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Review Article

Skin Dysbiosis in Atopic Dogs: Is Phage Therapy an Alternative to Antibiotics?

Key words

dysbiosis;
pyoderma;
canine atopic dermatitis;
bacteriophages;
phage therapy

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Abstract: Bacterial overgrowth, also known as dysbiosis, is a common concomitant of canine atopic dermatitis. Microbial diversity is decreased and coagulase-positive staphylococci are more abundant in dogs with canine atopic dermatitis compared to healthy dogs. Antimicrobial therapy restores the diversity of the skin microbiome; however, this effect can diminish after treatment is discontinued. Therapies for skin dysbiosis have traditionally included antibiotics and antiseptic medications. Due to increasing microbial resistance to antibiotics, the era of novel antimicrobial agents for the treatment of skin infections has already begun. Recent research highlights potential new treatment options, of which one of the most promising appears to be the use of bacteriophages. Bacteriophages are viruses that can infect and kill bacteria without having negative effects on human or animal cells. This article provides an update on human and veterinary research on phage therapy as a potential approach for the treatment of bacterial infections, with a focus on the treatment of skin dysbiosis in atopic dogs. The clear clinical potential of phage therapy, its advantages and disadvantages, and the legal, biological, technical, and economic challenges it faces for its further implementation and wider application are outlined.

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Introduction

Many skin diseases in humans and animals are associated with an imbalance in the skin microbiome, recently termed dysbiosis. The subtle stability of the skin's commensal community maintains the healthy state of the skin as it affects immune system functions and can rapidly change in response to environmental changes (1). The term dysbiosis describes "an altered composition of the commensal microbiome that is detrimental to the host" (2).

Canine atopic dermatitis (cAD) is similar to human atopic dermatitis, sharing clinical signs, altered epidermal barrier function, immune system dysregulation, and microbiome dysbiosis (3-11). Atopic dermatitis is the most common chronic inflammatory skin disease in humans and dogs, affecting around 20% of children, 2–7% of adults, and 10–15% of dogs worldwide, with local prevalences varying by region (12, 13). The diagnosis of atopic dermatitis is primarily a clinical diagnosis, based on clinical signs (on the face, intertriginous regions (e.g., axillae and groin), feet, and flexor surface of joints) and the exclusion of differential diagnoses (14, 15). The updated definition of cAD describes this disease in more detail as follows: a hereditary, typically pruritic and predominantly T-cell-driven inflammatory skin disease involving interplay between skin barrier abnormalities, allergen sensitization, and microbial dysbiosis (16).

Bacterial overgrowth (i.e., dysbiosis) and bacterial skin infection (i.e., pyoderma) are secondary in atopic dogs (see figure 1) (17, 18). It is not yet entirely clear whether dysbiosis is a trigger for or consequence of atopic dermatitis, or perhaps both (19). In human atopic dermatitis, *Staphylococcus aureus* has been shown to promote lesion formation (20, 21), and toxins produced by *S. aureus* are thought to trigger or exacerbate inflammation in atopic dermatitis (22). One such toxin is delta toxin, which has recently been shown to trigger mast cell degranulation and promote inflammatory skin disease (23).

