Current approach to exit-site infections in patients on peritoneal dialysis

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Exit-site case study

John Hershey is a 25-year-old man with ESRD secondary to interstitial nephritis. He has a swan-neck, coiled peritoneal dialysis catheter implanted 10 weeks ago and is doing nightly tidal peritoneal dialysis and still has good residual renal function. A week ago John called his primary nurse at the PD clinic to report ‘I think I hurt my exit site. It is red, and there was some drainage’. A culture of the exit site was taken and the patient was given a prescription for oral ciprofloxacin 500 mg twice daily for 10 days. Mr Hershey was also advised to apply mupirocin ointment to the exit once daily.

Today Mr Hershey has an exit-site assessment as part of a routine clinic visit. He has completed 7 days of antibiotic therapy. There is a small amount of clear drainage on the exit-site dressing. The external exit site (Figure 1) has slightly exuberant granulation tissue from 1 to 3 o’clock and this area looks moist. Some purplish-pink discoloration is seen adjacent to the granulation tissue. The sinus visible in Figure 2 has no epithelium, there is fleshy granulation tissue from 2 to 5 o’clock. It is difficult to differentiate whether the moisture between the granulation tissue and the catheter is drainage or mupirocin ointment. The exit has deteriorated since the trauma, in spite of local and systemic antibiotic therapy. There was no growth on the exit-site culture, 8 days ago. The granulation tissue is cauterized with a silver nitrate stick. Figure 3 shows the whitish-grey appearance of the granulation tissue after cauterization. Mr. Hershey is told to complete the course of ciprofloxacin and continue using mupirocin ointment daily.

One week later Mr. Hershey returns to the clinic for exit-site evaluation. The external exit site (Figure 4) looks good with small crusts and some flaky skin between 12 and 4 o’clock. The sinus (Figure 5) is now partly covered with epithelium; the granulation tissue deeper in the sinus appears to be slightly exuberant.
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The case presented above is a common problem in patients receiving peritoneal dialysis therapy. Catheter exit-site and tunnel infections can lead to morbidity, prolonged treatment, recurrent peritonitis, and catheter

Fig. 3. Appearance of granulation tissue after cauterization with silver nitrate. Note typical whitish-grey colour.

Fig. 4. External exit site 1 week after cauterization of granulation tissue. Small crusts and some flaky skin between 12 and 4 o’clock.

Fig. 5. Sinus 1 week after cauterization of granulation tissue. Sinus is partly covered with epithelium; the granulation tissue deeper in the sinus (arrows) appears to be slightly exuberant. Moisture visible deep in the sinus is probably mupirocin ointment.

Fig. 6. External exit 2 weeks after cauterization of granulation tissue. Colour natural from 7 to 2 o’clock; darker from 2 to 5 o’clock. Minimal crust between 2 and 4 o’clock.

Fig. 7. Sinus 2 weeks after cauterization of granulation tissue. Epithelium covers most of sinus; plain granulation tissue or mucosal epithelium can be seen deeper in the sinus (arrow).

(fleshy’). The moisture visible deep in the sinus is probably mupirocin ointment. This exit site is markedly improved and can now be classified as equivocal. Mupirocin ointment was continued.

The exit site was re-evaluated the next week. The external exit (Figure 6) has a more natural colour and minimal crust between 2 and 4 o’clock. Sinus (Figure 7) is mostly covered with epithelium, plain granulation tissue or mucosal epithelium can be seen deeper in the sinus (arrow). The exit is now classified as good and mupirocin ointment is discontinued.

Comment

The case presented above is a common problem in patients receiving peritoneal dialysis therapy. Catheter exit-site and tunnel infections can lead to morbidity, prolonged treatment, recurrent peritonitis, and catheter
failure. With the reduced incidence of peritonitis since the introduction and widespread acceptance of the Y-connector, the problem of exit-site and tunnel infections has become the primary infectious complication of peritoneal dialysis [1–3]. This review will present practical aspects of design, implantation, diagnosis, treatment, care, and monitoring of catheter-related infections.

Catheter tunnel healing

Initial tissue reaction to a skin-penetrating foreign body

The tissue reaction begins immediately after an incision in the integument is made. Bleeding from capillaries and body fluids forms a coagulum of a hydrophilic fibrin–fibronectin gel and cellular debris. Various cytokines co-ordinate subsequent entry of inflammatory cells, fibroblasts, and the formation of new blood vessels [4]. Polymorphonuclear leukocytes phagocytize local bacteria and participate in the formation of a scab, which is desiccated coagulum. Healing of wounds starts with transformation of the coagulum into granulation tissue, composed mostly of new vessels and fibroblasts. New epithelial cells spread upon this tissue.

