



## Deactivation of Palacos R Bone Cement with the Addition of Rifampin Antibiotic Powder An In-Vivo Experience

### -Case Report-

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Use of antimicrobial impregnated polymethylmethacrylate (PMMA) bone cement in the treatment of orthopaedic infections is widely accepted.<sup>1</sup> Antibiotic powder is routinely added to PMMA, and formed into beads or spacers when treating infected bone or periprosthetic infections. Antibiotics placed into the PMMA elute via a water diffusion process.<sup>2</sup> This results in high local doses of the antimicrobial agent with reduced systemic toxicity.<sup>3</sup> Two stage reimplantation protocols utilizing antibiotic loaded PMMA cement generally provide the highest rates of successful treatment.<sup>4,5</sup> With the increasing number of resistant organisms, success of this treatment protocol requires antimicrobial therapy targeted at the specific organism found. There exists a great deal of data on the use of certain antimicrobial agents in PMMA cement.<sup>1,6,7</sup> However, there are few published reports of the addition of rifampin. This is the first clinical report on the failure of Palacos® R cement (Heraeus Kulzer GmbH, Wehrheim, Germany) to set when rifampin is added.

### Case Report:

A 67 year old female was treated for a recalcitrant infection involving her left total knee arthroplasty (TKA). Her primary TKA was resected. An antibiotic spacer was not placed. At resection, cultures were positive for atypical mycobacterium and coagulase negative staphylococcus. Risk factors for infection included insulin dependent diabetes, obesity (body mass index 44.3) with chronic

thalassemia.<sup>5</sup> Before reimplantation, multiple aspirations of the left knee were negative. Multiple c-reactive protein measurements were normal and clinical exam of the knee was benign. At reimplantation, the left knee was re-debrided and reconstructed with a constrained non-hinged knee implant system. The components were cemented in a serial fashion, starting with the tibia. For reimplantation, we mixed 600 milligrams (mg) of rifampin (Bedford Laboratories, Bedford, Ohio) with each bag of Palacos® R cement. The cement turned a dark violet-brown color. The cement was inserted with an injection gun, and the tibial component was implanted. After 35 minutes, the cement was still doughy in texture and the tibial implant was extracted. The cement was easily removed from the bone and prosthesis. The implant was reinserted employing 1 gram vancomycin per bag of Palacos® R cement, which hardened in a typical fashion. All reimplantation cultures were negative. The patient remains free of infection at three year follow up.

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A follow up study was conducted in the operating room. Under constant temperature and humidity, two preparations of Palacos® R cement were evaluated for time to hardening. One bag was mixed with 600 mg of rifampin, with the other used as an unaltered control. These were mixed for approximately one minute, and injected five minutes apart into two sterile emesis basins. Separate mixing bowls and injection guns were used to prevent cross contamination. Evaluation consisted of probing the cement with sterile tonsil forceps to judge the consistency of the cement. The plain Palacos® R cement was evaluated every minute for the first 10 minutes, then every 15 seconds until set. It achieved a non-stick doughy consistency at 5 minutes, firm rubbery consistency at 10 minutes, and set completely at 13.5 minutes. The Palacos® R with rifampin was evaluated every minute for the first 10 minutes, then in increasing intervals after it was evident that there was little progress towards setting. It achieved a non-stick doughy consistency at 5 minutes, a semi-firm surface with spongy interior at 30 minutes, and a firm rubbery consistency at 5 days (fig 1). The cement remained in a firm rubbery state when checked every 5 days up to 30 days. The cement never completely hardened.



Fig 1a. Sample of Palacos® R-rifampin as it appears after five days of curing. Its outer crust of 0.5 mm feels firm, but can be easily indented.

## Discussion:

Use of antibiotic impregnated PMMA bone cement is an important treatment method for orthopaedic infections.

Infection caused by microorganisms with antimicrobial resistance is increasingly common, and has resulted in the addition of various antibiotics mixtures to bone cement. There is limited guidance for surgeons when using novel combinations, and scant literature regarding the addition of rifampin to PMMA bone cement. One study briefly mentions a resulting tarry composite that took several days to set, but does not describe the type of cement used or the testing method.<sup>4</sup> Another study states only that rifampin is adversely affected by cement curing.<sup>8</sup> Another recent study reports that complete curing was prevented when rifampin was added to Simplex P™ cement.<sup>3</sup> However, this report was not available at the time of this case. None of these studies elaborate on the potential mechanism by which polymerization is affected.

PMMA polymerization is initiated by the reaction of two agents, dibenzoyl peroxide (BPO) in the powder and dimethyl-p-toluidine (DmpT) in the liquid monomer. Although the mechanism of inhibition of this process is not known, rifampin has been described as a scavenger of reactive oxygen species.<sup>9</sup> We propose that the rifampin reacts with the BPO and/or DmpT to become oxidized rifampin. The initiators are then unable to react with the methyl methacrylate and radical polymerization is inhibited. This results in failure of the cement to set.