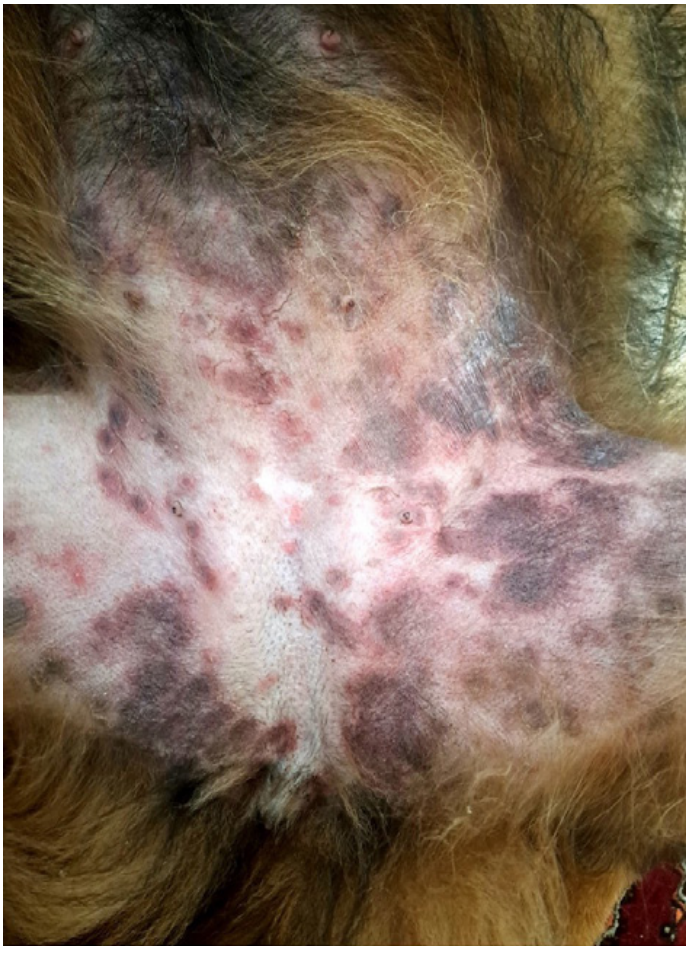

Figure1: Skin dysbiosis in a dog before treatment

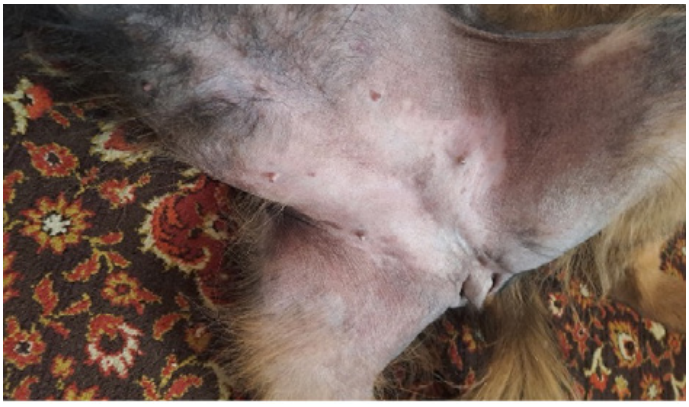

Figure 2: Clinical improvement in the same dog after treatment

The skin and nasal mucosa of humans (24-28) and dogs (9, 29-31) with atopic dermatitis are more frequently colonized with *S. aureus* and *Staphylococcus pseudintermedius*, respectively, compared with healthy patients. Veterinary studies demonstrate a significant decrease in microbial diversity and a higher abundance of coagulase-positive staphylococci in dogs with cAD (even on their apparently healthy skin) compared to healthy dogs (8, 9, 32, 33). Antimicrobial therapy can restore skin microbiome diversity (see figure 2 in comparison to figure 1, which displays dysbiosis in the same dog before treatment with antiseptic shampoo) (9, 24, 28, 34); however, the effect may diminish after treatment is discontinued (9).

Moreover, microbial resistance to antibiotics is increasing, and thus the era of novel antimicrobial agents for treating skin infections has already arrived. In line with the One Health approach, efforts should be made to efficiently manipulate the skin microbiome without the use of antibiotics, as this would significantly contribute to the prevention of bacterial resistance (35).

