Expanded Phage Case Histories

Introduction

Chronic wounds by definition are wounds that fail to progress through normal expected patterns of healing by remaining in a chronic inflammatory state. Multiple reasons have been put forward as to why chronic wounds fail to heal such as diabetes, white cell dysfunction, peri vascular cuffing, malnutrition, repetitive trauma, poor perfusion, infection, and many others. Yet in spite of these diverse barriers to healing, chronic wounds have a surprising similarity. At a biochemical level, chronic wounds display increased proinflammatory cytokines, increased matrix metalloproteases in a specific pattern, low levels of tissue inhibitors of matrix metalloproteases, low levels of growth factors cytokines along with degraded receptors on the cells constituting the wound bed (senescent cells). The best explanation for this biochemical pattern is the presence of biofilm, which is ubiquitous in chronic wounds and can be considered the final common pathway for non-healing wounds. Biofilms demonstrate remarkable colony defenses against antibiotics, biocides, human immuno defenses, and most of the current wound care products used to treat chronic wounds today. Therefore, a novel approach to treat chronic wounds must be developed.

Biofilms and their amazing multicellular survival strategies were relatively unknown until 1978. Over the next decade it became clear that biofilms were the preferred form for bacteria to organize into on any surface. This colony organization gives them defenses against ultraviolet light, environmental extremes of hot, cold, drying, predators such as bacteriophages and amebas, antibiotics, and very importantly mammalian host defenses. It is the biofilm’s ability to form on the surface of the wound and evade our host defenses that makes it such a serious problem in human disease. The Centers for Disease Control estimates that 65% (the National Institute of Health’s estimate is 80%) of all human infectious disease is secondary to biofilm. Chronic undulating infections such as sinusitis, endocarditis, osteomyelitis, prostatitis and many other human diseases are biofilm based. It has now become clear that wounds remain open because of the presence of biofilm. It has become very important for new tools to be developed to combat biofilm.

A free-floating (planktonic) bacteria with no colony defenses is what we commonly envision colonizing the surface of a wound. However, once the bacteria attaches to the wound surface it quickly divides and forms a gooey protective substance, which further attaches it to the surface. This gooey substance is called “extracellular polymeric substance” (EPS) and it is nothing more than long chains of polysaccharides produced by the bacteria to form a cocoon around itself that will tightly adhere to the surface and protect it from the outside environment. Once the microcolony has evaded the host defenses and formed this early cocoon, the bacteria within the microcolony communicate with one another, which causes them to change their phenotype depending on the layer in which they are present. Roughly three layers have been identified in a biofilm with each layer defending the other from different types of attack. Biofilms have defenses that protect it against biocides, antibiotics, UV light, dehydration, and phages.

The ability of bacteriophages to lyse bacteria embedded in biofilms has first been examined in 1956 by Adams and Park (Adams and Park, 1956). More recently, Doolittle et al. (Doolittle et al., 1995) demonstrated that phage T4D+ infects and replicates inside E. coli growing within its biofilm. Similar findings were later reported (Corbin et al., 2001) using a closely-related T4 bacteriophage which reduced the density of an E. coli K-12 biofilm by 10-fold in as little as 90 min, as assessed in a Modified Robbins' Device (MRD) and confirmed by scanning confocal laser microscopy. Studies of phage-biofilm interactions have also been performed with other bacterial pathogens, including Enterobacter agglomerans, Listeria monocytogenes, Staphylococcus aureus, Yersinia ruckeri, and Pseudomonas aeruginosa.