Mechanical factors, hypoxia, perfusion

The coagulum and necrotic tissue are gradually removed from the tunnel. Part of the necrotic tissues is absorbed, part is drained out of the tunnel. The tunnel should not be too tight, to allow free drainage of necrotic tissue and to prevent tissue oedema, which decreases local perfusion and $O_2$ tension, which are critical for the wound healing process [5]. On the other hand, too large an incision prolongs healing by the sheer volume of repair needed. In addition the movement of the catheter in a wide tunnel causes mechanical stress that slows the healing process [6]; thus the catheter should be relatively tightly anchored in the tunnel and also well immobilized externally, especially during the break-in period. Constricting sutures which can cause pressure necrosis with skin sloughing must not be used. Perfect haemostasis during implantation is extremely important because a large haematoma interferes with healing.

Systemic factors interfering with healing

Impaired nutrition, diabetes mellitus, uraemia, and corticosteroids are all known factors decreasing wound healing by decreasing fibrosis [7]. In our study on quality of exit healing these factors did not play a major role, except for obesity and diabetes mellitus [8]; however, our study groups did not include severely uraemic or malnourished patients.

Exit colonization

Infection is the major cause of impaired wound healing [9]. It has been well established in the surgical literature that wound infection is the result of major disturbance in the balance between host defences and bacteria [9]. Not only the number of bacteria but bacterial virulence are important; *Staphylococcus aureus* or *Pseudomonas aeruginosa* are more likely to induce an inflammatory response than is *Staphylococcus epidermidis*.

Our study clearly demonstrated the importance of delayed colonization for optimal healing, reduced exit infection and peritonitis rates, and catheter survival. [8]. Positive cultures from either washout or peri-exit smears 1 week after implantation were associated with early exit infections, higher peritonitis rates, and high probabilities of catheter loss due to exit/tunnel infections [8]. The early infected exits were more likely to have Gram-negative bacteria and *Staphylococcus aureus* in the first positive culture.

Appearance of healing exits

Table 1 summarizes signs and symptoms characterizing the quality of healing. Systematic descriptions of healing exit appearances with 96 colour photographs have been published recently [10]. In optimally healing exits, at 1 week post-implantation, slight tenderness is present in about one-third of exits, a scab is visible in almost all exits, and the epidermis surrounding the exit orifice is pale pink or pink. A small amount of serosanguineous, bloody or serous drainage is visible around the exit. Drainage inside the sinus is visible in almost all cases, and is similar in character to that seen outside. There is no epithelium visible in the sinus; the sinus is lined with a white tissue, which resembles aponeurosis. Granulation tissue is not yet formed at week 1.

Table 1. Signs and symptoms characterizing quality of healing

<table>
<thead>
<tr>
<th>Sign or symptom</th>
<th>Good healing</th>
<th>Poor healing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain (tenderness)</td>
<td>Decreases</td>
<td>Remains same or increases</td>
</tr>
<tr>
<td>Scab</td>
<td>Decreases</td>
<td>Remains same or recurs</td>
</tr>
<tr>
<td>External granulation tissue</td>
<td>Absent</td>
<td>May be present</td>
</tr>
<tr>
<td>Exit skin colour</td>
<td>Pale pink or pink</td>
<td>Erythema may be present</td>
</tr>
<tr>
<td>Exudate</td>
<td>None, serosanguineous or serous</td>
<td>Bloody or purulent</td>
</tr>
<tr>
<td>Progression of epithelium</td>
<td>Fast</td>
<td>Delayed, slow or interrupted</td>
</tr>
<tr>
<td>Sinus lining</td>
<td>Plain: white → mottled → pink</td>
<td>Soft → fleshy → proud flesh</td>
</tr>
<tr>
<td>Exit culture</td>
<td>Negative in early weeks</td>
<td>Positive in early weeks</td>
</tr>
<tr>
<td>Organism (if present)</td>
<td>Staph. coagulase negative</td>
<td><em>S. aureus</em>; Gram negative</td>
</tr>
</tbody>
</table>
External drainage abates by week 2, and is absent by week 3. Scabs diminish by week 3 and are not seen after week 4. Exit colour remains pale pink or pink throughout the 6-week period. Drainage in the sinus diminishes and most sinuses are dry at week 6. Sinus lining remains flat, but is gradually transformed into plain granulation tissue. Sometimes as early as week 2 the vessels become visible and/or the surface appears mottled (partly white and partly pink). The colour gradually changes to pink, but sometimes remains white as late as at 6 weeks.

Epithelium starts entering the sinus at weeks 2 or 3, progresses steadily, and covers at least half of the visible sinus tract by 5 weeks after implantation. Epithelium is fragile and pale pink or occasionally white.

Early infected exits do not show signs of healing (progression of epithelium, decrease in drainage amount). Instead, tenderness/pain increases, drainage changes to purulent, sinus lining becomes composed of granulation tissue at weeks 1 or 2 and the tissue becomes slightly or frankly exuberant.