New options for skin dysbiosis treatment

Recent research indicates possible new treatment options (Table 1). Among the most studied new therapies is the use of bacteriophages (i.e., phage therapy). Bacteriophages are viruses that can infect and kill bacteria without negative effects on human or animal cells (72, 73). Their narrow spectrum of action avoids the main problems associated with antibiotics, such as affecting the entire microbiome by eliminating potentially beneficial bacteria, overgrowth of secondary pathogens, and the emergence of resistant bacteria (72). In addition, their ability to replicate only in target bacteria and their inability to infect mammalian cells makes their use much safer (74). The use of bacteriophages could also be more cost-effective than the use of antibiotics targeting multidrug-resistant pathogens (75). This article provides an update on human and veterinary research on phage therapy as a potential approach to the treatment of skin dysbiosis, particularly in cAD.

Phage therapy

Bacteriophages are the most common biological entity (76, 77). Similar to their bacterial hosts, bacteriophages are cosmopolitan, and an estimated 10^7 bacteriophage particles can be present in 1 mL of natural sample (78). Bacteriophages are found ubiquitously, anywhere bacteria survive, i.e., on marine and terrestrial surfaces and in soil, water, sewage, extreme environments, hospitals, and animal and human tissues (76). Several thousand bacteriophages have been described and classified according to their morphological characteristics, nucleic acid content, habitat, target bacterial species (75), and biological cycle (79). Classification based on biological cycle is the most useful, as it distinguishes between lytic (i.e., virulent) and lysogenic (i.e., temperate) bacteriophages and thus highlights differences regarding attachment to and invasion of bacteria (80). Lytic bacteriophages are of interest for the treatment of bacterial infections in humans and animals.

Bacteriophage activity is characterized by absolute specificity (75). To initiate binding, bacteriophage structures must match strain-specific variants of bacterial receptors. Both bacteriophages and bacteria are subject to constant mutations, resulting in a limited number of binding combinations,

Table 1: Alternatives to antibiotic treatment, apart from phage therapy

Antibiotic alternative	Aim of the studies	Results	Reference numbers
Probiotics	To review the current state of knowledge about gut microbial communities, advances in probiotic therapies, and whether the composition of the gut microbiome influences the composition of the skin microbiome and the pathogenesis of skin diseases.	Probiotics can help strengthen barrier function, reduce sensitivity, and modulate the immune system of the skin, enabling skin homeostasis.	36-40
Quorum quenching	To review natural anti-biofilm mechanisms recently identified in pathogenic, commensal, and probiotic bacteria.	Bioactive molecules that inhibit growth, interrupt quorum sensing, and/or prevent bacterial adhesion can prevent skin infections.	41-50
Antimicrobial peptides	To test whether various peptides can be used as diagnostic markers and for the treatment of different skin diseases.	Peptides have potential as diagnostic markers and for the treatment of skin diseases; however, further research is needed.	51-59
Gut and skin microbiome transfer (bacteriotherapy)	To investigate whether various skin diseases, such as atopic dermatitis, can be influenced by transmitted bacteria.	Transplantation of feces can suppress atopic dermatitis symptoms. Some bacterial strains can suppress *Staphylococcus aureus* in atopic dermatitis and improve inflammation.	10, 60-71

Table 2: The advantages and disadvantages of phage therapy

Advantages	Disadvantages
The ability to infect and kill bacteria without having negative effects on human or animal cells (77).	Preparation for clinical use is difficult (75, 113).
Significantly more effective than antibiotics owing to a very specific mechanism of action (75).	Bacteriophages might transfer antibiotic-resistant genes (75).
The occurrence of resistant bacteria is less likely (77).	The emergence of bacterial resistance to bacteriophages is possible (75, 123).
The entire microbiome is not affected, and potentially beneficial bacteria are not eliminated (77).	The activity of bacteriophages may be reduced by the response of the mammalian immune system to bacteriophages, and the specific bacteriophage activity for a particular bacterial strain may be absent regardless of the response of the mammalian immune system (75).
Only very few doses are needed (81, 82, 111).	
The effects are limited to accessible infection sites (83).	
Further advantages can be achieved with genetic engineering (93).	
May be less costly than antibiotic treatment (75).	

