

RECOMMENDATIONS FOR TREATMENT OF EXIT -SITE P A THOLOGY

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Detailed evaluations of over 800 healing or healed exit sites of peritoneal accesses resulted in our identification of seven categories of exit appearances. These can be combined into two broad types of exit sites: healthy (healing or healed) and pathological (1-6). The skin color around a healthy exit site was either natural or dark/pale pink with a diameter less than 13 mm. Its sinus tract epithelium was partly or completely keratinized (strong and mature epidermis). The unkeratinized part of the sinus tract was either covered with a fragile mucosal epithelium or devoid of any epithelium exposing the plain granulation tissue. The visible sinus tract might be dry or moist with a minute amount of thick drainage, which on shedding and drying was evident as specks of crust on the dressing. When a healthy exit site was at least 6 months old and its entire visible length of sinus tract covered with the keratinized epithelium, it was termed "perfect." Otherwise, it was classified as "good." A healthy exit site had none of the features of acute or chronic infection.

A pathological exit site had either clear or equivocal evidence of infection. An obvious infection could be either acute or chronic. An acutely infected exit site could be painful, swollen, and red with erythema greater than 13 mm in diameter. Exuberant granulation tissue, which bled easily upon touch, was visible around the exit and/or in the visible sinus where the epithelium had receded. The external drainage was purulent and/or bloody. The infection was termed chronic when it persisted more than 4 weeks. The signs of acute infection

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(such as pain, redness, and swelling) were absent unless acute exacerbation accompanied chronic infection.

Infection of the external cuff indicates a chronic infection that is focused primarily in and around the cuff. The visible sinus and the exit site often appeared normal and showed evidence of chronic infection intermittently. Goopy/gluey drainage (i.e., extremely sticky, viscous, thick, and partially dried) was a feature unique to this condition.

During the early stages or the recovery phase of an acute infection, the signs were minimal. External drainage could be evident only on squeezing the sinus tract. The equivocal signs made it difficult to ascertain a diagnosis with certainty. If left untreated, these infections progressed to acute infections. These were called "equivocal exit sites."

HEALING EXIT SITES

It is important to be aware of some features of a healing healthy exit site that could be misinterpreted as indications of an acute infection. For example, it is normal for the patient to experience exit pain immediately following catheter insertion. The pain abates quickly, but slight tenderness may persist for 2 or 3 weeks. Serosanguineous, bloody, or serous drainage may be copious in the beginning; however, it should diminish gradually and cease altogether by week 3. Such drainage is visible both externally and in the sinus. Similarly, scab formation stops completely by the third to fourth week. Swelling around the exit subsides by the first week. The lining of the sinus is devoid of any epithelium and appears white during the first week. With the development of granulation tissue and formation of new vessels, the sinus color changes to pinkish white or pink by week 2. Exceptionally, the sinus color may remain white for up to 6 weeks. The epithelium begins to appear in the sinus by week 2 and may cover over half of the sinus by the sixth week. Wrinkling of the sinus surface suggests the presence of epithelium.

A healing exit-site infection may differ from a mature exit-site infection. In contrast to a healed exit, equivocal signs of infection in a healing exit are a clear indication of infection and should be treated aggressively. The first sign of infection is the cessation of healing, and this is indicated by halting or regression of sinus epithelialization. Change in the character of drainage to purulent and/or the presence of granulation tissue is an early indication of acute infection in a healing exit site. Evidence of infection may be localized in the sinus only. Epithelialization of the sinus ceases to progress or regresses.

It is pertinent to review some principles of early exit care here. Healthy exits are more likely to be colonized by Gram-positive than Gram-negative bacteria. Good hemostasis and irrigation of the wound prior to closure are essential in order to minimize hematoma formation. A systemic antibiotic, preferably with broad coverage, is preferred to topical therapy during the early postimplantation period for both prophylaxis and acute infection. The copious drainage from the exit during the early postimplantation period would wash out topical antibiotics. Catheter immobilization is of great importance to promote uninterrupted healing. To promote free drainage from the sinus, it is best to avoid occlusive dressings; instead, use several layers of high-absorbency gauze. By minimizing dressing changes to once a week, the catheter is kept immobilized and the exit is protected from bacterial contamination. The skin surrounding the exit and the sinus should be cleansed with a nonirritating solution such as a nonionic surfactant. At bacteriocidal concentrations, the usual disinfectant solutions are cytotoxic to mammalian cells and granulation tissue. Monitoring the healing process for about 6 weeks is an important step in the care of healing exit sites. Slow healing or complete cessation of healing is an early indication of infection. Even equivocal signs of an infection should prompt aggressive treatment.

