

# **Cutibacterium acnes (formerly Propionibacterium acnes) and Shoulder Surgery**

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## **Abstract**

Infection is a rare but serious complication of shoulder arthroplasty. The most prevalent cause of patient infections is *Cutibacterium acnes* (formerly *Propionibacterium acnes*), a commensal skin bacterial species. Its presentation is often non-specific and can occur long after shoulder arthroplasty, leading to delay in diagnosis. This bacterium is difficult to culture, typically taking 14 to 17 days for a positive culture and often does not exhibit abnormal results on a standard laboratory workup for infection (eg, ESR, CRP, and synovial WBC count). Male patients are at particularly high-risk due to having a greater number of sebaceous follicles than females. While it is difficult to diagnose, early diagnosis can lead to decreased morbidity, appropriate treatment, and improved clinical outcomes. Current options for treatment include antibiotics, one stage implant exchange, or two stage implant exchange, although success rates of each are not currently well described. A better understanding of the prevention, diagnosis, and treatment of *C. acnes* infection could lead to better patient outcomes from shoulder arthroplasty.

## **Keywords**

*Cutibacterium acnes*, *Propionibacterium acnes*, surgical site infection, shoulder surgery

## **Introduction**

Infection after shoulder surgery is a rare but potentially catastrophic complication. Patients that develop postoperative wound infections are 60% more likely to spend time in the intensive care unit and experience twice the mortality rate.<sup>1</sup> Synovial joints are at risk for infection given both their relative absence of immune cells and the presence of nutrient-rich synovial fluid. Several species of commensal bacteria are known to cause the majority of shoulder infections. These include *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Cutibacterium acnes* (formerly *Propionibacterium acnes*).<sup>2</sup>

Recently, it has been noted that the common pathogen in shoulder infection post-arthroplasty is *Cutibacterium acnes*.<sup>3</sup> *C. acnes* infection is also associated with arthroscopy, fracture fixation, injections, cuff repair, and Latarjet procedures.<sup>4</sup> *C. acnes* is a gram-positive, anaerobic bacteria that normally occupies the hair follicles and sebaceous glands and colonizes the shoulder at increased rates compared to the knee and hip.<sup>5,6</sup> Earlier studies reported a rate of *C. acnes* infection after shoulder arthroplasty presenting as a classical periprosthetic infection of 0%-15% of patients, but these studies recognized that this have been an underestimate of the true rate, as diagnosis of *C. acnes* can be difficult and unreliable.<sup>7</sup> More recent studies, usually with

longer durations of culture, have been positive at higher levels for *C. acnes* at the time of revision ranging from 16% to 70%<sup>4,7,8</sup> with the most common estimates around 50%-60%.<sup>4,8,9</sup> In one study, the total infection rate was 1.9% with 89% caused by *C. acnes*.<sup>10</sup> Similarly, in a study of deep infection after rotator cuff injury, *C. acnes* was found to be the most prevalent cause of infection, causing 51% of the post-surgical infection cases.<sup>11</sup>

## **Cutibacterium acnes Biology**

First described by Paul Gerson Unna in 1865, *C. acnes* is a slow-growing, facultatively anaerobic, non-spore forming gram-positive rod-shaped bacterium.<sup>12</sup> *C. acnes* is part of the normal flora of the skin, oral cavity, gastrointestinal, and genitourinary tract. There are three proposed sub-types of *C. acnes* (I, II and III).<sup>4</sup> The production of propionic acid from lactose gave this species its prior name, *Propionibacterium*. *C. acnes* has been shown to be implicated in the pathogenesis of endocarditis, endophthalmitis, septic arthritis, osteomyelitis, chronic prostatitis, sarcoidosis, synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome.<sup>13-20</sup>

In healthy skin, *C. acnes* plays a commensal role.<sup>5,21</sup> It outcompetes other bacteria on the skin and colonizes the acidic, anaerobic environment of the sebaceous gland deep in the dermis. Through its digestion of the sebum, it produces free fatty acids which are secreted with the sebum onto the skin. This helps produce an overall acidic pH of the skin, which inhibits pathogenic bacteria such as *Staphylococcus aureus* and *Streptococcus pyogenes*, while favoring other commensal bacteria such as coagulase negative staphylococcus and corynebacteria.

