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The Authors' Reply

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Our recent study showed that the contagious nature of *Pneumocystis jirovecii* allows development of outbreaks of *Pneumocystis* pneumonia (PCP) in immunosuppressed kidney transplant recipients without prophylaxis. Although short-term prophylaxis at developing of PCP is effective in controlling transient outbreak, recurrence of PCP outbreak may arise under free anti-*Pneumocystis* regimens. We asserted that implementation of lifelong prophylaxis is required for prevention of repeated PCP outbreak in kidney transplant recipients.[1]

A recent Letter to the Editor by Momoko Kono, MD, et al: "A case of a *Pneumocystis* pneumonia twenty-four years after living kidney transplantation due to withdrawal of Sulfamethoxazole/Trimethoprim prophylaxis" supports our study.[2]

Guidelines for kidney transplant recipients recommend anti-*Pneumocystis* prophylaxis for all recipients for at least 6 to 12 months posttransplant. However, this is only directed to protect individuals against PCP infection soon after transplantation, but not for long-term prevention of PCP outbreak. Because kidney transplant recipients account for the largest proportion of organ transplant recipients, they are at high risk of exposing each other through their contact in the outpatient clinic. Once a patient developed PCP in these populations, who are taking standard immunosuppression, an outbreak of PCP may easily occur. Although a 3-month prophylaxis provided to all recipients (universal short-term prophylaxis) is sufficient to control the outbreak, intermittent new PCP outbreaks caused by different genotypes are not prevented in our experience.[1]

There are 3 ways of acquiring PCP: (1) via direct transmission from patients with active PCP, (2) from asymptomatic carriers, or from (3) environmental exposure.

P. jirovecii is currently classified as a fungus, not a protozoan. Because a culture system for *P. jirovecii* in vitro has not yet been established, the life cycle of *P. jirovecii* remains poorly defined. *Pneumocystis* organisms differ depending on mammalian species, so that strains from one host mammal do not transmit to a different one. Reports of evidence for the cysts as the agent of transmission of *P. jirovecii* have also been shown by aerial route from host to host in mice.[3,4] Accordingly, the reasons for emergence of PCP among immunocompromised host can be explained by the reactivation developing from de novo infection or reinfection with different genotypes. In PCP lungs, trophic forms are the most abundant, whereas cysts which are detected in the bronchial lumen may be the major form through colonization.

Trimethoprim-sulfamethoxazole (TMP-SMX) remains the first drug of choice for PCP prophylaxis, as well as for treatment. The TMP-SMX is an antiprotozoal agent, not meant to target fungus, but is highly effective for PCP (trophic forms) treatment. Unlike trophic forms, as cysts are not sensitive to TMP-SMX, colonies of *P. jirovecii* in the bronchial lumen cannot be eliminated. Macrophages which are phagocytic immune cells have a function for clearance of activated *P. jirovecii*, but those in kidney transplant recipients are basically suppressed. Thus, susceptible kidney transplant patients are ready to import any genotypes of *P. jirovecii* that they are exposed to in the outpatient clinic.

Although short-term administration of TMP-SMX effectively blocks the onset of PCP which changes from cysts to trophic forms, it is impossible to eradicate the nest of *P. jirovecii*. Therefore, lifelong administration could be approved to protect recipients from PCP outbreaks by different genotypes in a transplant facility where many immunosuppressed patients visit.

Previously, we experienced repeated outbreaks of PCP in the past decade, but no PCP outbreaks have been observed over a 40-month period after a lifelong prophylaxis strategy was adopted in our kidney transplant center.

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