**Sinus epithelialization as an indicator of healing**

Sinus epithelialization is an excellent indicator of the quality of healing. Delayed epithelialization is a sign of poor healing. Regression of epithelium is an early sign of impending infection. At the same time granulation tissue becomes exuberant. Whereas epithelium may spread over plain granulation tissue, exuberant granulation tissue not only inhibits progression of epithelium but almost always causes regression of epithelium. It looks as if exuberant granulation tissue is ‘pushing’ epithelium out of the sinus [8].

**The healed catheter tunnel**

**Morphology**

In most uninfected peritoneal dialysis catheter tunnels the epithelium covers only the external part of the sinus tract while the deeper part is covered with granulation tissue [11]. The epithelium may reach the cuff located less than 15 mm from the exit. The outer cuff limits spreading of granulation tissue and/or epithelium beyond the cuff. In the deeper part of some sinus tracts, a fibrous sheath replaces the granulation tissue. A dense capsule surrounds the cuff. Giant multinucleated cells and mature collagen fibres surround polyester fibres of the cuff in well-healed catheters. Only islands of mononuclear infiltrates are seen in the cuff.

During the healing period, only the part of the cuff adjacent to the tissue is invaded by fibroblasts and macrophages coalescing into giant cells. Immature collagen fibres are also deposited. The part of the cuff adjacent to the tubing is filled with a clot. Gradually the clot is reabsorbed, giant cells surround polyester fibres and mature collagen fibres become intertwined with polyester fibres.

Infection causes formation of granulocytic infiltration which propagates through the tunnel along the catheter and is usually confined within the fibrous capsule.

**Bacterial colonization of the sinus**

Late colonization, after the healing process is completed, is inevitable and mostly harmless, provided that the defence mechanisms are intact. Almost all healed catheter sinuses are colonized by bacteria [12]. The number of bacteria entering deeper into the sinus depends on the number and species of bacteria at the exit site, exit direction, as well as sinus tract length, the latter an important contributing factor in the amplitude of catheter movement in the sinus. Defence mechanisms, after the sinus is healed, are best in undamaged epidermis and granulation tissue; trauma to these structures may tilt the balance toward attacking micro-organisms and allow their rapid multiplication.

**Staphylococcus aureus nasal carriage**

The importance of *S. aureus* as an aetiological agent of peritoneal catheter exit-site infection has been well established [13,14]. Nasal carriage status of *S. aureus* is reported to be common in patients undergoing haemodialysis, [15] and peritoneal dialysis [16,17]. A recent multicentre study found an increased incidence of exit-site infections in nasal carriers of *S. aureus*; in 85% of these infections the strain from the nares and the strain causing the infection were similar in phage type and antibiotic profile [18]. In contrast, we found that even though *S. aureus* was more likely to be detected in nares of patients with exit infections, by antibiotic profile, the strain causing exit infection and the strain cultured from nares were different [8]. Judging from these data, there is an increased probability of exit infection in patients who carry *S. aureus* in nares, but the strain is usually different.

Whereas our patients usually showed colonization of nares and the exits by different strains, in other series the strains were more uniform. Hands are probably the major means of spreading bacteria to distant parts of the integument. Variations in habits, hygiene, exit-site care, and/or surgical practices are among the possible explanations why our results differ from those of others.

**Diagnosis of exit-site infection**

**Background**

There is no difficulty in the diagnosis of peritonitis; dialysate contains either a small number of cells when uninfected or a large number of cells, mostly granulocytes, when infected. Normal dialysate does not contain micro-organisms; a correctly performed culture is usually positive in peritonitis. Bacterial peritonitis cannot be cured without antibiotics. Attempts to classify exit
appearance into two categories (infected and not infected) is difficult, if not impossible, because infected and uninfected exit appearances overlap. This overlap is due to the peculiarity of tissue reaction to the foreign body penetrating the skin and stems from the delicate balance between bacteria in the sinus and host defences. The presence of a small amount of exudate causing crust formation does not indicate infection, but if the bacterial attack is more severe then the amount of exudate increases; granulation tissue proliferates, becomes more vascularized, epithelium regresses and signs of infection become obvious. Low-grade exit infection may abate without systemic antibiotics.

Attributes used in classification

The classification relies on the cardinal signs of inflammation: calor (heat), rubor (redness), turgor (swelling), and dolor (pain). Additional features of inflammation, specific for an exit of any skin-penetrating foreign body, are drainage, regression of epidermis, and exuberance (profuse overgrowth) of granulation tissue (‘proud flesh’).

Improvement or deterioration of inflammation is associated with respective decreases or increases of pain, induration (swelling), drainage, and/or exuberant granulation tissue, and/or regression or progression of epithelium in the sinus. Increased lightness (pink, pale pink) or darkness (purplish, brown, or deep black) and decrease in colour diameter indicate improvement, increase in red colour saturation and diameter indicate deterioration.

