positive on removal, 61% developed bloodstream infections.

Issue: Parents report having witnessed a child's death following an injection for the treatment of fever and convulsions in rural Tanzania, and some traditional healers who would refer a child with uncomplicated malaria for Western biomedical treatment are convinced that injections are fatal for a child with convulsions. Injection drug users learn aseptic technique to avoid what is called a 'dirty hit', a systemic infection that is felt immediately after injecting, indicating sudden deterioration is likely in a sick child if an IV injection is unsafe. Community mistrust of injection providers has been too casually attributed to superstition; to address parents' concerns, injection safety should be a priority in rural health services. Intravenous injections carry a 0.2% risk of acute bacteremia when given with unsterile equipment, while unsafe infusions carry a 3.7% risk of infection, much greater than the risk from intramuscular injections of vaccine. Sepsis should be considered an important adverse event in the management of severe malaria, but the diagnosis of nosocomial bloodstream infections is a challenge in hospitals that cannot culture for bacteria. When the auto-disable syringe was introduced, patient safety improved at a Tanzanian district hospital; a reduction in the burden of serious secondary infections large enough to reduce the average inpatient length of stay was observed. Nosocomial bloodstream



infections are a common cause of fever in Tanzanian hospitals. In Tanzania, bacteremia is sometimes associated with more deaths in hospitals than malaria.

Lessons learned: Although other obstacles to appropriate treatment for malaria may be more important in rural Tanzania, the belief that injections will kill a child is suggestive of avoidable adverse events. The intensity of malaria treatment in rural areas and frequent recourse to informal sector health care presented a significant challenge for the prevention of adverse events including sepsis and HIV transmission. A household survey in rural Tanzania found that 27% of malaria treatment occurs at drug stores, and 30% of patients seek treatment at a general shop. A majority of rural patients evaluated for malaria in the formal sector have taken chloroquine before coming to the clinic. A new national injection safety policy banning the import of non-auto-disable syringes prevents injection equipment re-use in the informal sector. Improving injection safety in rural Tanzania through the introduction of auto-disable syringes will ensure that parents have nothing to fear from quinine injections and infusions that are usually life saving.

Key words: auto-disable syringe, bacteremia, convulsions, fever, injections, malaria, nosocomial infections, parenteral infusions, septicemia, traditional medicine.

Context

Injection safety has improved in Africa largely due to efforts to prevent HIV transmission. In some rural clinics and remote pharmacies, however, disposable syringes are still re-used, although heat sterilization damages the plastic ring at the base of the needle and is limited by the availability of fuel. A study of HIV transmission risks in Mbeya, Tanzania revealed that 33% of sterilized equipment prepared for re-use was contaminated with bacteria, introduced by handling the needle in preparing the next injection¹. This finding has serious implications for patient safety when IV injections are administered for the treatment of malaria. In a prospective study of patients receiving venous injections with catheters that were culture positive on removal, 61% developed a bloodstream infection². However, low recognition of resulting secondary infections is to be expected in rural areas, because sepsis and malaria are indistinguishable by clinical examination; and WHO guidelines for managing childhood illnesses typically fail to identify 50% of bacteremia cases in Africa³. The purpose of this review was to explore the clinical significance of a traditional proscriptio of injections ('I know if I take my convulsed child to hospital they may inject him and this practice is known to kill children') in treating cerebral malaria (known as *degedege* in Tanzania⁴). The hypothesis of this review

was that the belief that injections will kill a child with *degedege* arises from the occurrence of injection associated infections resulting in fatal sepsis, and that recognizing and redressing problems with infection control may improve parents' and traditional healers' willingness to refer sick children for quinine injections.

Issue

A systematic search of the peer reviewed literature was completed in January 2010 using Medline and the search terms 'sepsis', 'septicemia', 'bacteremia', 'catheter', 'nosocomial' and 'degedege', together with the search term 'Tanzania'. All English-language articles published since 1995 were screened (167 records), and the reference lists of relevant articles were reviewed, identifying a further 9 articles. Only 25 articles met the inclusion criteria by providing quantitative or qualitative data on the incidence of nosocomial bloodstream infections or the nature of *degedege*. The authors of one article with an aberrant description of *degedege* were contacted for clarification. Five articles that did not meet the inclusion criteria were deemed relevant because they provide information on the management of malaria and diseases misdiagnosed as malaria in rural Tanzania. Three additional searches were performed to assess the incidence of bacteremia in African



patients receiving treatment via an IV line, the incidence of bacteremia in vaccine trials, and the mortality rate for nosocomial bacteremia in developing country hospitals; and to review all records on nosocomial bacteremia in developing countries, and adverse events in vaccine trials in Africa.