The prevalence and burden of *C. acnes* has been found to be greater in the axilla and acromion than at the hip or knee.<sup>5</sup> The prevalence and burden of *C. acnes* is also greater at the anterior and posterior acromion than the axilla in men, but not women. In general, men also have a greater prevalence and burden of bacteria than females.

Pathophysiologically, *C. acnes* bacteria feed on lipids and triglycerides producing fatty acids as a byproduct, as well as secrete cytotoxic chemicals and enzymes which can degrade the shoulder capsule.<sup>12</sup> *C. acnes* uses antigens to adhere to cells, biofilms, and surfaces, which can initiate an inflammatory response on the inside of the joint.<sup>22,23</sup> *C. acnes* forms biofilms within the body, which aids in micro-colony formation, evasion

of macrophage engulfment, avoidance of phagocytosis.<sup>9,22</sup> *C. acnes* may persist within macrophages for up to 8 months in vitro. Over half of *C. acnes* cultures now carry resistance to more than one antibiotic.<sup>24</sup>

### **Cutibacterium acnes Clinical Characteristics**

*C. acnes* infection increases the risk of needing revision surgery, morbidity and mortality. The total cost to treat an infected shoulder prosthesis has been estimated at \$46,745.<sup>25</sup> Surgical debridement is often not sufficient alone to eliminate *C. acnes* infection and excess scar tissue from repeated surgery can lead to less functional outcomes.<sup>2,26</sup> It is important to note that *C. acnes* infections do not typically elicit typical host inflammatory responses. Classic signs of swelling, erythema, drainage, tenderness, and sinus tract are less common. Rather, common presentations include unexplained pain, stiffness, and component loosening after an initially good outcome and the usual period for acute postoperative infection has passed. *C. acnes* may not present symptoms for two years or more post operatively. Good recovery of function and pain control followed by increase in pain and stiffness suggest *C. acnes*, particularly in males.<sup>24</sup> A number of studies have pointed to *C. acnes* infection as a possible cause of prosthetic loosening.<sup>27,28</sup> In established *C. acnes* infections involving a prosthesis, exchange of the prosthesis may yield the best clinical outcome.<sup>6</sup>

*C. acnes* may enter the surgical field via surgical incision through the pilosebaceous glands in the deeper layers of the skin.<sup>29,32</sup> There has been no difference found in bacterial colonization for different types of pre-operative preparation including ChlorPrep (2% chlorhexidine gluconate and 70% isopropyl alcohol; Enturia, El Paso, Texas), DuraPrep (0.7% iodophor and 74% isopropyl alcohol; 3M Healthcare), or providone-iodine scrub and paint, (0.75% iodine scrub and 1.0% iodine paint; Tyco Healthcare Group, Mansfield, Massachusetts).<sup>29-31</sup> Using a rigorous technique, Koh et al.<sup>30</sup> demonstrated that use of 4% chlorhexidine gluconate showers only reduced the skin culture positivity rate to 40%, and even after the ChlorPrep had dried the skin positivity rate for *C. acnes* was 27%. At the end of the case, the skin culture positivity rate rose again to 43%.