Pathomechanism of exit attributes

Well healed, uninfected exits and sinus tracts are usually colonized by bacteria. The part of the sinus tract covered with epithelium constitutes an excellent barrier to bacterial invasion as does the rest of the body integument. The part of the sinus covered with granulation tissue appears to respond to bacteria by constant exudation of serum with white blood cells. The serum and white blood cells suppress bacterial proliferation and curb penetration of bacteria into the deeper sinus. This small amount of exudate becomes desiccated and forms a crust, which may be seen in the external part of the sinus or around the sinus rim. This crust is easily washed away during routine exit care but may be visible if the exit care has been performed some time before examination of the exit. Such a crust is easily removed during examination, particularly from the exits where the whole visible sinus is completely covered with mature epithelium.

As mentioned previously the number and virulence of bacteria is crucial in invoking inflammatory response. It seems logical to postulate that if the number of bacteria, particularly virulent ones, deeper in the sinus increases, then the inflammatory response ensues. The process begins with vasodilatation, increased blood flow, and increased vascular permeability in response to such mediators as histamine, kinins, and interleukins. Various growth factors co-ordinate subsequent entry of inflammatory cells, fibroblasts, and the formation of new blood vessels [4]. Polymorphonuclear leukocytes phagocytize local bacteria and macrophages dispose of accumulated debris. As the amount of exudate increases the drainage becomes more liquid (purulent), cannot desiccate in the sinus, and becomes visible in the sinus or around the skin exit. Epithelium in the sinus tract regresses toward the sinus rim when granulation tissue becomes slightly or frankly exuberant due to overgrowth of capillary buds, macrophages, neutrophils, and fibroblasts. As the infection extends toward the exit, the exit site also becomes inflamed as evidenced by the cardinal signs of acute inflammation: erythema, heat, swelling, and pain. The severity of infection and the extent of the inflammatory response determine the intensity of signs and symptoms.

If bacterial invasion is restricted by local defence mechanisms and treatment, the inflammatory response subsides, fibroblasts produce collagen, which shrinks the granulation tissue and allows the epithelium to spread into the sinus. Blood flow slows down in capillaries, causing higher extraction of oxygen from haemoglobin, higher concentration of bluish deoxyhaemoglobin, and change of skin hue from red to purplish.

As the inflammatory process subsides the keratinocytes in the area of inflammation are stimulated to proliferate; the number of keratinocytes increases, they phagocytize more melanin granules and the skin becomes darker [19]. When acute inflammation subsides, colour changes to brownish in people with fair skin and deep black in people with dark skin. Gradually all signs of inflammation subside and skin assumes a normal appearance.

Chronic infection is characterized with less vasodilatation and vascular permeability but more proliferation of capillary buds and increased cellularity, particularly fibroblasts but also macrophages, granulocytes, and lymphocytes. Such an inflammatory reaction leads to formation of exuberant granulation tissue (‘proud flesh’ or granuloma) in the sinus and around the exit with regression of epithelium. The epidermis around the granuloma may look completely normal.

A cuticle may form around exits with mild or moderate inflammatory reactions. Cuticle around the exit probably results from accelerated skin turnover and increased keratinization. Similar to eponychium (which is a cuticle at the base of a nail) a cuticle at the exit is difficult to detach and the exit may bleed if the cuticle is forcibly removed. If exudate mixes with the cuticle a crust is formed which is difficult to remove. Frequently such a crust or crust mixed with a scab covers slightly exuberant granulation tissue around the exit. Removal of such a crust exposes slightly exuberant granulation tissue that will bleed. Distinctly exuberant granulation tissue (‘proud flesh’) is usually covered with purulent drainage, which cannot desiccate to form a crust or scab. Unlike slightly exuberant granulation tissue, cuticle does not form around ‘proud flesh’.
Appearance of healthy and infected exit sites

Exit evaluation technique

Visual attributes are best discerned by viewing with 3–5 times magnification and good illumination provided by a white light source. This can be achieved with an inexpensive, hand-held lighted magnifying lens. Magnification and good lighting amplify exit and sinus features: colours are intensified, drainage is more easily seen and the initial impression is that the exit is ‘worse’ than when assessed with the unaided eye [20]. Most of the attributes are not discrete but continuous, e.g. skin colour may range from natural, through shades of pink to red, drainage ranges from barely visible moisture in the sinus to copious external drainage. Sometimes it is difficult to differentiate within the spectrum of a particular attribute; therefore, two experienced evaluators may grade an attribute differently. These differences are usually no more than one level apart and the classifications of the exit-site appearance based on all features are almost always the same.