The recommendations for the care of healthy exit sites are given in the accompanying paper (7). This section describes management recommendations of pathological exit sites.

ACUTELY INFECTED EXIT SITE

It is essential to culture and to perform sensitivity testing on exudate from the infected exit site. This step is important for several reasons:

1. Culturing allows the organism(s) responsible for infection to be identified.
2. Sensitivity testing facilitates the selection of a specific antibiotic to treat the identified organism.
3. Identifying the organism may provide clues to the source(s) of infection.

Several studies suggest that recurrent *Staphylococcus aureus* exit-site infection and nasal carriage state have a cause-and-effect association (8-16). In several studies the strains in nares and exits were found to be identical in a high percentage of patients. By restriction endonuclease subtyping, Pignatari *et al.* (13) showed that 95% of patients with both nasal and pericatheter colonization were colonized with the same subtypes at both sites. Brown *et al.* (17), using three typing methods, found very low agreement among strains of coagulase-negative staphylococci recovered from hands, exit site, and dialysate. In yet another study (16), by antibiotic profiles, there was only 21% agreement between the micro-organism cultured from nares and washouts from the sinus tract of the catheter tunnel. A significantly better, 49% agreement, was found between the organism cultured from sinus washouts and the pericatheter abdominal wall (16). These results indicate that it is important to take a culture swab from the drainage coming from the sinus tract without touching the skin around the exit site.

The patient should begin a course of systemic antibiotics as soon as a clinical diagnosis of an acute exit-site infection is made. Gram-positive organisms are frequently the cause of exit-site infections. Accordingly, oral cephalosporin was commonly selected as the initial antibiotic, but more recently quinolones have become the initial antibiotic of choice. The antibiotic prescription should be adjusted after the infection-causing organism is identified and the antibiotic sensitivity results are available. The antibiotic is initially prescribed for a period of 7-10 days, the time required to heal (achieve a good appearance) in an uncomplicated acute infection. If there is no improvement after this period, another appropriate antibiotic is substituted or a second synergistic antibiotic is added. Rifampin is frequently used as a second antibiotic for *Staphylococcus aureus* infections. Antibiotic therapy is continued for 7 days after achieving the healthy appearance of an exit.

Conditions that delay healing or make therapy ineffective are cuff and/or tunnel infection, a foreign body in the vicinity (e.g., infected stitch), infection with a resistant organism or virulent pathogens (such as *Staphylococcus aureus*, *Pseudomonas* species, and *Candida*), patient noncompliance, and use of an inappropriate antibiotic.

Exuberant granulation tissue (proud flesh) is cauterized with a silver nitrate stick, a procedure widely used in surgical practice (4,18). No more than one or two applications may be necessary in acute infection. This procedure speeds up the healing process and facilitates epithelialization. Cauterization should be restricted to granulation tissue only, and accidental touching of the adjacent epithelium should be avoided.

Use of a magnifying glass aids in precise cauterization. This can be done safely by a physician or nurse.

Recommendations for the care of infected exit sites are based on sound surgical practices, anecdotal experiences, and survey results. Increasing the frequency of dressing changes to one or two times a day helps the healing process, especially in those with copious drainage. A 1991 survey of 320 centers indicated that 75% of the centers preferred twice daily dressing changes during acute infection (19). Changing the cleansing agent was recommended by 38% of centers in the same survey. An infected exit is covered with a sterile dressing to absorb drainage, protect against trauma, and shield against further inoculation by micro-organisms.

Topical treatments are essentially recommendations based on anecdotal experiences. They include application of soaks to the exit 2-4 times daily as well as the application of dry heat (19-22). Soaking solutions include normal saline, hypertonic saline, sodium hypochlorite, dilute hydrogen peroxide, povidone iodine, and 70% alcohol. Local application of povidone iodine ointment, mupirocin, and Neosporin cream, ointment, or ophthalmic solutions has been recommended. It is our belief that topical antibiotics are of limited value in treating acute or chronic infection with copious drainage because of their inability to achieve high enough local concentrations.