In at least some of these studies, the ability of bacteriophages to degrade biofilm was associated with their encoding an enzyme with strong EPS-degrading ability. For example, a bacteriophage specific for E. agglomerans has been shown (Hughes et al., 1998) to possess a polysaccharide depolymerase specific for the bacterium’s EPS, and phage-elicited biofilm disruption was found to be caused by a combination of (i) EPS degradation by the depolymerase, and (ii) infection and subsequent bacterial lysis by the phage. Scanning electron microscopy confirmed that the phages extensively degraded susceptible biofilms and continued to infect biofilm bacteria while EPS degradation occurred.
The enzyme responsible for this phenomenon has been partially purified, and it has been shown (Hughes et al., 1998) to be an endo-glycanohydrolase. Similar results have been reported (Roy et al., 1993; Hibma et al., 1997) for *L. monocytogenes*-specific phages; e.g., they inhibited biofilm formation on stainless steel, and they were as effective as lactic acid (130 ppm) in inactivating pre-formed *L. monocytogenes* biofilms (Hibma et al., 1997). In another similar study, *P. aeruginosa*-specific bacteriophages were found (Hanlon et al., 2001) to diffuse through alginate gels and to produce a 2-log reduction in the cell numbers in 20-day-old biofilms of *P. aeruginosa*. In addition, bacteriophage treatment elicited a significant (up to ca. 40%) time- and concentration-dependent reduction in the viscosity of commercial alginate samples, and it reduced the number of viable *P. aeruginosa* in biofilms by ca. 99%, despite the presence of EPS (Hanlon et al., 2001). The WPP-201 preparation contains strong lytic phages targeted against some of the most notorious, biofilm-forming bacterial pathogens – including *P. aeruginosa* and *S. aureus*. Although the ability of WPP-201 to degrade biofilms has not been rigorously determined, the above-cited studies suggest that various bacteriophages (including *P. aeruginosa*- and *S. aureus*-specific phages) contained in WPP-201 may provide an exciting new tool for managing wound infections by combinational effect of (i) lysing wound-infecting bacteria, and (ii) reducing biofilm levels in the wounds.

Case histories have been a valuable tool in clinical medicine since its beginnings. Case histories have the advantage of providing insights into the efficacy of a particular treatment.

Because of the variations from case to case, it is difficult for a clinician to develop a firm opinion with just one case. Therefore, it is important to group a number of cases relative to a specific treatment to develop a clearer picture of its efficacy. The disadvantage of case histories is the bias of the observer. A specific case history is evaluated by the observer understanding what is happening clinically with a specific treatment, and then comparing it to what the observer feels would be the most likely clinical course with standard treatment. This added bias of the observer is best managed looking at multiple cases.

**Phage Therapy of Chronic Wounds With Associated Epithelial Islands**

**Case History**

NAME: R.T.
ACCT: 10171

A.H. is a very pleasant 53-year-old white female with a very painful venous leg ulcer for over a year. The patient was treated with phage cocktail in March and showed very rapid closure of the wound. Her pain was rapidly relieved over a 24- to 48-hour period. Granulation tissue rapidly filled the defect, and re-epithelization began out in the mid portion of the wound. The wound rapidly covered with epithelium, healing within 12 weeks. This is much more rapid closure than expected, and the pattern of re-epithelization was unexpected.
**Case History**

**NAME:** A.H.  
**ACCT:** 2965

A.H. is a very pleasant 73-year-old white male with a long history of recurrent venous leg ulcers. The area of this venous leg ulcer is very sclerotic from 30 years of recurrent wounds. The patient had application of phage cocktail the first week in February. Within three weeks the patient has an epithelial island, and through the course of his healing he developed another island in the 2:00 position. The photographs document the development of the island.

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**NAME:** R.B.  
**ACCT:** 4146

The patient is a very pleasant 60-year-old white male with lymphedema in the bilateral lower extremities, uncontrolled noninsulin dependent diabetes mellitus and nonhealing wounds on his lower extremities for many years. The patient’s first visit to our clinic was 06-26-2002 with a very painful highly exudative wound. He failed to respond to comprehensive wound management.

The patient was readmitted in May of 2004 with dramatic increase in pain. The wounds were much deeper and more exudative. The patient had multidrug resistant *P. Aeruginosa* bacteria. He was depressed, and ended up losing his job. The patient was started on biofilm based wound management along with bacteriophage therapy with specific phages against *P. Aeruginosa*. The patient showed dramatic improvement in his wounds over the course of six weeks.