Classification of exit-site appearance

The classification of healed exit sites into seven categories evolved from 565 evaluations of 61 healed exit sites in 56 patients [12]. Five basic categories of catheter exit appearances were identified: acute infection, chronic infection, equivocal (low grade) infection, perfect and good exit. Two special categories were also described: cuff infection with or without exit infection, and exit trauma. The characteristics for each category of catheter exit sites are summarized in Table 2. Exit culture may be negative in infected exits in patients receiving antibiotics; positive peri-exit smear culture, if present in exits without signs of inflammation, indicates colonization not infection.

Acute catheter exit-site infection. Purulent and/or bloody drainage from the exit site, spontaneous or after pressure on the sinus; and/or swelling; and/or erythema with diameter 13 mm or more from border to border; and/or regression of epithelium in the sinus. Acute catheter inflammation lasts less than 4 weeks and may be accompanied by pain, exuberant granulation tissue around the exit or in the sinus and the presence of a scab or crust.

Chronic catheter exit-site infection. Purulent and/or bloody drainage from the exit site, spontaneous or after pressure on the sinus; and/or exuberant granulation tissue around the exit and/or in the sinus; and regression of epithelium in the sinus. Chronic infection persists for more than 4 weeks and crust or scab is frequently present. Swelling, erythema, and/or pain indicate exacerbation, otherwise are absent. Exit culture may be negative in patients receiving antibiotics.

Equivocally infected catheter exit site. Purulent and/or bloody drainage that cannot be expressed outside the sinus, accompanied by the regression of epithelium, and occurrence of slightly exuberant granulation tissue around the exit and/or in the sinus. Erythema with a diameter less than 13 mm from border to border may be present, but pain, swelling, and external drainage are absent. Exit culture may be negative in patients receiving antibiotics.

Perfect catheter exit. At least 6 months old with its entire visible length of sinus tract covered with the keratinized (mature) epithelium. Exit colour is natural or dark and there is no drainage. A small, easily detachable crust may be present in the sinus or around the exit.

Good catheter exit. Exit colour is natural, pale pink, purplish or dark and there is no purulent or bloody drainage. Clear or thick exudate may be visible in the sinus. Mature epithelium covers only part of the sinus; the rest is covered by fragile epithelium or plain granulation tissue. Pain, swelling, and erythema are absent.

External cuff infection without exit infection. Intermittent or chronic, purulent, bloody or gooey drainage, spontaneous or after pressure on the cuff and induration of the tissue around the cuff. Exuberant granulation tissue may be seen deep in the sinus; sinus epithelium may be chronically or intermittently macerated. Exit site may look normal on external examination. Ultrasound may show fluid collection around the cuff, but negative ultrasound does not rule out cuff infection.

Traumatized exit. Features of traumatized exit depend on the intensity of trauma and time interval until examination. Common features of trauma are: pain, bleeding, scab and deterioration of exit appearance (e.g. perfect exit transforms to good or equivocal or acutely infected).

Catheter exit care recommendations

Catheter exit care and treatment recommendations are based on our long-term experience with various peritoneal catheters [21–24], particularly that acquired during the last 7 years of exit-site study [8,12]. Caudal direction of the external exit facilitates drainage during the early post-implantation period and later in case of infection with copious exudate. Catheters with a permanent bend between cuffs offer an advantage because they allow implantation of catheters in an unstressed condition in an arcuate tunnel with both internal and external exits directed downward. Implantation of a straight catheter in an arcuate tunnel predisposes to external cuff extrusion [23]. Compared to the abdominal exit, localization of the exit in the parasternal or presternal area using swan-neck presternal catheters provides better overall results, particularly regarding exit and tunnel infections. The catheter is suitable for any patient commencing peritoneal dialysis and is particularly useful in extremely obese patients (BMI >40 kg/m²) and those with ostomies [24].

Implantation

Prior to implantation the exit should be marked in such a way that the catheter would not be subjected
Table 2. Characteristics of each category of exit site appearance