Legend: The numbers in brackets stand for the respective references

such that it is possible that a single bacteriophage binds to only a single bacterial strain (80). By contrast, in theory, no bacterium exists that cannot be lysed by at least one bacteriophage. Indeed, bacteriophages are much more effective than antibiotics due to their high specificity of action, which is their most attractive property (75). Unlike antibiotics, bacteriophages do not need to be administered in short succession over several days, as they can remain and multiply in the human or animal body for the duration of the infection (81, 82). As such, very few doses are required because the concentration of bacteriophages at the site of infection increases after the first administration (82). Unlike antibiotics, their effects are limited to the accessible site of infection (83).

Bacteriophages only kill the pathogen they can recognize, whereas antibiotics mostly have a very broad spectrum of action (75). Nevertheless, the idea of using bacteriophages in combination with antibiotics to treat bacterial infections has emerged (77). However, this can lead to antagonism because antibiotics often interfere with bacterial processes that are required for successful bacteriophage infection.

Additionally, antibiotics reduce the number of bacteria and thus decrease the ability of bacteriophages to proliferate (84, 85). By contrast, simultaneous treatment with bacteriophages and antibiotics at low (subinhibitory) concentrations can lead to so-called phage-antibiotic synergy (84-89). In an interesting study, a lytic bacteriophage was selected for *Pseudomonas aeruginosa* that uses an outer membrane porin that is part of a multidrug efflux system as a receptor, pressuring the host to mutate toward increased drug sensitivity to escape the bacteriophage (90). This is an approach that aims to resensitize multidrug-resistant pathogens to conventional antibiotics. Selected bacteriophages can be administered together with the antibiotic(s) to which they increase bacterial susceptibility (90-92). The advantages and disadvantages of phage therapy are summarized in Table 2, which clearly demonstrates the benefits of phage therapy.

Genetic engineering of bacteriophages

Genetic engineering can increase the therapeutic potential of bacteriophages (93). This can be directly achieved by modifying the host range (e.g., by homologous recombination or mutagenesis of tail fiber genes), bacteriophage infection (e.g., by deleting or deactivating genes required for lysogenic cycles), or the bacteriophage capsid (e.g., by selecting bacteriophages that can remain in the bloodstream longer). Bacteriophages can also be modified to enhance the antibacterial effects of conventional antibiotics, e.g., by enabling the production of factors that interfere with quorum sensing or enzymes that degrade biofilm matrices (84). For example, Lu and Collins modified a bacteriophage to express a biofilm-degrading enzyme that is effective against biofilm-producing *Escherichia coli* (94). Furthermore, it is possible to develop bacteriophages that combat bacterial resistance to antibiotics (75).

Bacteriophage-derived enzymes (enzybiotics)

Another therapeutic possibility is the use of bacteriophage-derived enzymes called enzybiotics. Currently, the greatest advances have been made with bacteriophage-encoded peptidoglycan hydrolases, which are highly effective against many clinically relevant pathogens. Interestingly, peptidoglycan hydrolases generally have broader specificity compared to whole bacteriophages (95, 96). Formulation options for enzybiotics range from liquids to dry powders, all of which can be stored for extended periods of time. Bacteriophage enzymes also tend to remain stable over wide pH ranges as well as at 4 °C and −80 °C (97). Junjappa et al. tested enzybiotic P128 hydrogel in 17 dogs with staphylococcal pyoderma. Daily treatment for 8 days resulted in complete recovery with no recurrence of symptoms for 2 months (96). Jun et al. tested the safety of the peptidoglycan hydrolase endolysin SAL-1 administered intravenously with increasing dosages once weekly in four dogs. Authors noted adverse side effects in 18.7% of administrations (3/16) when higher dosages were administered. Adverse events included subdued behavior, prone position, irregular breathing, vomiting, and transient changes in cardiovascular function (98). Overall, more comprehensive studies on phage therapy are needed to determine the safety and efficacy of enzybiotics.