Teaching Point: The patient has multi drug resistant *P. Aeruginosa* and only responded to phage therapy. Of interest, his wound developed epithelial islands throughout the center of the wound, which coalesced and filled the wound in, which is a different healing pattern than normally seen.
Case History

NAME: E.G.
ACCT: 211

E.G. has been making a 250-mile round trip to the Southwest Regional Wound Care Center for over five years. The patient is a quadriplegic and has had many decubitus ulcers on his legs, ankles, feet and even his upper extremities. These have been treated with traditional therapies and have healed rapidly. However, the decubitus ulcer of his sacrum showed no signs of healing or getting worse for over four years. The patient was treated with phages in March. It was noticed that epithelial migration started cascading down the walls of the decubitus ulcer, which was almost four inches deep. Once the keratinocytes arrived at the wound bed, they spread out over the wound bed. The wound is now mostly healed, but the pattern is unexpected. Usually, granulation tissue fills the defect and then re-epithelization occurs. For some reason, angiogenesis has not taken place in this wound, yet the keratinocytes have migrated out and have almost covered the defect. This is an unexpected pattern.

Case History

NAME: A.W.
ACCT: 9163

A.W. is a very pleasant 36-year-old male with a large decubitus ulcer at the end of his spine. The patient had a hemicorporectomy, which is removal of the pelvis in both lower extremities. This was done for advanced osteomyelitis of the pelvis and hips. The patient has had a longstanding decubitus ulcer in the area. He was treated with phages in April and has shown several positive signs. First, the wound is contracting and is much smaller. Next, there is much less exudate. The area around the wound is much firmer, which allows the patient better sitting balance. And, he has the presence of re-epithelization in the base of the wound. The patient has multiple epithelial islands throughout the wound. Because of the significant wound moisture, these islands are macerated and appear white. There is not much in the way of angiogenesis, and the wound bed color remains a yellowish or pale color. The appearance of re-epithelization in the mid portion of the wound in the midst of heavy exudate with very little granulation tissue and very deep below the surface of the skin is quite unusual. However, this phenomenon is seen frequently after treatment with phage cocktail.
CASE HISTORY:

NAME:  R.C.
ACCT:  10589

The patient is a 79-year-old Latin American male with a 20-year history of diabetes. She is a resident of a nursing home. The patient has coronary artery disease and congestive heart failure. The patient was found to have methicillin resistant Staph Aureus in the wound of the right great toe. The patient was started on Vancomycin on 3/4/05.

The patient had failed to respond to three months of conservative wound care and then had a resection of the right great toe. That wound site dehisced and worsened over about a 6 week period of time and the patient was referred to The Wound Care Center.

The patient was started on biofilm based wound care along with hyperbaric oxygen. The wound responded.

The wound healed in 5 weeks.

Teaching Point: Managing wound healing barriers such as hypoxia along with biofilm based wound care is important.

In a study that reviewed 27,630 diabetic foot ulcers, 47% of the ulcers healed in 20 weeks. (Am J Med Vol 115 (8), Dec 2003, Margolis, DJ, et al.)

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CASE HISTORY:

NAME:  D.L.
ACCT:  10378

The patient is a very pleasant 53-year-old Latin American male with a longstanding history of diabetes mellitus on dialysis. The patient has diabetic peripheral neuropathy involving the foot. The patient presented with gangrenous changes to his right foot. TCOMS showed a TCpO2 of 5 at the right foot and 10 at the right calf. The left leg showed good perfusion and oxygenation. The patient was cultured out to have Group D Enterococci and multidrug resistant Pseudomonas in the right foot. The patient underwent aggressive debridement, biofilm management of his wound and phage therapy.

Teaching Point: The patient responded rapidly to phage therapy. A wound is never hopeless.

In a study that reviewed 27,630 diabetic foot ulcers, 47% of the ulcers healed in 20 weeks. (Am J Med Vol 115 (8), Dec 2003, Margolis, DJ, et al.)
CASE HISTORY:

NAME: L.D.
ACCT: 7726

The patient is a very pleasant 52-year-old black male with a nonhealing transmet amputation. The patient is an insulin dependent diabetic. He had poor blood flow into the left foot. He has diabetic peripheral neuropathy.

The patient’s wound dehisced. Those sutures were removed and the wound was allowed to open. He had methicillin resistant Staph Aureus. The patient had phage applied weekly.

The patient’s wound stayed fairly clean, free of biofilm and went on to complete healing within 10 weeks of opening the wound.

