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Q Fever in Young Children, Ghana

To the Editor: Recently, experts identified Q fever, caused by the small, gram-negative bacterium *Coxiella burnetii*, as an important underdiagnosed childhood disease (*1*). Studies on Q fever in children <5 years of age are scarce, especially with respect to sub-Saharan Africa. The only available study from Niger reports a seroprevalence of 9.6% (*2*). Throughout Africa, prevalence of Q fever in adults shows considerable variability and is highest in countries with prominent stockbreeding (*3*).

Clinical manifestations of Q fever in children are similar to those of malaria (*1,4*). In malaria-endemic areas, most fevers are attributed to *Plasmodium falciparum* infection and presumptively treated with expensive combination therapies (*5*). In this context, other neglected fever-causing pathogens need to be given appropriate consideration.

We studied the prevalence of Q fever antibodies in 219 randomly selected children living in 9 rural villages of the Ashanti region, Ghana. Plasma was obtained by venous puncture from 2-year-old children after they had participated in a malaria control study and had been clinically monitored for 21 months. Clinical, parasitologic, socioeconomic, and Global Positioning System information was recorded as described elsewhere (*6,7*). In addition, 158 healthy adult volunteers from the same area were included. Plasma was stored at −20°C until microimmunofluorescence assays (IFA) (*Coxiella burnetii* I+II, Vircell SL Microbiologists, Granada, Spain) were performed according to manufacturer's instructions. To identify all children with Q fever titers, we regarded the following as positive fluorescence reactions to plasma dilutions: ≥1:64 for phase II immunoglobulin (Ig) G and ≥1:24 for phase II IgM with sensitivity (specificity) of 97.2% (100%) and

100% (56.3%), respectively. IgM testing was only performed on IgG-positive children. Positive and negative controls were run on each IFA slide. Relative risks (RR) for characteristics of children were calculated by χ^2 test; p<0.05 was considered significant. Informed consent was obtained from all participants or their parents. The study protocol was approved by the committee on human research and publication, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

Positive *C. burnetii* phase II IgG responses were observed in 37 (16.9%) of 219 children and 14 (8.9%) of 158 adults (Figure, panels A and B). In comparison to adults, more children had IgG titers ≥64 (Figure, panels C and D). On the day of the serosurvey 71 (32.4%) of 219 children had fever (measured body temperature >38°C or reported fever within the previous 48 hours). Test outcome did not appear to be influenced by *P. falciparum* infection, since 4 of 37 IgG-positive children (23 of 182 IgG-negative children) had clinical malaria, 11/37 (62/182) had asymptomatic parasitemia, and 6/37 (38/182) had fever without parasitemia, and there were no significant differences between groups. The frequency of prior malaria episodes also did not influence antibody response. Three aparasitemic children had positive phase II IgM titers (24, 96, and 1,536; phase II IgG 64, 64, and 4,096, respectively). The child with the high IgM and IgG titers was clinically ill with nonsevere *C. burnetii* pneumonia. This child was among 10 (27%) of 37 phase II IgG-positive children with detectable anti–*C. burnetii* phase I antibodies. Of all sociodemographic characteristics under consideration, only maternal illiteracy was associated with positive phase II IgG testing (RR 2.1, 95% confidence interval 1.0–4.2, p<0.05).

A considerable proportion of Ghanaian children had anti–*C. burnetii* antibodies, which indicates that Q fever might be a common event in
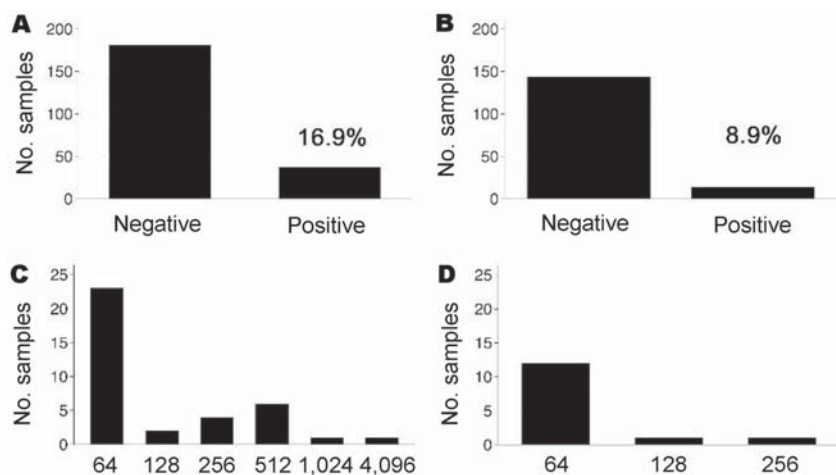
Figure. Seroprevalence of immunoglobulin (Ig) G antibodies against *Coxiella burnetii* phase II tested by microimmunofluorescence assays (IFA). A) Results of serologic tests of children, a cutoff titer of ≥64 for *C. burnetii* phase II IgG was applied; B) results of serologic tests of healthy adults (cutoff ≥64); C) distribution of *C. burnetii* phase II IgG titers in all positive children; D) distribution of IgG titers in all positive healthy adults.

this age group. Antibodies were more frequently detected in children than in adults. In adults, Q fever IgG antibodies reach a maximum 4–8 weeks after onset of symptoms and gradually decrease over months to finally fall below the detection limit (8).

A long period since infection is less likely in young children, which could result in higher seropositivity. Children, especially those of illiterate mothers, could also be more frequently exposed to the pathogen. Consumption of unpasteurized dairy products can result in infection or seroconversion without clinical disease (9). However, because consumption of raw milk in the Ashanti region is regarded as being uncommon by local health authorities, we consider dairy products an unlikely source of the disease. Although participants were intensively exposed to *P. falciparum,* which causes polyclonal B-cell stimulation, malaria episodes and parasitemia with and without symptoms at time of the serosurvey did not influence testing (10). This finding is important because commercially available test kits have only been evaluated in Europeans not exposed to parasites. We cannot completely rule out the possibility that other infectious agents, which are either only prevalent or more prevalent in African populations, could have resulted in false-positive results. Nevertheless, the test method we used and existing data on cross-reactions weaken this hypothesis (8).