Catheter immobilization is a sound practice. Immobilizing a catheter protects it from accidental trauma. Trauma leads to bleeding, and blood is a good medium in which micro-organisms can multiply. Catheter immobilization should be continued during the acute infection stage or implemented (if not already in practice). Catheter removal is indicated when acute exit-site infection leads to tunnel infection and peritonitis.

PROGNOSIS AND OUTCOME OF THERAPY

Most acute infections respond favorably to therapy (5). An exit site with an acute infection in association with proud flesh and bleeding requires prolonged antibiotic therapy. Association with a positive nasal culture had no influence on the outcome. Recurrent infections that progress to chronic infection and/or cuff infection are associated with a poor prognosis.

CHRONICALLY INFECTED EXIT SITE

The work-up leading to the proper diagnosis of a chronically infected exit site is similar to that performed to diagnose acute infection. Ultrasound examination of the tunnel is a valuable tool in the diagnosis of cuff infection. While positive findings with ultrasound examination help to establish a diagnosis of

tunnel infection, a negative examination does not rule out the existence of an infection. As outlined for acute infection, an antibiotic is started immediately after diagnosis. Once the culture and antibiotic sensitivity results are available, an appropriate antibiotic is chosen. A combination of synergistic antibiotics is preferred to a single agent to avoid emergence of resistant organisms, since the therapy is given over a prolonged period. In chronic infection, the bacterial flora or the antibiotic sensitivity may change during the course of long treatment. Therefore, an unresponsive exit site may have to be cultured repeatedly for timely diagnosis. The response to treatment is usually slow. The features of the chronic infection change very slowly to those of an equivocal exit and then eventually to those of a good exit site. The antibiotic therapy and local care of the exit site are continued until the desired features of a good exit are achieved. In some cases exit features change to equivocal and remain as such for a long time. In such cases the systemic antibiotic may be discontinued, and local care alone is continued.

Local care should include a topical antibiotic. Chronic infection requires cauterization of exuberant granulation tissue more than once. Typically, weekly cauterization for several weeks is necessary. The cauterization is continued as long as the proud flesh persists. The cauterization will discolor the proud flesh from red to gray. Some cases of chronic infection may require long-term (6 months to several years) suppressive doses of a systemic antibiotic. Typically, these cases show reinfection on discontinuing the systemic antibiotic.

Local care is similar to that used in treating acute infection. After achieving the features of an equivocal exit, the frequency of local care may be reduced to once a day. Cuff infection responds to therapy slowly, if at all, and a complete cure is unlikely. Local care has to be given aggressively. Deroofing the sinus tract and cuff shaving have been practiced with some success (23). These procedures serve as temporary measures that merely delay catheter loss. In our experience cuff shaving prolonged catheter life for approximately 6-12 months. These temporary measures may be suitable for patients who are expected to stay on therapy for a short period, for example, patients awaiting transplant. However, cuff infection is a strong indicator for catheter removal in long-term peritoneal dialysis (PD) patients. Delaying catheter removal in these patients amounts to inviting peritonitis (5,24). Lately, catheter removal and replacement are being done in one procedure if there is no active peritonitis. The preliminary experience of combining the two procedures is promising. Anecdotal reports suggest that cuff shaving may provide better results in presternal catheters (25,26). This may be related to the presence of three cuffs and a

long tunnel in the presternal catheter. Shaving of the subcutaneous cuff leaves two cuffs as a double barrier against periluminal bacterial penetration.

OUTCOME AND PROGNOSIS

Most chronic exit-site infections of abdominal catheters, particularly with inadequate treatment, end in peritonitis. The cuff infection is a strong indicator of impending peritonitis. Even aggressive therapy may not cure a chronic infection with cuff involvement, but may prolong the life for a short time. However, this prolongation comes with the risk of peritonitis. Catheter removal in chronic infection with cuff involvement may be individualized based on the patient's expectancy of PD therapy.