Teaching Point: Surfaces favor biofilms. Getting the wound opened and the surfaces exposed decreases the time for wound healing. Also it allows the surface biofilm to be managed.

CASE HISTORY:

NAME: C.D.
ACCT: 10788

The patient is a very pleasant 45-year-old female with a 35-year history of insulin dependent diabetes mellitus. She has had multiple wounds lasting for over a year at a time on her feet. The patient developed a right great toe wound three months prior to seeking help. The patient had multiple rounds of antibiotics and wound interventions, which failed to heal the wounds.

The patient was found to have coag negative staph on admission to The Wound Care Center. Vascular studies were good. Phage therapy was employed.

The wound healed in 3-1/2 weeks.

Teaching Point: The patient showed much faster healing than she had in the past as well as the ability to heal this particular wound using phage therapy.
CASE HISTORY:

NAME: G.G.
ACCT: 6949

The patient is a very pleasant 63-year-old Latin American male with diabetic foot ulcer. The patient had an ulcer on the plantar surface of his foot, which penetrated through the tendon and to the bone. The patient has been an insulin dependent diabetic for over 20 years and has severe peripheral neuropathy and severe peripheral arterial disease. He is allergic to Vancomycin and Levaquin.

The patient underwent 8 doses of Cubicin along with 20 treatments of hyperbaric oxygen. Wound care included frequent debridement, use of ultrasonic debridement, Phages and antibacterial biofilm agents. The patient had two Dermagraft grafting.

Teaching Point: This extensive plantar ulcer of the left foot despite severe hypoxia, severe peripheral neuropathy and insulin dependent diabetes mellitus for many decades showed good clinical response in four months with phage and a biofilm based wound care regimen.

In a study that reviewed 27,630 diabetic foot ulcers, 47% of the ulcers healed in 20 weeks. (Am J Med Vol 115 (8), Dec 2003, Margolis, DJ, et al.)

CASE HISTORY:

NAME: E.G.
ACCT: 10112

The patient is a very pleasant 34-year-old Latin American male with the acute onset of infected wound of his left chest. This came up rapidly over about a 10 day period. The patient does have contact with nursing home patients in his work. The wound was cultured and found to have methicillin resistant Staph Aureus, which may be community acquired. When the patient presented he was on Levaquin. The wound was draining, painful and progressive. The wound was debrided. A culture was taken and Phages applied. Cubicin 4mg/kg was started at the initial visit empirically. By day 5, the patient’s wound showed dramatic decrease in edema, erythema, drainage and the pain was basically gone. The patient went on to heal the wound in about 20 days.

Teaching Point: Multiple strategies including biofilm-effective anti-MRSA antibiotics, staph bacteriophage and a mixture of anti biofilm topicals were used on the wound and it showed rapid healing.
Case History

NAME: C.M.
ACCT: 10375

C.M. is a very pleasant 60-year-old white male with multiple sclerosis and other autoimmune disease. The patient is on high-dose prednisone and methotrexate. The patient sustained a burn from a heating pad prior to Christmas. The eschar was allowed to remain and it was felt that it would heal off. After two months the patient sought comprehensive wound care. The patient did have methicillin resistant staph aureus.

The wound was debrided February 17. Phages were applied weekly. The patient went on to complete healing in 11 weeks. This is good healing in a patient with immunosuppression.

CASE HISTORY:

NAME: R.M.
ACCT: 3392

The patient is a very pleasant 48-year-old Latin American male. The patient has had previous renal transplant and is on immunosuppressant medications. He is an insulin dependent diabetic with severe peripheral neuropathy. He has a previous left below-knee amputation. The patient was presenting with the post surgical wound starting to dehisce. Culture showed methicillin resistant Staph Aureus. The patient had a total of 42 days of Cubicin, biofilm based wound management, and phage therapy.

Teaching Point: The patient is on very potent immunosuppressants along with long-standing diabetes. Yet healing of this extensive wound took less than 3 months. This demonstrates that host-healing mechanisms remain robust despite advanced disease.
CASE HISTORY:

NAME: S.P.
ACCT: 4920

The patient is a very pleasant 67-year-old white male with venous insufficiency in the right lower extremity. The patient has a right medial ankle ulcer, which has been present for almost two decades. The patient was found to have a TCpO2 of 13 at the right foot. The wound was growing coag negative staph resistant to methicillin. A biofilm based wound management program plus the use of bacteriophage produced rapid healing.