The history of phage therapy

The first reports on bacteriophages were published in 1898, and a clear interest in using bacteriophages to treat bacterial infections in humans emerged after the researchers Twort and d'Herelle published their work in 1915 and 1917, respectively. In 1919, d'Herelle successfully used bacteriophage preparations to treat children suffering from bacterial dysentery, and phage therapy was widely used to treat bacterial infections in humans and animals in the 1930s, long before penicillin became available. Another study on phage therapy in humans was conducted and published as early as 1921 by the physician Bruynoghe and others (99).

The first program for phage therapy for human diseases was opened in what is now Tbilisi, Georgia, followed by another in Wroclaw, Poland; both programs still exist today. The G. Eliava Institute of Bacteriophages, Microbiology, and Virology in Tbilisi still houses a collection of bacteriophages isolated from environmental sources and collected in a bacteriophage bank. The collection provides a large repertoire from which bacteriophages can be either incorporated into preformulated products or selectively matched against bacterial isolates for personalized therapies (100). However, after World War II brought penicillin to the market in the early 1940s, phage therapy stopped in the West. The broad-spectrum activity of penicillin and later antibiotics against bacterial infections was considered an advantage over bacteriophages that require bacteria to express specific surface molecules to which the phage can bind. In addition, bacteria have intracellular defense mechanisms that can inactivate bacteriophages after invasion (101). The Cold War between the Eastern and Western blocs after World War II had a detrimental effect on scientific exchange between European countries and contributed to phage therapy being considered useless.

The new age of phage therapy research

Following the introduction of the last new family of antibiotics in 1987 and the emergence of resistant bacteria, researchers have once again started to focus on phage therapy. The number of clinical trials on the therapeutic use of bacteriophages is steadily increasing (101). Recent studies on human phage therapy have covered life-threatening diseases such as *P. aeruginosa* septicemia after liver transplantation (102), *P. aeruginosa* pulmonary infections in

cystic fibrosis (103), osteomyelitis in diabetic patients (104), infective endocarditis (73), and nontuberculous mycobacterium infections (105). Furthermore, reviews (100, 106) have covered more than 120 studies involving around 4000 human patients between 2000 and 2023 (107). These studies mostly reported cases of compassionate treatment. However, one prospective clinical trial involved patients with urinary tract infections treated with an adapted commercial bacteriophage drug provided by the George Eliava Institute of Bacteriophage, Microbiology and Virology, Tbilisi, Georgia (108).

Phage therapy is suitable for compassionate use due to its long-standing historical use, apparent lack of side effects, and supportive evidence from published research. Increasing media coverage and scientific articles have raised public awareness of the potential of phage therapy. However, compassionate phage therapies remain limited to a small number of experimental treatment centers or are performed by individual physicians and researchers. By establishing guidelines and increasing the availability of bacteriophages, we could enable compassionate phage therapies for more people in need (100). It is encouraging that the European Medicines Agency published guidelines on the quality, safety and efficacy of veterinary medicinal products specifically designed for phage therapy in October 2023 (109).

Phage therapy of skin dysbiosis

The case study series by DeWit et al. provide interesting clinical results regarding phage therapy of human skin dysbiosis with Staphefekt, an endolysin with endopeptidase and putative amidase activity. Rescue treatment with Staphefekt resulted in significant clinical improvement, with clinically relevant decreases in *S. aureus* abundance but not complete eradication (110). One clinical study included 24 patients suffering from chronic otitis externa for 2–58 years owing to infection with multidrug-resistant P. *aeruginosa*. Patients were randomized into two groups (of 12 patients each) treated with either a single dose of the commercial six-bacteriophage cocktail (Biophage-PA) or placebo. Significant clinical improvements and decreased *Pseudomonas* counts from baseline were observed in the phage-treated but not the placebo group. The study demonstrated bacteriophage replication in the patients and did not report any adverse reactions or local or systemic toxicity (111).