We conclude that children in rural sub-Saharan Africa become exposed to *C. burnetii* early in life and that Q fever, which is clinically indistinguishable from malaria, may develop in an unknown proportion of them. The incidence of Q fever in relation to malaria, the route of infection, and appropriate serologic cutoffs for sub-Saharan Africa must be defined further. Currently, a prospective diagnostic study is investigating neglected infections, including human Q fever, as a cause of illness in Ghanaian children.

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Early Diagnosis of Disseminated *Mycobacterium genavense* Infection

To the Editor: Nontuberculous mycobacteria are environmental organisms that cause life-threatening diseases, particularly in immunocompromised hosts. They are increasingly recognized for causing problems in the management of solid-organ transplant recipients, due to improved diagnostic methods as well as increasing numbers and life expectancy of these patients (1). The slow-growing *Mycobacterium genavense* is a ubiquitous nontuberculous mycobacterium; it is reportedly isolated from tap water, pets, and the gastrointestinal tract of healthy humans (1,2). It was first recognized as a human pathogen in a patient with AIDS but has not yet been found in heart transplant recipients (3). We report early diagnosis of disseminated *M. genavense* infection in a heart transplant recipient.

A 37-year-old man was hospitalized in September 2001 for abdominal pain, sweats, and weight loss; he had received a heart transplant 3 years earlier. Immunosuppressive treatment, which began immediately after transplantation, consisted of tacrolimus (5 mg) and mycophenolate mofetil (2 g) daily; concurrent steroid therapy was tapered off over the next 6 months. A computed tomographic (CT) scan showed numerous large lymph nodes in his abdomen (Figure). Endoscopic examinations showed diffuse inflammation of the mucosa of the duodenum, ileum, and colon. Multiple biopsy samples were submitted for histologic analysis, culture, and molecular biological analysis. Immediate 16S rRNA gene amplification that used universal primers (4) and sequencing of samples taken directly from the biopsy material led to the identification of *M. genavense*. A 475-bp fragment was sequenced, and 99% homology with the gene of type strain ATCC 51234 (GenBank accession no. X60070) was found. PCR results were positive for 2 of the 4 samples tested. The molecular identification was compatible with the subsequent histologic finding of profound macrophage infiltration without granuloma and the presence of Ziehl-Neelsen–positive bacilli. Five weeks later, the molecular diagnosis was confirmed by blood cultures and cultures of the intestinal mucosa samples (Inno-LiPA Mycobacteria test, version 2, Innogenetics, Courtaboeuf, France). The direct molecular diagnosis of *M. genavense* enabled immediate treatment of the patient with the combination of moxifloxacin, ethambutol, clarithromycin, and amikacin; mycophenolate mofetil was discontinued. Clofazimine was added to the treatment regimen 3 months later, when a control CT scan showed that some of the enlarged mesenteric lymph nodes had increased further. After 5 months, the clinical signs resolved, and after 9 months, the lymph nodes were substantially smaller. CT scan results were within normal limits after 12 months of treatment; only ethambutol and clarithromycin were continued for an additional 6 months. There was no sign of *M. genavense* infection relapse 3 years after the diagnosis had been made.

Nontuberculous mycobacteria in persons who have received heart or other solid-organ transplants remain a rare cause of late infectious complications and occur ≈3.5 years after transplantation (1,4). In the subgroup of heart transplant recipients, skin disease is the most common clinical manifestation, followed by pulmonary and disseminated disease; *M. kansasii, M. avium* complex, and *M. haemophilum* infections are most frequently encountered (1,5).

M. genavense causes up to 12.8% of all nontuberculous mycobacteria infections in AIDS patients; these infections are clinically similar to those caused by the *M. avium* complex (1,6).
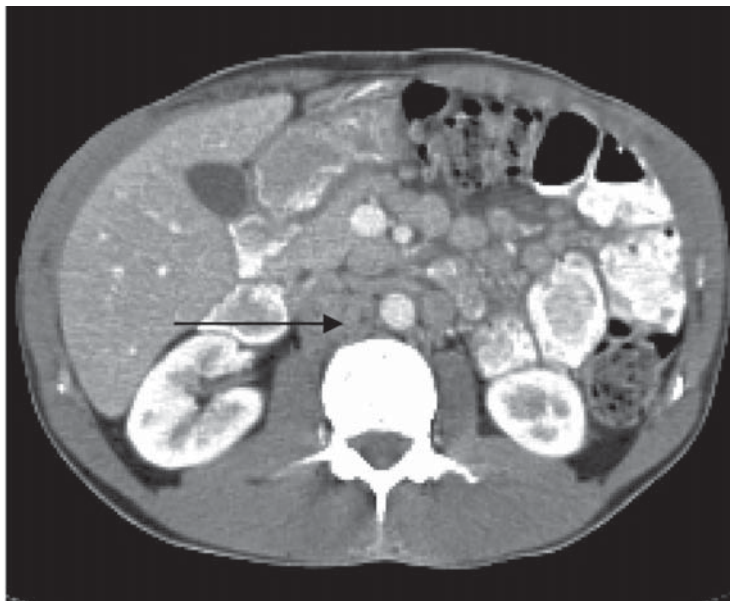

Figure. Initial computed tomographic scan of the abdomen, performed after intravenous injection of contrast dye, showing numerous enlarged para-aortic lymph nodes (arrow).