Currently, oral medication is prescribed for uncomplicated malaria in Tanzania, but severe malaria still requires parenteral therapy because convulsions are often accompanied by weakness or vomiting. This presents a particular problem in Tanzania because a fever with convulsions is popularly understood in rural areas as *degedege*, believed to be a condition that must never be treated by injection^{5,6}. The defining symptoms of *degedege* are those of cerebral malaria, with additional symptoms that include rolling eyes, a stiff body, lethargy, no urine, and no stool, cold feet, babbling, shouting, and frothing at the mouth^{7,8}. These additional symptoms are mentioned only by some traditional healers, however, and all the symptoms universally attributed to *degedege* according to traditional definitions are the symptoms of cerebral malaria.

Degedege is considered to be a spiritual malady associated with the spirit of a bird, and it is not traditionally associated with malaria in Tanzania, for which biomedical treatment is usually sought promptly by the same parents who would go first to a traditional healer to treat a child with convulsions^{9,10}. A similar proscription of treating a child with convulsions by injection exists in Burkina Faso⁶; whereas in Ghana and Nigeria, cerebral malaria with convulsions is also attributed to the spirit of a bird, but no similar proscription of injections exists⁶. In Cameroon *degedege* ('Idalgdalgui') is understood to be malaria and hospital treatment is believed to be effective¹¹.

Tanzanian mothers interviewed in some studies testified to the belief that injections will kill a child with *degedege*, and attributed this to their own experience⁸. Individuals who had not witnessed a sudden death in hospital following antimalarial injections had heard of the occurrence. One mother said, 'I could not take her to hospital as in the

hospital they treat by injecting drugs, the practice which results to sudden death of children under such treatment'¹². A traditional birth attendant who would refer patients with uncomplicated malaria for biomedical care reported that she would not refer a child with convulsions, because she believed that injections are fatal for this condition¹². In other Tanzanian settings, some traditional healers and rural mothers have been persuaded that malaria causes *degedege* and that antimalarials should be a first-line treatment⁹. That this transition has been difficult to achieve has been attributed to an irrational fear arising from the disappointment of parents who brought their child to the hospital too late, only to see the child die on arrival⁸.

In reality, sudden illness from an injection is a probability in unsterile conditions; the incidence of nosocomial bacteremia in patients receiving treatment via an IV line is reported to be as high as 54% in prospective studies of African hospitals, and of these infections 71% were matched to a culture from the IV catheter tip at the hospital recording the highest incidence. Table 1 presents the incidence of catheter-associated infections in five studies conducted in African hospitals. In many rural Tanzanian communities where injections are proscribed for *degedege*, the first line treatment for fever and convulsions is an IV infusion of quinine. Bloodstream infections in the developing world are usually associated with an IV line^{12,13}. In the absence of any other source of infection, a clinical bloodstream infection after admission in a patient receiving IV therapy is, by definition, an injection associated infection¹⁴. In this instance the definition is unhelpful, because the clinical signs of a bloodstream infection are indistinguishable from the presenting condition of cerebral malaria. The causal association between IV lines and nosocomial bacteremia has been established in risk factor analyses, however. The unadjusted relative risk for a bloodstream infection in patients with a peripheral venous catheter in US hospitals was reported as 10.9 (95% CI 10.8-11.1)¹⁵. A similar study of risk factors for cephalosporin-resistant bacteremia in hospitalized patients in Madagascar found an unadjusted odds ratio of 7.5 (95% CI 1.0-59) for the presence of a venous catheter¹⁶.



Table 1: Incidence of catheter-associated nosocomial bacteremia in African hospitals¹⁷⁻²¹

Reference	Country	Year	Patients	Incidence (%)
17	Egypt	2003	83	54
18	Ethiopia	1997	2417	7
19	Mali	2003-2004	1024	0.2
20	Nigeria	1980	20 382	2
21	South Africa	2001	800	10.4

The incidence of nosocomial bacteremia is high in Tanzanian hospitals that have the facilities to diagnose bloodstream infections, explaining 6-8% of fevers at the national referral hospital in Dar es Salaam^{3,22,23}. Nosocomial bloodstream infections develop in 1.5% of admissions to the intensive care unit²⁴. In 2006, bacteremia caused more deaths in children than malaria at this hospital³.