EQUIVOCAL EXIT SITE

For all practical purposes, the equivocal exit site is a subclinical form of infection. If left untreated, most equivocal exits will progress to acute infection. Therefore, aggressive management of equivocal exits assumes great importance. Aggressive local care with a topical antibiotic may cure most equivocal exit sites. Exits with external, slightly exuberant granulation tissue, which usually progress to acute infection, require systemic antibiotics. Cauterization of the slightly exuberant granulation tissue in the sinus may be necessary. An acute infection may acquire equivocal features during the recovery phase. Such an exit site warrants less aggressive therapy compared to one with acute infection; discontinuation of the systemic antibiotic and once-a-day local care is continued in such a situation. Local therapy with topical antibiotics is the mainstay of treatment for such an equivocal exit site. A topical antibiotic is chosen based on the exit swab culture results. The topical antibiotics that we have successfully used include mupirocin, Neosporin, and tobramycin. This effectiveness is due to the absence of copious drainage from the sinus tract. Free-flowing drainage in both acute and chronic infections washes away the topically applied antibiotic. Systemic antibiotic may be used in cases unresponsive to topical therapy.

PROGNOSIS AND

OUTCOME

If untreated, most equivocal exit sites will progress to acute infections. Response to therapy is excellent, with cure occurring in almost all instances.

MANAGEMENT OF TRAUMATIZED EXIT

SITE

Trauma with bleeding at the exit site may occur in a healthy exit as a result of an accident. Such events

are rare. A healing exit may be traumatized by movements (i.e., turning from side to side, twisting), pressure, and by catheter manipulations. Such trauma with minute bleeding may be the inciting factor for infection in a healing exit site. Therefore, prevention of trauma at a healing exit site is the most important step in the care of a healing exit site. Immobilization is essential for trauma prevention.

The features of a traumatized exit are pain, bleeding, and distorted exit appearance. Extravasated blood is a good medium for bacterial growth. Bacteria that have colonized the exit multiply rapidly in the presence of decomposing blood and infect the disrupted tissue. Infection may occur as early as 24-48 hours after trauma. The prompt administration of an antibiotic, chosen based on the past history of skin colonization, may prevent acute infection. In the absence of the information about previous skin colonies, an antimicrobial agent sensitive to Gram-positive organisms, such as a cephalosporin or a quinolone, may be chosen. Therapy may have to be continued for about 7 days after achieving a good appearance. Aggressive treatment is necessary in every instance of trauma reported by the patient. Local care requires gentle cleansing of all blood from the exit site.

Bleeding may also occur in an exit that is acutely or chronically infected. The highly vascularized proud flesh bleeds easily on touch. Even a minimal manipulation can initiate bleeding. Therapy for such bleeding has been described in the section dealing with management of infections.

ROLE OF PROPHYLACTIC ANTIBIOTICS IN THE PREVENTION OF EXIT-SITE INFECTIONS

Healthy exit sites usually do not get infected unless traumatized. Therefore, a prophylactic antibiotic is not recommended for healthy exit sites. A prophylactic antibiotic is indicated for the management of accidentally traumatized exits and equivocal exits. The value of such therapy was discussed earlier in this paper.

The other indication for prophylaxis is the chronic infection where discontinuation of systemic antibiotics results in reappearance of the infection. In such a case long-term prophylaxis with a suppressive dose of an antibiotic is useful. In nasal carriers of *Staphylococcus aureus* randomized trials showed decreased infectious complication in patients treated with prophylactic systemic trimethoprim-sulfamethoxazole (15) or rifampin (16). Topical intranasal application of antibiotics against *Staphylococcus aureus* is less likely to prevent exit infection, unless there is a high probability of micro-organism transfer from the nares to the exit on fingers or by other means. Although the role of prophylactic antibiotics

during the healing period has not been established in noncarriers of *Staphylococcus aureus*, the association between early exit colonization and exit infection would indicate that such approach may be beneficial (6).

SUMMARY

Good local care including measures to prevent trauma keeps healthy exit sites free of infection. Acute infection can be cured with aggressive therapy. Chronic infection may progress to cuff infection, which even when treated, may progress to peritonitis. Cuff and tunnel infections require deroofting, cuff shaving, and/or catheter removal. Therapy may prolong the life of a catheter. An equivocal exit site requires aggressive therapy in order to achieve cure. Local care of the exit should include measures to prevent trauma. Should trauma occur, aggressive therapy that includes a systemic antibiotic should be instituted immediately. Aggressive therapy is particularly indicated during the healing period. Prophylactic antibiotics, systemic or topical, are indicated in trauma, recurrent infection, and may be beneficial during the healing period.

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