Treatment of *P. aeruginosa*-infected ear canals of dogs with the same bacteriophage cocktail used in the clinical study by Wright et al. described above (Biophage-PA) decreased clinical scores by 30% and *P. aeruginosa* counts by 67% in just 48 h. The numbers of bacteriophages increased compared to the administered dose by a mean of 99.1-fold (range 2.8–433.3-fold). No treatment-related inflammation or other adverse events were observed during the trial period (82). Recently, Silva et al. prepared a gel containing lytic bacteriophages for *S. pseudintermedius* suitable for transdermal permeation in dogs (112). A promising paper by Slovenian researchers has reported 20 staphylococcal-specific bacteriophages isolated from wastewater by enrichment with *Staphylococcus epidermidis* or *S. aureus* (113), and tests with *S. pseudintermedius* are continuing. These and other veterinary phage therapy trials are summarized in Table 3.

Commercial preparations of bacteriophages

Bacteriophages against *P. aeruginosa*, *Staphylococcus*, *Salmonella* spp., and other bacteria are commercially available in the US and EU markets (123). In Europe, Lysando AG has developed Artilysins®—endolysin-based drugs with antibacterial properties against Gram-positive and Gram-negative pathogens (97). Two commercial bacteriophage products are currently available for the treatment of skin infections, one for use in humans and the other for use in animals. Staphage Lysate (SPL)® (Delmont Laboratories, Swarthmore, PA, USA) is currently the only product approved for use in *Streptococcus canis* skin infections in the US (123). A phage lysate against *S. aureus* infections is available on the EU market under the trade name Stafal® (124). This product has been approved by the Czech State Institute for Drug Control for the topical treatment of staphylococcal skin infections in humans (125).

Limitations and challenges of phage therapy

Phage therapy can be considered the third important intervention for the treatment of bacterial infections after vaccines and antibiotics (84, 126). Although phage therapy has clear clinical potential, it faces regulatory, biological, technical, and economic challenges for its further implementation and wider adoption (84, 91).

Regulatory challenges

In the US, bacteriophages and their products (lysins) are considered drugs and should thus undergo the same process as chemical drugs to obtain regulatory approval for commercial production and use. In the EU, bacteriophages are considered medicinal products, defined by the European Medicines Agency as "a substance or combination of substances intended to treat, prevent or diagnose a disease or to restore, correct or modify physiological functions by exerting a pharmacological, immunological or metabolic action" (126). However, both US and EU regulators agree, at a minimum, that therapeutic bacteriophages should be

