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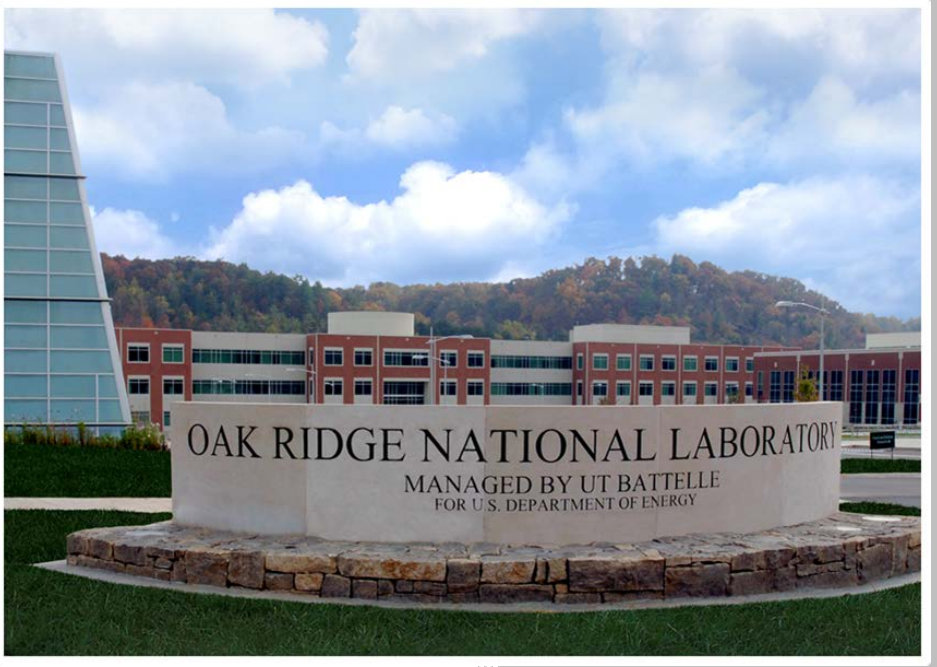
Topical Pathogens, Topical (Skin) Infections, and Cosmetics

Periodic Update (July 1, 2016 to June 30, 2017)



Anthony Q. Armstrong
Jennifer L. Goldberg
Marilyn E. Langston
Dana F. Glass-Mattie

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OAK RIDGE NATIONAL LABORATORY
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Environmental Sciences Division

TOPICAL PATHOGENS, TOPICAL (SKIN) INFECTIONS, AND COSMETICS
Periodic Update (July 1, 2016 to June 30, 2017)

Anthony Q. Armstrong
Jennifer L. Goldberg
Marilyn E. Langston
Lee Ann Wilson

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Prepared by
OAK RIDGE NATIONAL LABORATORY
Oak Ridge, TN 37831-6283
managed by
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Periodic Update (July 1, 2016 to June 30, 2017)

Executive Summary

A literature search was conducted of PubMed/Medline and MESH databases to support analyses and investigations of the relationship between microorganisms associated with human topical (skin) infections (including opportunistic pathogens) and cosmetics. Key terms for literature searches included; microbial genera and species of interest (bacteria, viruses, fungi, protozoans, parasites), opportunistic pathogens, human skin disease and infection, specific skin diseases (e.g., dermatomycoses, candidiasis, ecthyma, impetigo, etc.), surgery, infants, pregnant women, geriatric, immunocompromised, HIV and polymicrobial. The number of journal articles for defined searches was summarized and journal citations and abstracts were cataloged and incorporated into a searchable information system (MS Access). A periodic update to literature searches was completed in July 2017 and observations from the update indicate the most commonly associated bacteria with topical (skin) infections/diseases were *Staphylococcus* spp., *Streptococcus* spp., and *Pseudomonas* spp. Also, the literature searches indicate the most commonly associated fungi with topical (skin) infections/diseases were *Tinea* spp., *Candida* spp., and *Aspergillus* spp. A relative rank of occurrence of microorganisms associated with topical (skin) infections/disease in the literature citations was: Herpes simplex virus, *Staphylococcus aureus*, *Tinea* spp., *Candida* spp., Human papillomavirus, *Pseudomonas aeruginosa*, *Leishmania* spp., *Streptococcus* spp., *Aspergillus* spp., and *Treponema pallidum*. Literature searches for opportunistic microorganisms and emerging pathogens for this update identified several articles on dermatomycotic species including Candida yeasts (*Candida albicans*), dermatophytes (*Aspergillus*, and *Trichophyton*) and other opportunistic yeasts (*Malassezia* spp. and *Rhodotorula* spp.) associated with topical (skin) infections/diseases. A few of the opportunistic pathogenic Enterobacteriaceae more prevalent in citations were *Klebsiella* spp. and *Enterobacter* spp. Although the literature searches focused on microorganisms, key topical (skin) diseases noted in the citations were dermatomycoses, leishmaniasis, eczema, candidiasis, and impetigo.