<table>
<thead>
<tr>
<th>Exit</th>
<th>Perfect</th>
<th>Good</th>
<th>Equivocal</th>
<th>Acute infection &lt;4 weeks</th>
<th>Chronic infection &gt;4 weeks</th>
<th>Cuff infection without exit infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain/tenderness</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>May be present</td>
<td>Only if exacerbation</td>
<td>May be present over cuff</td>
</tr>
<tr>
<td>Colour</td>
<td>Natural, pale pink or dark</td>
<td>Natural, pale pink or dark, bright pink &lt;13 mm</td>
<td>Bright pink or red &lt;13 mm</td>
<td>Bright pink or red &gt;13 mm only if exacerbation</td>
<td>Natural, pale pink, purplish or dark, bright pink &lt;13 mm</td>
<td>Typically absent</td>
</tr>
<tr>
<td>Crust</td>
<td>None or small, easily detached or specks of crust on dressing</td>
<td>None or small, easily detached or specks of crust on dressing</td>
<td>Present, may be large and difficult to detach</td>
<td>Present</td>
<td>Present, may be difficult to detach</td>
<td></td>
</tr>
<tr>
<td>Scab</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>May be present</td>
<td>May be present</td>
<td>Absent</td>
</tr>
<tr>
<td>Drainage</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>May be present</td>
<td>May be present</td>
<td>Absent</td>
</tr>
<tr>
<td>Swelling</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>May be present</td>
<td>Occurs only if exacerbation</td>
<td>Cuff induration may be felt on palpation; negative ultrasound does not rule out the diagnosis</td>
</tr>
<tr>
<td>Granulation tissue</td>
<td>None</td>
<td>None</td>
<td>Plain or slightly exuberant</td>
<td>Slightly exuberant or 'proud flesh' may be present</td>
<td>'Proud flesh' or slightly exuberant typically visible</td>
<td>None</td>
</tr>
<tr>
<td>Sinus</td>
<td>Perfect</td>
<td>Good</td>
<td>Equivocal</td>
<td>Acute infection &lt;4 weeks</td>
<td>Chronic infection &gt;4 weeks</td>
<td>Cuff infection without exit infection</td>
</tr>
<tr>
<td>Epithelium</td>
<td>Strong, mature. Covers visible sinus</td>
<td>Strong, mature at rim. Fragile or mucosal deeper</td>
<td>Absent or covers part of sinus</td>
<td>Absent or covers only part of sinus</td>
<td>Absent or covers only part of sinus</td>
<td>Covers most or all of sinus. May be macerated</td>
</tr>
<tr>
<td>Granulation tissue</td>
<td>None</td>
<td>Plain beyond epithelium</td>
<td>Slightly exuberant</td>
<td>Slightly exuberant or 'proud flesh' slightly exuberant</td>
<td>'Proud flesh' or slightly exuberant typically visible</td>
<td>None or exuberant deep in sinus</td>
</tr>
<tr>
<td>Drainage</td>
<td>None or barely visible Clear or thick</td>
<td>None or barely visible</td>
<td>Purulent or bloody. Clear or thick</td>
<td>Purulent or bloody</td>
<td>Purulent or bloody</td>
<td>Purulent, bloody, gluey. May be seen only after pressure on cuff. Clot or dried blood in sinus</td>
</tr>
</tbody>
</table>

Trauma may result in pain, bleeding, scab, and deterioration of exit appearance. Exit appearance depends on intensity of trauma and time of evaluation.

to excessive motion with the patient’s activities and there will be no pressure on the tunnel by a belt or a tight garment or when the patient bends forward. These depend on the size and shape of the abdomen. Additional considerations include the presence of scars and the patient’s preference.

A prophylactic antibiotic, preferably 1 g vancomycin or a cephalosporin should be given by slow intravenous infusion [25]. This will provide a good antibiotic level in the coagulum and decrease the bacterial load in the wound.

General anaesthesia should be avoided if possible, because it predisposes to vomiting and constipation, and requires voluntary coughing during the
postoperative period as a part of pulmonary atelectasis prevention; coughing, vomiting and straining markedly increase intra-abdominal pressures and predispose to abdominal leaks [26].

A meticulously sterile surgical technique of implantation is mandatory. Perfect haemostasis, preferably using cautery, is required, because in our experience a wound haematoma is a risk factor for early exit infection. Post-implantation the catheter is covered with several layers of gauze and anchored with air-permeable tape. The dressing is left in place for a week. Peritoneal dialysis exchanges are performed to check the patency of the catheter, and remove residual blood from the peritoneal cavity, if present. The exchanges are continued until the dialysate is clear.

Early post-implantation care

A pericatheter dialysate leak interferes with fibrous tissue ingrowth into the cuff and should be avoided. Therefore, ambulatory peritoneal dialysis is delayed for at least 10 days after the implantation, but peritoneal dialysis in the strict supine position may be started immediately after in and out exchanges are completed. One litre volumes of dialysis solutions are used for the first supine peritoneal dialysis.

Daily dressing changes post-implantation are not necessary. There are two reasons for less frequent dressing changes: first, each dressing change may contaminate the exit with bacteria even though aseptic technique is used; second, each dressing change requires manipulation of the catheter, increasing the risk of catheter movement and subsequent trauma.

We do weekly dressing changes for the first few weeks after catheter implantation if there is no excessive drainage. Once the exit is colonized, between weeks 2 and 3 in the majority of cases [12], more frequent dressing changes are indicated. We recommend every other day dressing changes after 2 weeks post-implantation.

Aseptic technique, including wearing both masks and sterile gloves, should be used for postoperative dressing changes. The skin surrounding the exit should be cleansed with a non-irritating agent to remove the risk of exit contamination [24].