Teaching Point: The patient’s severe, prolonged chronic venous leg ulcer complicated by peripheral arterial disease only started healing when a focused biofilm management strategy was employed.

Case History

NAME: L.P.
ACCT: 10647

L.P. is a very pleasant 55-year-old white female who was in a severe motor vehicle accident with traumatic injury to her calf. The patient had severe tissue loss. The patient developed methicillin resistant staph aureus during her hospital stay. She underwent two large surgical split thickness skin grafts. The patient continued to have swelling, heavy exudate and pain. The patient was offered limb amputation. On April 1, 2005 we saw the patient. The wound was debrided, anti biofilm agents were begun, and phage therapy instituted. By Day 5 after treatment there was significantly less drainage, no pain, the color was much better, and there was rapid epithelization of the wound. Three weeks after initiation of phage therapy, the patient had 90% coverage of the wound, no exudate and no pain with pretty much complete healing by 7 weeks.

The patient had been in the hospital for over 7 weeks with continuous IV antibiotics. IV vancomycin was given the entire time with several other IV antibiotics co-administered with the vancomycin. None of these controlled the methicillin resistant staph aureus. Treatment with phage therapy showed a very quick turnaround in the wound.
CASE HISTORY:

NAME:  F.R.  
ACCT:  9221

The patient is a very pleasant 87-year-old white female with a prolonged history of a venous leg ulcer on the right medial ankle. The patient had this for a number of years; it was painful with quite a bit of drainage. The patient showed adequate circulation and responded well to phage and a biofilm based management program. She healed in 8 weeks.

Teaching Point: Even with advanced age and prolonged chronic wound, biofilm based management shows rapid healing.

CASE HISTORY:

NAME:  C.R.  
ACCT:  10613

The patient is a very pleasant 78-year-old Latin American male status post CVA with a decubitus ulcer of the right heel. The decubitus ulcer had been present since hospitalization prior to Christmas (about four months). The patient demonstrated good oxygenation and perfusion. Culture showed *Staph Aureus* sensitive to Methicillin. The patient responded well to phage and biofilm based wound management. It healed in 4 weeks.

Teaching Point: Without other barriers to healing, wounds can heal in a very rapid manner with biofilm management strategy.
CASE HISTORY:

NAME: M.S.
ACCT: 10585

The patient is a very pleasant 84-year-old white female status post right foot surgery approximately two months prior to admission. The patient had fourth toe resection and a partial fifth ray resection. The wound dehisced approximately two weeks postop. It has failed to heal and continues to show progressive necrosis. The patient’s vascular studies were good. The wound grew out Strep Viridans. The patient is a regent for George Washington University and opted to seek care in Lubbock.

The wound healed in 7 weeks.

Teaching Point: The patient had osteomyelitis and a deteriorating foot. She was offered an amputation but opted for a comprehensive wound management program. A biofilm based wound program including phages achieved rapid healing.

CASE HISTORY:

NAME: D.S.
ACCT: 10393

The patient is a very pleasant 72-year-old white male with gout. He received an injection in his right great toe, and this became infected. The patient subsequently underwent I&D. He had over nine months of conservative management of the foot and then was referred to The Wound Care Center. The patient showed good vascular studies and had no neurologic deficits. The patient grew out methicillin resistant Staph epi. He received two weeks of Cubicin, phages and aggressive biofilm based management. X-rays had shown bony destruction and involvement of the joint. The patient, however, went on to heal quickly with aggressive surface management and anti biofilm agents.

The wound healed in 8 weeks.

Teaching Point: Wound healing is possible even with severe disease such as gout and local osteomyelitis.
CASE HISTORY:

NAME: D.W.
ACCT: 10090

The patient is a very pleasant 47-year-old white male who is a Ph.D. candidate in molecular biology. The patient underwent neck surgery and for two months postoperatively had a draining, non-healing wound. The patient was treated with Levaquin, Vancomycin and other antibiotics. The wound failed to heal. The patient was referred to The Wound Care Center.