Topical Pathogens, Topical (Skin) Infections, and Cosmetics

Periodic Update (July 1, 2016 to June 30, 2017)

A literature search was conducted of PubMed/Medline and MESH databases to support analyses and investigations of the relationship between microorganisms associated with human topical (skin) infections (including opportunistic pathogens) and cosmetics. Key search terms were identified by Office of Cosmetics and Colors (OCAC) of U.S. Food and Drug Administration and Human Health Risk and Environmental Analysis staff of the Oak Ridge National Laboratory (ORNL). The search terms included: microbial genera and species of interest (bacteria, viruses, fungi, protozoans, parasites), opportunistic pathogens, human skin disease and infection, human skin infections, specific skin diseases (e.g., dermatomycoses, candidiasis, ecthyma, impetigo, etc.), surgery, infants, pregnant women, geriatric, immunocompromised, HIV and polymicrobial. This report describes results from literature searches conducted of PubMed/Medline and MeSH databases covering the period of July 1, 2016 to June 30, 2017. Periodic updates of the literature searches and associated information system are planned to maintain current information.

The number of journal articles for defined search terms were compiled and summarized. In addition to collecting numbers of journal articles (total of 1,957 articles), relevant citations and associated abstracts were cataloged and incorporated into a searchable MS Access information system. There were 1,369 citations and associated abstracts added to the information system during this update. Results of the literature searches from this periodic update indicate the most commonly associated bacteria with topical (skin) infections/diseases were *Staphylococcus* spp., *Streptococcus* spp., and *Pseudomonas* spp. Table 1 lists the key bacteria identified in the literature searches and provides a relative rank of occurrence with respect to other bacteria associated with skin infections. Also, a relative rank of occurrence of each genus or species of bacteria among all key microorganisms from the literature searches is included. Occurrence of *Staphylococcus* spp. ranked second, *Streptococcus* spp. is sixth, and *Pseudomonas* spp. is eighth, when compared to all key microorganisms from this update of literature searches.

Table 2 lists the key fungi identified in the literature searches and provides a relative rank of occurrence with respect to other fungi associated with topical (skin) infections. Results of the literature searches indicate the most commonly associated fungi with skin infections/diseases are *Tinea* spp., *Candida* spp. and *Aspergillus* spp. Also, a relative rank of occurrence of each genus or species of fungi among all key microorganisms from the literature searches is included. When compared to all key microorganisms from the literature searches, *Tinea* spp. ranks third and *Candida* spp. is fourth.

Table 1. Summary of key bacteria identified in the literature searches from July 1, 2016 to June 30, 2017 for microorganisms associated with topical (skin) infections. Relative rank of each bacterial species based on occurrence in literature citations to other bacteria and all microorganisms is provided.

