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CORRESPONDENCE

Diagnosis of *Kingella kingae* Arthritis by Polymerase Chain Reaction Analysis

SIR—We read with interest the report by Stähelin et al. [1] that describes the diagnosis of septic arthritis caused by *Kingella kingae* by amplification of constant regions of parts of a gene coding for 16S rRNA, followed by direct sequencing of the amplicon. Although conventional culture of synovial fluid was negative, the young age of the patient, benign clinical course, and prompt and complete recovery with antimicrobial therapy are compatible with invasive infection caused by *K. kingae* [2]. This gram-negative bacterium was traditionally considered a rare cause of human infection. In recent years, inoculation of synovial fluid specimens from children younger than 2 years of age who had arthritis into BACTEC (Becton Dickinson, Sparks, MD) blood culture bottles resulted in improved isolation of the organism, which appears to be a common cause of joint infection in this age group [2]. In our experience, despite routine inoculation of synovial fluid samples into blood culture media, about one-third of these cultures remain negative, indicating that alternative approaches based on strategies other than culture should be attempted for patients with suspected joint infections. The approach described by the Stähelin et al. is potentially capable of detecting minute amounts of foreign DNA. At present on the basis of our knowledge, however, detection of bacterial DNA sequences should not be considered irrefutable evidence of a specific bacterial etiology.

In a recent study by Soderlund et al. [3], DNA from human parvovirus B19 was found in 28% of synovial tissue specimens from children with chronic arthropathy. However, an even higher fraction (48%) of tests performed for the control group was also positive. In a second study by Dagan et al. [4], the clinical relevance of PCR detection of pneumococcal DNA in serum samples from children was studied. Serum specimens from all 13 patients with culture-proven invasive pneumococcal infections (bacteremia or meningitis) were positive. Serum samples from 16 (32%) of 50 healthy infants and children who carried pneumococci in the nasopharynx and 8 (15%) of 52 children in whom the organism could not be demonstrated in the respiratory tract were also positive. These results suggest that DNA from colonizing or persisting organisms may be detected in normally sterile body fluids in the absence of clinical disease when exquisitely sensitive techniques are used.

We have shown that *K. kingae* is also carried in the oropharynx by up to 50% of healthy infants and toddlers attending a day care center and that, similar to pneumococcus, the age associated with the peak carriage rate coincides with that associated with invasive infection [2]. It seems then rational that in the absence of isolation of *K. kingae*, the significance of detecting specific DNA from the organism should be validated before a positive result can be considered evidence of infection. A suitable control group should be tested to determine the specificity of the procedure. Obviously, performance of joint taps on healthy children is ethically unacceptable. We suggest that synovial fluid specimens obtained from young children with culture-proven septic arthritis caused by organisms other than *K. kingae* may constitute appropriate controls. Failure to detect DNA sequences specific to *K. kingae* in these controls will support the usefulness of PCR amplification and sequencing for solving the diagnostic dilemma of "culture-negative" septic arthritis.

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Clinical Infectious Diseases 1999;29:704
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1058–4838/99/2903–0053$03.00

Reply

SIR—We fully agree with Yagupsky that the presence of bacterial DNA does not necessarily reflect a causative role of the particular organism found. This view was nicely illustrated in the studies of Dagan et al. [1], who found pneumococcal DNA in serum samples from healthy children with and without culture-proven pneumococcal infection in the nasopharynx, and Söderlund et al. [2], who found human parvovirus DNA in synovial membrane (but not synovial fluid) samples from both patients with chronic arthropathy and controls. Nevertheless, there is compelling evidence that *Kingella kingae* was indeed the causative agent in the patient we described [3]. The overall clinical picture was compatible with infection by *K. kingae*, which is often difficult to isolate from joint fluid [4]. Furthermore, the broad-spectrum PCR approach used is not "exquisitely sensitive" as implied by Yagupsky, which is mainly due to the fact that a relatively large DNA fragment (~800 bp) is amplified, resulting in sensitivity lower than that of species-specific PCR systems.

According to our own unpublished findings of patients with Lyme borreliosis, broad-spectrum PCR analysis revealed DNA in only one of six synovial fluid specimens containing *Borrelia*-specific DNA, as shown by species-specific PCR analysis with use of bacterial DNA from the flagellin gene. Consequently, a relatively high number of organisms must have been present in our

patient's joint fluid. Furthermore, with this methodology, other bacterial DNA would be detected if they were present in sufficient amounts, further supporting our conclusion that *K. kingae* (and not another bacterium) was the cause of infection.

The study proposed by Yagupsky in which children with culture-proven septic arthritis caused by organisms other than *K. kingae* would be the controls could not be carried out as such. Broad-spectrum PCR analysis would fail to detect *K. kingae* because of the presence of other organisms. In addition, the significantly higher sensitivity of a putative *Kingella*-specific PCR system would invalidate a comparison with the broad-spectrum system that we use.

In summary, we are convinced that our initial judgement of the patient was correct and that broad-spectrum PCR analysis is a powerful tool for the detection of bacteria in specimens obtained from sterile body sites when cultures remain negative.

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Clinical Infectious Diseases 1999;29:704–5
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1058–4838/99/2903–0054$03.00

Disseminated Toxoplasmosis After Liver Transplantation

SIR—I read with interest the article *Disseminated Toxoplasmosis After Liver Transplantation* by Lappalainen et al. [1]. In their article, Lappalainen et al. present the case of a patient who died of disseminated toxoplasmosis following liver transplantation and review reports of similar cases in the literature. As evidenced by their review of the literature, toxoplasmosis is rare following liver transplantation. Despite this rarity, they recommend that liver transplant candidates undergo screening for antibodies specific to *Toxoplasma*, a procedure that is not routinely performed in most liver transplantation programs. Instead, in liver transplantation programs such as ours, pretransplantation serum samples from donors and recipients are stored for future analysis and, thus, are readily available to test for antibodies to such agents as *Toxoplasma gondii* if needed.

Many liver transplantation programs employ trimethoprim-sulfamethoxazole as prophylaxis for *Pneumocystis carinii* infection. At the Mayo Clinic (Rochester, MN), for example, we routinely administer trimethoprim-sulfamethoxazole at a dosage of one single-strength tablet daily for the first 6 months following liver transplantation. There are little published data to support the efficacy of this regimen in preventing *T. gondii* infection in liver transplant recipients. However, on the basis of experience with patients with AIDS in whom trimethoprim-sulfamethoxazole has been shown to be effective in preventing toxoplasmic encephalitis and the experience with *T. gondii* serologically mismatched heart transplant recipients in whom trimethoprim-sulfamethoxazole as prophylaxis for *P. carinii* infection also prevents primary toxoplasmosis, the prophylactic efficacy of trimethoprim-sulfamethoxazole for *T. gondii* infection in liver transplant recipients can be inferred [2–5]. In this regard, the use of prophylactic trimethoprim-sulfamethoxazole targeted primarily at *P. carinii* pneumonia in the patient described by Lappalainen et al. may have prevented the disseminated *T. gondii* infection reported. It is interesting that it is not evident that the other liver transplant recipients with disseminated toxoplasmosis whose cases were summarized by Lappalainen et al. received prophylactic trimethoprim-sulfamethoxazole [6–10].

In conclusion, I would disagree with the recommendation to screen liver transplant candidates for toxoplasma-specific antibodies. Although trimethoprim-sulfamethoxazole is not recommended solely as prophylaxis for *T. gondii* infection in liver transplant recipients, its use as a prophylactic agent for *P. carinii* infection may simultaneously prevent *T. gondii* disease.

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