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Photoactive dye could prevent infection during bone-repair surgery

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Despite extensive procedures to sterilize small and large bone fragments used in joint replacement or reconstructive surgeries, the rate of infection remains around 5 percent and can reach 11 percent or even higher in bone repairs for gunshot wounds or reconstruction after tumor removal. Infection after surgery is a serious complication that can require further surgery and can be life threatening. A new study demonstrates for the first time that an antimicrobial dye activated by light avidly adheres to bone to prevent bacteria from growing on bone fragments used in reconstructive surgery, and remove any bacteria that has already attached, thereby sterilizing the bone for surgery. The study was published online April 17 ahead of print in the journal of *Clinical Orthopaedics and Related Research*.

"We used a class of chemicals called porphyrins that are tolerated very well by the body in the dark and appear to have excellent antimicrobial properties in the presence of light," says Noreen Hickok, Ph.D., Associate Professor of Orthopedic Surgery at Thomas Jefferson University. "These properties allow sterilization during surgical procedures, which occur in bright light."

Surgeons often use bone chips or bone powder as a sort of putty during bone reconstruction to help areas of bone re-grow. Also, larger pieces of bone are used all over the world when a tumor or accident requires replacement of a large segment of bone. These bone materials can come either from the patient or a donor and are typically sterilized with a series of methods including various detergents and high pressure steam

sterilization. But bacteria can still creep in once the material is handled again. "Bacteria really love to hide and grow in the nooks and crannies of porous bone and bone fragments - it's one of the most perfect surfaces for bacterial growth," says Dr. Hickok.

The researchers took these bone chips and treated them with a green dye called TAPP (which stands for 5,10,15,20-tetrakis-(4-aminophenyl)-porphyrin). They showed that in the dark, TAPP is stable. But when the lights go on, TAPP becomes active, producing chemicals called reactive oxygen species, or ROS, that rapidly kill the bacteria. Dr. Hickok and colleagues first treated the bone putty with TAPP and then exposed those fragments to bacteria. As long as the lights were on, bacteria was unable to attach and grow on the surface of the bone.

The researchers then showed that TAPP not only prevents bacterial growth, but can also break up bacterial slime, or biofilms, already growing on the bone fragments. They demonstrated this by first allowing bacteria to colonize the bone and then treating with TAPP. Finally, Dr. Hickok and colleagues showed that the dye binds tightly to the bone, without any trace of leaching out into surrounding fluid, suggesting that it could be safe and non-toxic to normal tissue once implanted.

In theory, says Dr. Hickok, the TAPP dye could be added to the currently used protocols for sterilizing the bone prior to use in surgery. "Sterilization could then occur in two steps—one which was achieved with a targeted illumination, and the other would be the continuation of the activation in the bright lights of the surgical suite so that the sterilizing effects of the ROS release could continue well into surgery and implantation," says Dr. Hickok. "We need to continue testing in conditions that more closely resemble the surgical suite, but we think that this method could offer a more effective method to help improve patient outcomes by reducing infection rates."

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