Risk factors for *C. acnes* infection include male gender and surgery including a prosthesis or for treatment of trauma.<sup>24</sup> Other factors in the development of *C. acnes* infections include the suitability of the joint for infection, the size of the bacterial inoculum, the patient's immune response to the bacterium, and the relative proportion of pathogenic strains.<sup>4</sup>

Early treatment is important in treating *C. acnes* infection, even though it may not show symptoms for three or more years as it establishes a biofilm which is much more resistant to antibiotic therapy.<sup>3</sup> Unfortunately, there is no established antibiotic regimen for treating *C. acnes* infection and consultation with an infectious disease specialist is recommended.<sup>11,33</sup>

### **Cutibacterium acnes Testing**

Serological testing for infection may be unhelpful in laboratory evaluation for *C. acnes* infection—typical inflammatory markers, such as CRP and ESR, tend to be low or borderline while white blood cell count may be within normal limits.<sup>34</sup> Traditionally, *C. acnes* was cultured with a tissue swab under anaerobic conditions and held for up to 7 days. It has been noted that this method is insufficient to rule out *C. acnes* infection, however.<sup>7</sup>

Matsen, et al,<sup>4,35</sup> propose that testing for *C. acnes* in a failed shoulder should include more than 5 cultures including tissue and explant, sonication of explant, collection of revision specimens prior to antibiotics, sending cultures on both aerobic and anaerobic media, and holding the specimens for 17 days.

Intraoperatively, signs of inflammation are not usually seen. In some cases, cloudy fluid, osteolysis, a periprosthetic membrane, and component loosening may be present and are associated with increased likelihood of positive cultures, but absence does not preclude infection.<sup>35</sup> Frozen section has poor sensitivity for infection in cases of *C. acnes*.

A new, more sensitive technique involves using PCR.<sup>36</sup> This method utilizes restriction fragment length polymorphisms to create a clinically relevant assay that can detect *C. acnes* more easily, although controlling for false positives must be carried out carefully.<sup>36</sup> This new method only requires 24 hours and can be carried out in the average pathology laboratory. As a PCR based assay, it can detect as few as ten *C. acnes* cells when it was tested in an artificial tissue system.

### **Controversy: Cutibacterium acnes and Arthritis**

There are a number of controversies remaining in this field, including some questioning if *C. acnes* is present intraarticularly prior to surgery and if *C. acnes* may be responsible for some cases of arthritis.<sup>37</sup> However, when carefully controlled for contamination, a cause and effect relationship between *C. acnes* and osteoarthritis was not supported in a separate study.<sup>38</sup> Further study has found the bacteria only in skin tissue and not in the deeper tissues such as the rotator cuff and glenohumeral cartilage.<sup>39</sup> This suggests the bacterium is a contaminant from the skin during surgery. Whether the data support a link between *C. acnes* and arthritis is still an area that requires more investigation.

### **Recent Developments and Future Directions**

A number of strategies have been proposed as potential techniques to minimize infection and manage these infections. It has been suggested that a second change of gloves for the surgeon and re-draping, use of a skin barrier, along with hair

removal by electric clippers or depilatories, could reduce *C. acnes* infection.<sup>2,10,40</sup> Another preventative method being utilized is the application of vancomycin powder during shoulder arthroplasty to prevent *C. acnes* infection.<sup>25</sup> This was found to be highly cost effective. Another technique under development is the disruption of the *C. acnes* biofilm by using calcium sulfate cement beads loaded with tobramycin, vancomycin, or a combination of the two to deliver high local concentrations of antibiotic; so far testing has only been in vitro.<sup>3</sup> This was noted to be effective in eliminating both planktonic organisms and biofilms. Point-of-care testing could lead to improved outcomes for patients by informing decisions while still in the operating room. Changes in interleukin-6 (IL-6) levels, leukocyte esterase, and alpha-defensin are being investigated for correlation to *C. acnes* infection, although sensitivity and specificity have been lower.<sup>41-45</sup> More recently, topical benzoyl peroxide has been investigated as a preventative agent for *C. acnes*.<sup>46-48</sup> Presurgical treatment with topical benzoyl peroxide was found to be more effective than chlorhexidine gluconate in decreasing the skin burden of *C. acnes*, but was unable to completely eradicate it in any study.

## Conflicts of Interest

None of the authors identify any conflicts of interest.

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