Table 3: Clinical trials with phage therapy in veterinary medicine

Aim of the study	Results	Reference
Evaluation of bacteriophage treatment for chronic *Pseudomonas aeruginosa* otitis in dogs.	Topical administration of the bacteriophage cocktail in the ear resulted in lysis of *P. aeruginosa* without apparent toxicity and thus has potential to be a convenient and effective treatment for *P. aeruginosa* otitis in dogs.	82
Evaluation of the antibacterial effects of endolysin P128 on *Staphylococcus* isolates responsible for canine pyoderma.	The endolysin P128 proved to be an effective and practical drug for the treatment of staphylococcal pyoderma in dogs.	96
Evaluation of the lytic activity of the staphylococcal bacteriophage phiSA012 and its endolysin Lys-phiSA012 against antibiotic-resistant staphylococcal strains isolated from infected canine skin.	Lys-phiSA012 proved to be a potential therapeutic agent for various staphylococcal infections, including methicillin-resistant *Staphylococcus pseudintermedius* infections of canine skin.	114
Evaluation of the host range of phage isolates and their ability to lyse antibiotic-resistant *P. aeruginosa* isolated from canine diseases.	The isolated phages were able to lyse many *P. aeruginosa* strains (28/39), including strains with high resistance to fluoroquinolones (4/6).	115
Investigation of the feasibility of bacteriophage therapy to combat *Escherichia coli* urinary tract infections in dogs and cats.	Most uropathogenic *E. coli* were susceptible to lysis by naturally occurring bacteriophages.	116
Investigation of the antimicrobial efficacy of nebulized phage therapy in a porcine model of pneumonia caused by *P. aeruginosa*.	Administration of large amounts of active phages by nebulization during mechanical ventilation is feasible. Rapid control of in situ infection by inhaled bacteriophages was achieved.	117
Determination of the therapeutic efficacy of the PaVOA phage compared to a phage cocktail or the cephalosporin antibiotic ceftriaxone in a model of *P. aeruginosa* skin infection in New Zealand rabbits.	Wound healing studies showed that the phage cocktail resulted in a high healing rate and accelerated skin remodeling and was more effective than ceftriaxone. The phage PaVOA had the ability to kill bacteria quickly.	118
Evaluation of the use of phage therapy for the prevention and treatment of fracture-related infections in a clinically relevant rabbit model.	The study provided a proof of concept for the use of phage therapy in a clinically relevant model for fracture-related infections.	119
Isolation and evaluation of the efficacy of bacteriophages with specific lytic activity against *Staphylococcus aureus* strains with low cure rates (biofilm-producing, multidrug-resistant, and methicillin-resistant *S. aureus* strains) in bovine mastitis.	Two phages belonging to the *Podoviridae* family with specific lytic activity against *S. aureus* were isolated from dairy farm effluents. Strains were susceptible to *Staphylococcus* phage M8 as follows: multidrug-resistant (4/20; 20%), methicillin-resistant (4/13; 31%), and biofilm-producing *S. aureus* (1/10; 10%).	120
Evaluation of the current literature on bacteriophage treatment in poultry farming.	Current literature on the treatment of various infections in poultry farms with phages was collected.	121
Two previously isolated phages were used to study the therapeutic effects against *Pseudomonas plecoglossicida* fish infections.	The mortality of fish receiving PPpW-3, PPpW-4, PPpW-3/W-4, and control fish not receiving phages was 53%, 40%, 20%, and 93%, respectively. The daily mortality of fish decreased at a constant level.	122

Legend: MDR: Multidrug resistant; MRSA: Methycillin resistant *Staphylococcus aureus*; SA: *Staphylococcus aureus*

classified as biological therapies that require compliance with well-defined regulatory frameworks and manufacturing and production requirements.

Demonstrating the efficacy of phage therapies in controlled clinical trials, of which there are only a very limited number to date, has been crucial in accelerating the development of regulatory frameworks (84), at least for veterinary medicine (109). However, the lack of definitive guidelines and regulations has made bacteriophages less attractive to pharmaceutical companies and funding agencies, making it difficult to conduct large-scale clinical trials to demonstrate the efficacy, safety, and stability of bacteriophages and their products. Although countries such as Georgia, Russia, and Poland have practiced phage therapy since its discovery, since very recently, they had no regulatory guidelines. In Poland, phage therapy is considered an "experimental treatment" as defined by the 2011 Polish Journal of Laws, Article 1634 and Article 37 of the Declaration of Helsinki (127, 128). Veterinary bacteriophage production has recently been included in the European Medicines Agency guidelines, which specifically refer to bacteriophage products. However, bacteriophage-derived products (e.g., lysins or other enzymes) or magistral formulae consisting of bacteriophages are not within the scope of these guidelines (109).

Technical and biological challenges

The technical difficulty in the production of bacteriophage drugs is that the stability of the preparations for clinical use is strictly bacteriophage-dependent and that the

stabilization strategies must be optimized individually for each bacteriophage (129). This may lead to costly and time-consuming clinical trials, which discourage the pharmaceutical industry from researching and manufacturing bacteriophage preparations (75). Isolation of bacteriophages, usually from wastewater and feces, is the first step and is relatively straightforward (130). However, before identifying a bacteriophage as a potential therapeutic agent, its specificity to a particular bacterial strain must be demonstrated. This is quite challenging because detecting the lytic capacity of a bacteriophage depends on the interactions between the bacteriophage and bacterium and how they change over time along with the dose of bacteriophages used for the assay.