We use a non-ionic surfactant agent, poloxamer 188 (ShurClens®), that cleanses well, but is not harmful to the granulation tissue if allowed to enter the sinus. If these are used, care should be taken to use only on the intact skin surrounding the wound or granulation tissue [29]. We do not use povidone-iodine and hydrogen peroxide concentrations [27,28] and are harmful to granulation tissue if allowed to enter the sinus. If these are used, care should be taken to use only on the intact skin surrounding the wound or granulation tissue [29].

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Late exit care

Late care, after the healing process is completed, is simpler. The results of a prospective study indicate that cleansing with soap and water is the least expensive and tends to prevent infections better than painting with povidone-iodine and cleaning with hydrogen peroxide [32]. After cleansing, the exit has to be patted dry with sterile gauze and well immobilized. Most of our patients use a dressing cover for 6–12 months after implantation. One year after implantation patients are allowed to omit use of a cover dressing if desired.

We recommend that our patients use only a shower and avoid submersion in water, particularly in a jacuzzi, hot tub, or public pool, unless watertight exit protection can be implemented. Prolonged submersion in water containing high concentrations of bacteria frequently leads to severe infection with consequent loss of the catheter. Swimming in the ocean, and well-chlorinated private pools is less dangerous. Exit care must be performed immediately after a shower or water submersion, with particular attention to obtaining a well-dried exit. Patients with a presternal catheter may take a deep tub bath without any risk of exit contamination [24].

Treatment recommendations

General principles

A culture of exit-site exudate or, if there is swelling/erythema without expressible exudate, a smear culture of the skin surrounding the exit should be taken as soon as a clinical diagnosis of an exit-site infection is made. Antibiotics should be started before culture results are available. Gram-positive organisms are frequently the cause of exit-site infections; therefore local or systemic antibiotics for Gram-positive organisms should be used. Accordingly, an oral cephalosporin may be selected as the initial antibiotic, but more recently, quinolones have become the initial antibiotics...
Topical mupirocin is an initial choice for an equivocal exit. Conditions that delay healing or make therapy ineffective are cuff and/or tunnel infection, infection due to a resistant organism or virulent pathogens (such as S. aureus, Pseudomonas sp., Candida, etc.), and patient non-compliance. Exuberant granulation tissue (proud flesh) is cauterized with a silver nitrate stick, a procedure widely used in surgical practice, veterinary and human. [33,34]. 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 [35]. Chronic infection requires repeated cauterization of exuberant granulation tissue. 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 grey.

Recommendations for the care of infected exit sites are based on sound surgical practices and anecdotal experiences. Increasing the frequency of dressing changes to one or two times a day helps the healing process, especially in those with copious drainage. Non-irritating solution (e.g. non-ionic surfactant) is our preferred cleanser to remove drainage and reduce the number of micro-organisms. An infected exit should be covered with a sterile dressing to absorb drainage, protect against trauma, and shield against superinfection.

Topical treatments include application of soaks to the exit 2-4 times daily as well as the application of dry heat [25,36,37]. 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 have been recommended [36]. In our opinion, strong oxidants and other irritating solutions should not be used. It is our belief that topical antibiotics are of limited value in treating acute or chronic infection with copious drainage because of the inability to achieve high enough local concentrations [34]. Catheter immobilization is a sound practice. Immobilizing a catheter protects it from accidental trauma. Trauma leads to bleeding, and blood is a good medium for micro-organisms to multiply in. Catheter immobilization should be continued during the acute infection stage, or implemented if not already in practice.

**Specific recommendations for treatment of infection by categories**

Table 3 shows our recommendations for treatment of equivocal infection, acute infection, chronic infection, and cuff infection. Although the recommendations are mostly self evident a brief rationale for some of the recommendations is provided below.

**Equivocally infected exit**

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 or chronic 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 daily local care is continued in such a situation.

Local therapy with topical antibiotics is the mainstay of treatment for 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®, gentamicin, and tobramycin.

**Chronically infected exit site**

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 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 replaced with a topical antibiotic. 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. It is likely that such cases represent undiagnosed, low-grade, external cuff infection.