Culture showed a *Staph Aureus* sensitive to Methicillin. Cubicin 4mg/kg was given for a total of 14 doses. This along with phages biofilm based wound management changed the wound into a rapid healing trajectory.

Teaching Point: Even though the *Staph Aureus* was sensitive to Methicillin, the biofilm phenotype of *Staph Aureus* is very resistant to antibiotic. Cubicin has an advantage of being effective on the biofilm phenotype.

Case History

NAME: E.W.
ACCT: 10472

E.W. is an 89-year-old white male status post fall with hip fracture in February of 2005. The patient developed a decubitus ulcer of the right heel. There was quite a bit of pain and drainage on admission. The patient was started on anti biofilm agents and phage therapy on 3/16/05. Eight weeks later the wound was completely healed.

The patient had advanced age with immobility and recovering from a recent surgery, and healed a significant decubitus ulcer of the heel in 8 weeks. This was better than expected healing time.
Case History

NAME: G.W.
ACCT: 9241

G.W. is a very pleasant 65-year-old black female. She presented with necrosis of the right great toe with ischemia of all the toes of her right foot. The patient’s wound continued to progress through the mid foot until December of 2004. The first week in January the patient had initial phage application. She went almost two months before phage therapy was re-instituted on a weekly basis. From March to May of 2005 the patient has shown dramatic improvement of her wound and is expected to go on to heal.

The big change in the patient’s wound was once phage therapy was started. The patient had extensive osteomyelitis of the forefoot, severe peripheral neuropathy, poor perfusion of the foot and difficulty to control diabetes mellitus. It is important to note that the patient had several doctors recommend limb amputation throughout the entire course of her wound care. So, the expectation was for below-knee amputation and the fact that the patient will heal her wound is an unexpected outcome. The most change in the patient’s wound healing was after phage therapy was instituted.

Case History

NAME: C.Y.
ACCT: 10076

C.Y. is a very pleasant 93-year-old white female with a decubitus ulcer on the right upper buttocks. The wound was necrotic and appeared to be painful to the patient. After phage therapy was started on 1/13/05, the patient had less swelling of the wound, less exudate and less necrotic material just two weeks later. A month later the patient had a clean wound bed with obvious healing. The wound went on to heal sometime in March. We saw the patient back in May for another wound and a picture of the healed wound on the right buttocks was obtained.

The patient’s healing from 1/13/05 to 2/25/05 was faster than expected for an elderly, immobile patient.
CASE HISTORY:

NAME: R.M.
ACCT: 3392

The patient is a very pleasant 48-year-old Latin American male. The patient has had previous renal transplant and is on immunosuppressant medications. He is an insulin dependent diabetic with severe peripheral neuropathy. He has a previous left below-knee amputation. The patient was presenting with the post surgical wound starting to dehisce. Culture showed methicillin resistant Staph Aureus. The patient had a total of 42 days of Cubicin, biofilm based wound management, and phage therapy.

Teaching Point: The patient is on very potent immunosuppressants along with longstanding diabetes. Yet healing of this extensive wound took less than 3 months. This demonstrates that host-healing mechanisms remain robust despite advanced disease.

Case History

NAME: A.D.
ACCT: 3608

A.D. is a very pleasant 73-year-old female with longstanding diabetes mellitus and peripheral neuropathy. The patient has severe peripheral vascular disease. She bumped her toe, causing a wound. This wound has led to exposed bone on her initial visit on 2/28/05. The patient’s wound had deteriorated despite aggressive conservative management. The patient was treated with phage cocktail and showed a steady course towards healing and was healed in 10 weeks. This is much more rapid healing than would be expected given the patient had osteomyelitis, longstanding diabetes mellitus, peripheral neuropathy, and also took over a year and a half to heal a similar wound on the other foot.