Considering this limited experience, we recommend rifampin not be added to PMMA when bone cement is to be used for structural, long term fixation. However, we would consider its use in temporary nonstructural PMMA spacers (beads as opposed to cement blocks) if absolutely needed. Beforehand, a follow up elution study should be performed to confirm that an active rifampin agent is available for antibacterial action. Finally, we recommend caution when adding any antibiotic to PMMA that act as a reactive oxygen species scavenger to avoid similar difficulties with cement curing.

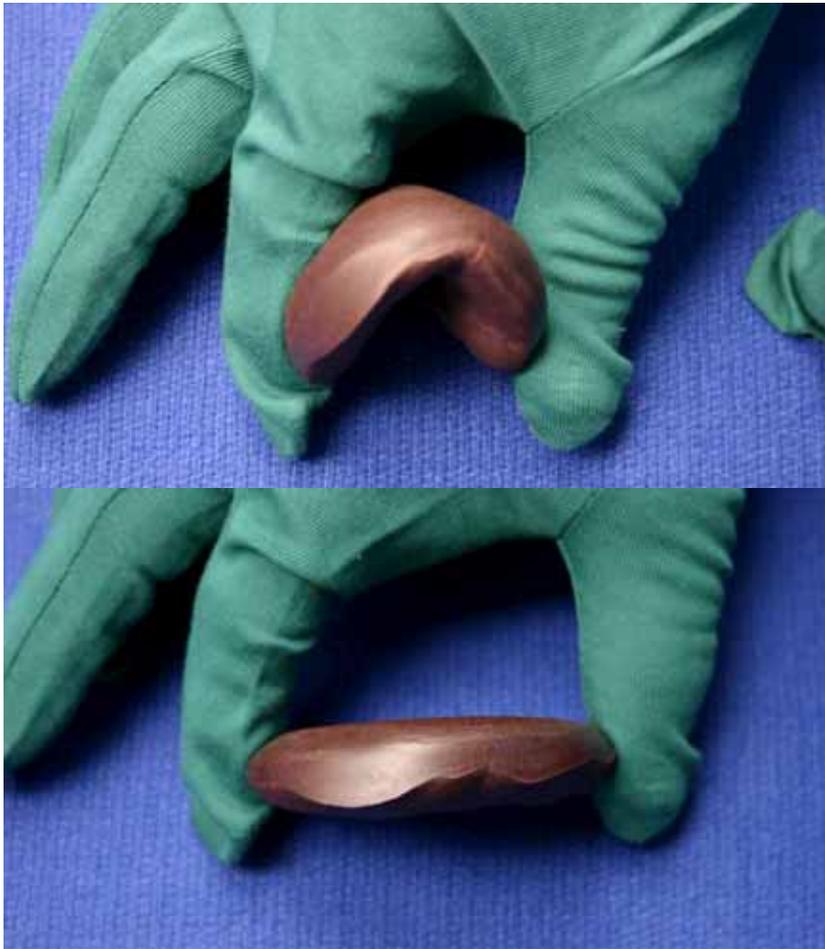
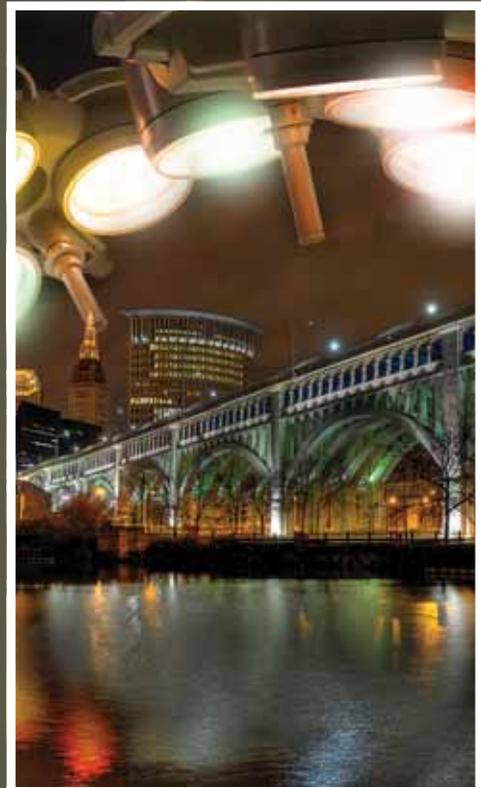


Fig 1b. Same sample of Palacos® R-rifampin showing how the cement puck easily bends without breaking. Once bending force is released, the specimen returns to its resting flat state.

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