The association between an IV line and secondary infection is captured in the experience of Temeke Hospital in Dar es Salaam, where the auto-disable syringe was introduced in 2005, ending the practice of routine syringe re-use. In a film produced as an informal intervention assessment, the chief medical officer reported that infections prevented by the auto-disable syringe saved the hospital approximately US\$280 for a 7 day course of antibiotics, bed charges and intensive care to manage the symptoms of a serious systemic infection²⁵. The average length of stay for non-surgical inpatients was significantly reduced by the injection safety intervention alone. Remarkably, before the injection safety intervention's impact was immediately apparent, injections were not considered a serious risk factor for infection at this hospital, as the background rate of secondary infections was not then appreciated.

The infection risk from an IV line is greater than from an IV injection, because the device remains in place for days at a time. The risk from an IV line is comparable to that from a contaminated central venous catheter (61% probability of infection), and can be adjusted by the rate ratio of infections per catheter-day for peripheral venous catheters, compared with central venous catheters (0.5:2.7)^{2,26}. This adjustment

gives an 11.3% probability of infection if injection equipment is contaminated with bacteria. From the contamination rate observed in Mbeya, Tanzania when injection equipment was being boiled and re-used, the incidence of nosocomial bacteremia should be 3.7% for malaria patients with an IV line, where injection equipment re-use is practiced¹. This estimate is somewhat higher than the average observed incidence of catheter-associated nosocomial bacteremia in African hospitals (2.9%).

An ordinary IV injection should be less likely to lead to infection than an IV line. The incidence of HIV in drug users who inject intravenously has been used to estimate the risk of nosocomial HIV transmission in an unsafe medical injection²⁷. The per-injection risk of a serious bacterial infection can also be estimated from the experience of injecting drug users, who learn aseptic technique to avoid a 'dirty hit,' a febrile infection felt by most users immediately after an injection²⁷. Among febrile injecting drug users admitted to a hospital in Baltimore, USA, 25% had culture-confirmed bloodstream infections²⁸. Among 94 cohorts of injecting drug users interviewed from 1999 to 2008 in Australia, Ireland, and Viet Nam using the Illicit Drug Reporting System, the average incidence of a 'dirty hit' over one month of daily injecting was 21% (range 14–54%). These reports support a per-injection risk of 0.2% in unsafe IV injections.

The search for records of sepsis in vaccine trials anywhere in Africa identified only two studies that reported cases of fatal sepsis classified as vaccine-related adverse events. One rotavirus trial reported two cases of fatal sepsis (0.06%



incidence)²⁹. One trial in a review of trials of preventive treatment for malaria recorded a 0.6% incidence of fatal sepsis but did not report the nature of other hospitalizations (12% of infants were hospitalized within 8 weeks of treatment) that may have been related to the intervention³⁰. These findings suggest that IV injections for the treatment of malaria carry a much greater risk of secondary infection than ordinary medical injections.

The US CDC estimates that 15% of episodes of bacteremia are fatal, but the attributable mortality rate for nosocomial bacteremia in developing countries may be somewhat higher³⁶. Prospective studies into the mortality rate of patients with nosocomial bacteremia in developing countries are presented (Table 2). The crude mortality rate is high even in pediatric patients with no signs of infection on admission.

Lessons learned

The findings of this review suggest that the prevention of secondary infections through the prevention of injection equipment re-use may substantially improve the safety and acceptability of life saving injections for the treatment of malaria in rural Tanzania. The prevention of injection equipment re-use by informal-sector injection providers poses a special challenge. Outbreak investigations in the USA have shown that re-use of injection equipment without sterilization usually occurs when health workers mistakenly believe³⁷ that:

- it is safe to reuse a syringe after changing the needle or after changing the syringe
- it is safe to reuse a needle or syringe on the same patient: for re-entering a multi-dose vial or saline bag; or when accessing an IV port separated from the patient by intervening IV tubing or heparin locks or valves
- it is safe to re-use finger-stick devices among different patients without sterilization

- cleaning injection equipment or shared devices is only necessary when blood or other contamination is visible.

These misconceptions are likely to be common among injection providers who have no formal training in injection safety.