The bacteriophage genome must also be sequenced and cannot contain integrase genes (as in the lysogenic type), antibiotic resistance genes, genes for phage-encoded toxins, or genes for other bacterial virulence factors (131). In addition, bacteriophage activity may be reduced due to the immune system's response to bacteriophages, and specific bacteriophage activity for a given bacterial strain may be absent regardless of the immune system's response (75). There is also the possibility of bacterial resistance to bacteriophages evolving, as bacteria possess and can evolve different mechanisms to prevent viral infections (84, 132). The development of bacterial resistance to bacteriophages can be reduced by using bacteriophage cocktails, administering a higher initial bacteriophage inoculum, or combining bacteriophages with antibiotics. A higher inoculum is associated with a lower risk of developing bacteriophage-resistant bacteria because the bacteriophages kill pathogens faster than they can replicate (133).

Although the development and marketing of bacteriophage-based products is difficult under current regulations in both the US and EU, so-called "compassionate use of phage therapy" is permitted on a case-by-case basis, particularly for patients who have not responded to conventional therapies and are unable to participate in clinical trials. In the EU, phage therapy in humans has been successfully implemented at the Ludwik Hirszfeld Institute of Immunology and Experimental Therapy in Wroclaw, Poland, and at the Queen Astrid Military Hospital in Brussels, Belgium (127).

Summary

For now, antibiotics will remain the standard clinical treatment for bacterial infections despite increasing antimicrobial resistance and multidrug-resistant infections. Nevertheless, in the near future, the search for new antimicrobial agents that act synergistically with antibiotics will be an important focus of drug development. It has already been demonstrated that subinhibitory concentrations of multiple antibiotic classes have a positive effect on bacteriophage plaque size and bacteriophage multiplication efficiency. However, a better understanding of the interactions between bacteriophages and antibiotics warrants further studies. Overall, combining bacteriophages with antibiotics can lead to synergies that should be exploited to improve antibiotic efficacy and add viable combination therapies to the clinical armamentarium.

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Disbioza kože pri atopičnih psih: ali je zdravljenje z bakteriofagi lahko alternativa zdravljenju z antibiotiki?

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Izvleček: Bakterijsko preraščanje, poimenovano tudi disbioza, pogosto spremlja atopijski dermatitis pri psih. Pri bolnih psih je v primerjavi z zdravimi opazna zmanjšana mikrobna raznovrstnost, prevladujejo pa koagulazno pozitivni stafilokoki. Protimikrobno zdravljenje sicer obnovi pestrost mikrobioma, vendar učinek lahko hitro mine, ko z zdravljenjem prenehamo. Disbiozo kože običajno zdravimo z antibiotiki in antiseptiki. Novi načini zdravljenja so zaradi naraščajoče odpornosti bakterij proti antibiotikom že našli svoje mesto v raziskavah. Med njimi se uporaba bakteriofagov zdi ena izmed bolj obetavnih potencialnih možnosti zdravljenja. Bakteriofagi so virusi, ki okužijo in ubijejo bakterije, ne da bi imeli negativen vpliv na živalske ali človeške celice. Članek povzema najnovejše raziskave v veterinarski in humani medicini s področja zdravljenja bakterijskih okužb z bakteriofagi. Še posebej se osredotoča na zdravljenje disbioze kože pri psih z atopijskim dermatitisom. V članku avtorici izpostavita jasen klinični potencial uporabe bakteriofagov pri zdravljenju, prednosti in slabosti tega zdravljenja ter pravne, biološke, tehnične in ekonomske izzive, s katerimi se raziskovalci soočajo v želji po uvedbi tega načina zdravljenja v širšo uporabo.

Ključne besede: disbioza; piodermija; pasji atopijski dermatitis; bakteriofagi; zdravljenje s fagi