Search Term (Bacteria)	Relative Rank to other Bacteria	Relative Rank among all Microorganisms
Acinetobacter spp.	13	23
Bartonella spp.	18	24
Brevibacterium spp.	21	31
Burkholderia cepacia	19	34
Chlamydia trachomatis	9	14
Citrobacter spp.	20	35
Corynebacterium	17	22
Enterobacter spp.	10	26
E. coli	23	37
Klebsiella spp.	12	25
Micrococcus spp.	16	30
Moraxella spp.	15	18
Mycobacterium spp.	8	11
Neisseria gonorrhoeae	25	28
Peptostreptococcus spp.	22	36
Propionibacterium spp.	11	17
Proteus spp.	24	38
Pseudomonas aeruginosa	5	8
Serratia marcescens	14	19
Staphylococcus spp.	1	
S. aureus	2	2
S. epidermidis	6	13
Streptococcus spp.	3	
S. pyogenes	4	6
Treponema pallidum	7	10

Table 2. Summary of key fungi identified in literature searches from July 1, 2016 to June 30, 2017 for microorganisms associated with topical (skin) infections. Relative rank of each fungal species based on occurrence in literature citations to other fungi and all microorganisms is provided.

Search Term (Fungi)	Relative Rank to other Fungi	Relative Rank among all Microorganisms
Alternaria	5	21
Aspergillus spp.	3	9
Blastomyces dermatitidis	12	40
Candida spp.	2	4
Fonsecaea pedrosoi	4	16
Fusarium spp.	6	12
Malassezia spp.	9	39
Penicillium spp.	8	27
Rhodotorula spp.	10	32
Sporothrix schenckii	7	29
Tinea spp.	1	3
Trichophyton spp.	11	33

Table 3 lists the key viruses, protozoans, and parasites identified in the literature searches. A relative rank of occurrence with respect to other microorganisms associated with skin infections indicates the most common viruses associated with skin infections are Herpes simplex, Human papillomavirus (HPV), Herpes zoster, and poxvirus. *Leishmania* spp. and lice (*Pediculus* sp., *Pthirus* sp.) were commonly associated with skin infections. When compared to all key microorganisms from the literature searches, Herpes simplex ranks first, HPV is fifth, and *Leishmania* spp. ranks seventh in association with skin infections.

Table 3. Summary of other key microorganisms or parasites identified in literature searches from July 1, 2016 to June 30, 2017 for microorganisms associated with topical (skin) infections. Relative rank of each virus, protozoa, or parasite based on occurrence in literature citations to other microorganisms and to all microorganisms is provided.

Search Term (others)	Relative Rank to others	Relative Rank among all Microorganisms
Bedbugs (*Cimex* sp.)	8	*
Herpes simplex virus	1	1
Herpes zoster virus	4	20
Human papillomavirus (HPV)	2	5
Leishmania spp.	3	7
Lice (*Pediculus* sp., *Pthirus* sp.)	5	*
Mites	7	*
Poxvirus (*Molluscum contagiosum*)	6	15
Scabies *(Sarcoptes* sp.)	9	*

* Not in the ranking of top 40 microorganisms for this periodic update (see Appendix A).

In addition, Table 4 lists the top 10 microorganisms and Appendix A lists the top 40 microorganisms identified in this literature search update by rank order of occurrence in the citations compared to all other microorganisms.

Table 4. Top ten microorganisms in this periodic update (July 1, 2016 to June 30, 2017) by rank order of occurrence in the citations from literature searches of microorganisms associated with topical (skin) infections.

Microorganisms	Relative Rank to all other Microorganisms
Herpes simplex virus	1
Staphylococcus aureus	2
Tinea spp.	3
Candida spp.	4
Human papillomavirus (HPV)	5
Pseudomonas aeruginosa	6
Leishmania spp.	7
Streptococcus spp.	8
Aspergillus spp.	9
Treponema pallidum	10

Several observations from this update of the literature searches indicate the prevalence of dermatomycotic species including Candida yeasts (*Candida albicans*), dermatophytes (*Trichophyton, Aspergillus* and *Microsporum*) and other opportunistic yeasts (*Malassezia* spp. and *Rhodotorula* spp.). A few of the opportunistic pathogenic Enterobacteriaceae more prevalent in citations were *Klebsiella* spp., *Citrobacter* spp. and *Enterobacter* spp. *Acinetobacter baumanii* occurrence with topical (skin) infections was also observed in this literature update. Based on the citations from this literature search update, the occurrence of these microbes with topical (skin) infections is noteworthy.