Informal-sector health care plays a prominent role in the treatment of malaria in Tanzania. Treatment seeking for malaria was comprehensively reviewed in one household survey of mothers and guardians in an endemic area of Tanzania³⁸. Of all individuals interviewed, 16% reported their children had experienced malaria in the previous 2 weeks, and 85% had sought treatment, most at a formal health facility but 27% at a drug store, and 30% at a general shop. The definition of malaria used in this survey included a traditional term sometimes understood to include a broader range of symptoms, such as respiratory or gastrointestinal illness (*homa*). The actual incidence of malaria is likely to be much lower than reported; however, the reliability of reported treatment-seeking behavior is considered good in retrospective surveys with a short recall interval.

The intensity of informal-sector treatment for malaria in Tanzania is evident from the high levels of chloroquine in the blood of patients presenting with malaria at hospitals and clinics in rural areas. Two studies evaluated levels of chloroquine already present in the blood of patients diagnosed with malaria. One study of primary healthcare facilities in eastern Tanzania (40 km north-west of Dar es Salaam) found that 98% of febrile children already had chloroquine in their blood when they presented for treatment³⁹. A follow-up study at public health facilities in the same region found that of sick children given chloroquine at the health facilities, 85% had recently taken chloroquine⁴⁰. Another study in the northern Highlands found that 51% of febrile patients seeking a malaria test had already taken antimalarials within the past 2 weeks.



Table 2: Crude and attributable mortality from nosocomial bacteremia in developing country hospitals^{22,31-35}

Reference no.	Design	Enrolment characteristics	Country	Patients	Mortality (%)
22	Crude mortality	Children with no signs of infection at admission	Tanzania	1798	43
31	Attributable mortality	Patients at nine hospitals	Colombia	125	18.5
32	Crude mortality	Neonatal intensive care unit patients	Mexico	868	37.7
33	Excess mortality	Intensive care unit patients	India	476	19
34	Crude mortality	Pediatric intensive care unit patients staying more than 48 hours	Tunisia	38	42
35	Crude mortality	Intensive care unit patients	Brazil	1004	38

In support of the Ministry of Health and Social Welfare policy on safe injections and healthcare waste management (effective from 1 May 2010) the Tanzania Food and Drugs Authority will no longer issue a permit for the importation of standard disposable syringes of 10 mL or less, unless these are meant for specific procedures, including blood drawing. Instead, only auto-disable syringes will be used for medical injections. The transition to importing only auto-disable syringes for ordinary medical injections is expected to improve injection safety at public, private and faith-based healthcare facilities, as well as in the informal sector.

Although fear of injections is not necessarily the most important barrier to seeking health care for fever with convulsions in Tanzania, injection fears in rural areas may reflect real risks associated with unsterile injections that can be redressed by improving infection control in the hospital. Other obstacles to receiving appropriate treatment for cerebral malaria must also be addressed. One study of treatment-seeking behavior in a rural area found that the most common explanation for a child's death due to delay in taking the child to a healthcare facility, was the perception that it was 'only ordinary fever', and not a severe episode of illness⁴¹. Other obstacles to obtaining timely treatment are a lack of access to transport and the high cost of professional medical care³⁸.

Conclusion

The clinical significance of the traditional proscription of treating *degedege* with injections is comparable to parents'

fears of injection-provoked paralysis, a rare but avoidable adverse event that can be prevented by safe injection technique. The estimated probability of infection when an IV injection is unsafe is 0.2%, and the estimated probability of infection when an IV infusion is unsafe is 3.7%^{1,2,26}. The observed average incidence of catheter-related nosocomial bacteremia in African hospitals supports a per-injection risk of 2.9%¹⁷⁻²¹. Vaccines carry a much lower risk of secondary infections^{29,30}. Nosocomial bacteremia has an attributable mortality rate of 19% in developing country hospitals, and accounted for more deaths in children than malaria at the national referral hospital in Tanzania in 2006^{3,31,33}. Low recognition of secondary bacterial infections at rural hospitals and a focus on HIV prevention in injection safety interventions have led to a general neglect of these serious adverse events, despite parents' fears that IV injections may kill a child. Attention to aseptic technique should be paramount where HIV transmission risks have been eliminated, as bacterial secondary infections can also be fatal. Bloodstream infections are a major burden on Tanzanian hospitals and their prevention through the use of auto-disable syringes may improve malaria treatment referrals in rural areas.

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