The patient was able to heal a difficult diabetic foot ulcer despite her comorbidities.
Case History

NAME: J.G.
ACCT: 3829

J.G. is a very pleasant 56-year-old Latin American male who is a Viet Nam vet. The patient did two tours of combat in Viet Nam and had significant fungal infections of his foot on and off for the years that followed. The patient developed severe diabetes mellitus and then developed an infected fissure between the great toe and second toe of the left foot. The patient had progressive necrosis of his great toe and then throughout the rest of the toes of his foot. He declined amputation. Eventually in late 2003 the patient had closure of his distal foot and effectively had an autoamputation in the transmetatarsal region. He had a functional foot and was able to walk on it. We saw the patient periodically over the next two years because of a draining and oozing necrotic wound, which was foul smelling on his distal foot. Over those two years his family physician and other physicians recommended amputation. He declined.

In January of 2005 and then again from February to July of 2005, the patient had debridement every two to four weeks with application of phage. The odor is significantly decreased. There is less necrotic material.

Repeated cultures come back with no growth or coag negative staph resistant to methicillin. He has had several other organisms including Klebsiella, Acetobacter and E. Coli present in the foot at some time over the last several years.

The nonhealing wound of the foot may be a prolonged fungal infection by nature; however, there obviously was secondary colonization with bacteria because there has been significant improvement with phage therapy over the last three months. This raises the question of a synergy between bacteria and fungus that would keep this wound open over that extensive period of time.
CP is a 57-year-old black female with a 30-year history of insulin dependent diabetes mellitus. The patient has worked as a nurse and administrator at the state school for mentally challenged and physically handicapped children. She has been extremely dedicated to her patients until her diabetes caused this severe complications. On March 24, 2005 the patient presented with a necrotic, black, draining right great toe. Three other toes were showing signs of necrosis. The patient was treated aggressively with IV antibiotics, hyperbaric oxygen and biofilm based wound care. Necrotic material was debrided on a weekly basis and by June 14, 2005 the patient’s foot had eroded back to just proximal to the metatarsal heads. The wound had stopped dying back as is apparent in picture A. There is still biofilm present and there is a pale color to the wound bed. The edge is not active.

However, the swelling in the foot, the severe pain and the copious drainage have all decreased. It was felt that the patient needed an active healing agent. On June 2, 2005 the patient had Dermagraft placed on the wound and within about 4-5 days because of odor, increased drainage and some increased pain the Dermagraft was removed. On 6/14/2005 Substance P was placed on the wound.

One month later on 7/12/05 there has been a dramatic transformation of the wound. In panel B, in the middle of the picture, is a large granulation growing up next to necrotic bone of the first metatarsal. The wound is smaller, it is obviously contracting and the necrotic material is still left on the surface of the wound. It is very soft and appears that autolysis is taking place. The wound is cleaning itself. There is no significant biofilm left and the edge is active. Panel C shows a 90-degree side view of the wound. The granulation tissue which is growing along the left side of the first metatarsal bone, which is the necrotic shiny surface at the 12:00 position, shows that the granulation tissue is raised about ¼ inch above the level of the bone and it is very active and trying to migrate and cover the bone. Panel D is a close up of the edge. The first metatarsal head, the exposed bone is still at the 12:00 position but this gives a closer view of the epithelial edge and at the 9:00 position and in the right hand corner it clearly shows migration of keratinocytes over the wound.

This is a dramatic example of the potency of Substance P. This is a patient that had nothing but a degenerative wound since March 2005. She had been offered amputation on several occasions. She failed to respond to several advanced technologies such as hyperbaric oxygen, Cubicin, dermal substitute (Dermagraft), UV light and anti biofilm agents. However, Substance P caused dramatic changes in the amount of granulation tissue, a decrease in biofilm and a decrease in necrotic tissue and a reduction in wound volume. The wound now has an active granulation bed and shows an active edge which is producing epithelialization of the wound margin. This is a dramatic response in four weeks in a diabetic foot ulcer.
CASE HISTORY:

NAME: E.G.
ACCT: 10330

The patient is a very pleasant 87-year-old female with a 3-month nonhealing surgical wound of the abdomen. The patient had an extensive abdominal surgery. She spent two weeks on IV antibiotics in the hospital even though her cultures were negative. The patient then was transferred to a long-term acute care facility. The patient was started on biofilm based wound care including phages on 2/14/05 and healed three weeks later.

The wound healed in 3 weeks.

Teaching Point: A patient with a well-perfused wound can heal very rapidly with biofilm management.