Although the literature searches focused on microorganisms, information on skin diseases was also collected. Table 5 lists the key skin diseases identified in the literature searches, and the ranking of occurrence indicates dermatomycoses is most commonly associated with microorganisms. Leishmaniasis, eczema, candidiasis, and impetigo round out the top five skin diseases in rank order.

Table 5. Summary of key skin diseases identified in literature searches from July 1, 2016 to June 30, 2017 for microorganisms associated with topical (skin) skin infections. Relative rank of each disease based on occurrence in literature citations is provided.

Search Term (Diseases)	Relative Rank to other Diseases
Candidiasis	4
Dermatomycoses	1
Eczema	3
Erysipelas	9
Hyalohyphomycosis	7
Impetigo	5
Leishmaniasis	2
Onychomycosis	10
Tuberculosis (cutaneous)	8
Warts	6

Microbial/Topical (Skin) Infection Literature Information System

To support analyses and investigations of the relationship between microorganisms associated with human topical (skin) infections (including opportunistic pathogens) and cosmetics, the citations and abstracts from the literature searches of PubMed/Medline and MESH databases described above were assimilated in a literature inventory. Journal citations and abstracts from the literature searches were cataloged and entered into a MS Access database to support queries and additional analyses to investigate the relationships between human skin diseases and microorganisms. Within the MS Access database, queries were developed and export functionality was included to allow results from queries (lists of citations or citations including abstracts) to be exported. The information system also supports investigations of microbial skin infection occurrence and clinical information on pathogenicity. Version 3 of the Microbial/Skin Infection information system (MS Access database) was delivered to FDA OCAC on October 31, 2017 via ftp. Version 3 contains 21,033 records. Based on discussions with FDA OCAC staff, additional functionality was incorporated to allow FDA OCAC staff to periodically update the database with information provided by ORNL. As part of the future updates, literature search terms will be reviewed and updated before the search is conducted. Cursory literature searches for opportunistic or emerging microbial pathogens not currently included in the Microbial/Skin Infection information system will be added as requested by FDA OCAC.

Appendix A.

Listing of microorganisms identified in literature searches of PubMed/Medline and MESH databases for microorganisms associated with topical (skin) infections by rank order of occurrence in the literature citations for the periodic searches.

Microorganism	Relative Rank to all other Microorganisms		
	May 31, 2015	June 30, 2016	June 30, 2017
Herpes simplex virus	1	1	1
Staphylococcus aureus	2	2	2
Tinea spp.	3	3	3
Leishmania spp.	4	5	7
Candida spp.	5	4	4
Pseudomonas aeruginosa	6	6	8
Streptococcus pyogenes	7	7	6
Mycobacterium spp.	8	8	11[a]
Fusarium spp.	9	10	12
Human papillomavirus (HPV)	10	9	5
Poxvirus (*Molluscum contagiosum*)	11	16	15
Sporothrix schenckii	12	25	29
Treponema pallidum	13	12	10
Chlamydia trachomatis	14	17	14
Staphylococcus epidermidis	15	13	13
Bartonella spp.	16	22	24
Moraxella spp.	17	20	18
Aspergillus spp.	18	11	9
Propionibacterium spp.	19	15	17
Penicillium	20	28	27
Fonsecaea pedrosoi	21	14	16
Serratia marcescens	22	21	19
Corynebacterium	23	18	22
Neisseria gonorrheae	24	29	28
Micrococcus spp.	25	31	30
Alternaria	26	23	21
Enterobacter spp.	27	30	26
Brevibacterium spp.	28	27	31
Trichophyton	29	26	33
Acinetobacter spp.	30	24	23
Peptostreptococcus spp.	31	34	36
Klebsiella spp.	32	32	25
Herpes zoster virus	33	19	20

E. coli	34	35	37
Rhodotorula spp.			32[b]
Burkholderia cepacia	36	33	34
Citrobacter spp.			35[b]
Malassezia spp.	38	36	39
Proteus spp.	39	37	38
Blastomyces dermatitidis			40[b]

[a]Highlighted cells indicate major differences from previous ranking.

[b]*Rhodotorula* spp., *Citrobacter* spp., and *Blastomyces dermatitidis* are new to the ranking of the top 40 microogranisms for this periodic update.