**External cuff infection with or without exit infection**

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 [38]. Others find these measures ineffective [39]. In our experience cuff shaving prolonged catheter life for approximately
<table>
<thead>
<tr>
<th>Category</th>
<th>Equivocal infection</th>
<th>Acute infection</th>
<th>Chronic infection</th>
<th>Cuff infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evaluation</td>
<td>Culture and sensitivities on peri-exit smear; Gram stain</td>
<td>Culture and sensitivities on exudate; Gram stain</td>
<td>Culture and sensitivities on exudate; Gram stain</td>
<td>Palpation of cuff and tunnel; Culture and sensitivities on exudate (spontaneous or after pressure on cuff); Ultrasound of cuff/tunnel</td>
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<tr>
<td>Initial therapy</td>
<td>Cauterize slightly exuberant granulation tissue</td>
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<td>Cauterize slightly exuberant granulation tissue</td>
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<td></td>
<td>Topical mupirocin</td>
<td>First-generation cephalosporin for Gram + organisms; Quinolone for Gram– organisms; Vancomycin for MRSA</td>
<td>First generation cephalosporin for Gram + organisms; Quinolone for Gram– organisms; Vancomycin for MRSA</td>
<td>Initial antibiotic therapy based on Gram stain results</td>
</tr>
<tr>
<td>48 h</td>
<td>Change to neosporin or gentamicin ointment if Gram – organisms on culture</td>
<td>Adjust therapy according to culture and sensitivities</td>
<td>Adjust therapy according to culture and sensitivities</td>
<td>Adjust antibiotic according to culture and sensitivities</td>
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<td>Follow up</td>
<td>If no improvement in 2 weeks, change to systemic antibiotic based on initial culture and sensitivities</td>
<td>Evaluate weekly; reculture if no improvement; Substitute another appropriate antibiotic or add a second, synergistic antibiotic. Use rifampicin as a second antibiotic for staphylococcal infections. Most acute infections respond favourable to therapy; continue achieving a good appearance. If accompanying peritonitis, consider catheter removal</td>
<td>Evaluate every 2 weeks; reculture every 2 weeks if no improvement on appropriate therapy. Add synergistic drug or change antibiotic according to culture and sensitivities. If infection recurs repeatedly after achieving a good appearance: (a) consider chronic antibiotic suppression; (b) if no improvement after a month of treatment, suspect cuff infection and treat as such If accompanying peritonitis, remove catheter</td>
<td>Re-evaluate every 2 weeks; reculture monthly. If no remission: (a) consider cuff shaving (b) consider catheter replacement. If accompanying peritonitis, remove catheter</td>
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<td>Continue therapy 7 days after achieving a good appearance</td>
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<tr>
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<td>Response to systemic antibiotic therapy is excellent with cure occurring in almost all instances</td>
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provide better results in presternal catheters [24,42]. Local antibiotics in acute or chronic infection are of sites. A prophylactic antibiotic is indicated for the ive that all patients and all episodes are counted. Systemic and local use of antibiotics for prophylaxis and complications, and (3) rate of peritonitis. It is imperat- that have colonized the exit multiply rapidly in the blood is a good medium for bacterial growth. Bacteria good, or perfect exits but are indicated only for equi- Traumatized exit

Bleeding is a common sequela of trauma. 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 h 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.

Systemic and local use of antibiotics for prophylaxis and treatment of exit infection

Healthy exit sites usually do not get infected unless traumatized. Therefore a prophylactic, systemic antibiotic is not recommended for good or perfect exit sites. A prophylactic antibiotic is indicated for the management of accidentally traumatized exits. In most cases of trauma this may be considered a treatment not prophylaxis, since in most reported trauma cases the exit deteriorates to equivocal, which is a subclinical form of exit infection. The other indication for prophylaxis is the chronic infection, where discontinuation of systemic antibiotics results in reappearance of the infection [43]. In such a case long-term prophylaxis with a suppressive dose of an antibiotic is useful.

In nasal carriers of *S. aureus*, randomized trials showed decreased infectious complication in patients treated with prophylactic systemic trimethoprim-sulphamethoxazole [44] or rifampicin [45]. Topical intranasal application of antibiotics against *S. 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. As mentioned above in our studies the strains are usually different in the nares and at the exit. Even if the strains were the same, it seems preferable to use topical antimicrobial agents on the exit, where the bacteria are harmful, instead of using it in nares.

Although the role of prophylactic antibiotics during the healing period has not been established in non-carriers of *S. aureus*, the association between early exit colonization and exit infection would indicate that such an approach may be beneficial [8]. A prospective randomized study of prophylactic antibiotics during the healing period is needed to clarify their role.

Local antibiotics in acute or chronic infection are of little value because they cannot achieve proper local concentrations before being washed away with large drainage; antibiotics administered systemically can pro- vide therapeutic concentrations locally by being excreted into the drainage. Local antibiotics can achieve high concentrations in the sinus in equivocal, good, or perfect exits but are indicated only for equivocal exits.

Monitoring and reporting results

The method of reporting exit infections as episodes per year or number of months between the episodes is inappropriate [46]. This method is suitable for analys- ing peritonitis rates because peritonitis is almost always easy to diagnose. Cases of chronic peritonitis or equivocal peritonitis are very rare. Because of the complexity of exit infections, presence of equivocal exits, chronic infections both treated and/or untreated, and recurrent infections, a simple rate is insufficient.

We think that a better practice would be to combine three reports [46]: (1) a yearly cross-sectional assessment of exit-site appearance according to our classi- fication, (2) rate of catheter removal due to infectious complications, and (3) rate of peritonitis. It is imperative that all patients and all episodes are counted.

The use of the classification system will result in early diagnosis of exit problems and treatment can be more specific.

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**References**

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