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Ocular Pathogens, Eye Infections, and Cosmetics

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

Anthony Q. Armstrong
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October 2017

OAK RIDGE NATIONAL LABORATORY
MANAGED BY UT-BATTELLE FOR THE US DEPARTMENT OF ENERGY

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Environmental Sciences Division

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OAK RIDGE NATIONAL LABORATORY
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Executive Summary

A PubMed literature search was conducted to support analyses and investigations of the relationship between microorganisms associated with human eye infections (including opportunistic pathogens) and cosmetics. Key terms for PubMed literature searches included; microbial genera and species of interest (bacteria, viruses, fungi, protozoans, parasites), opportunistic pathogens, human eye disease and infection, human ocular infections, specific eye diseases (keratitis, conjunctivitis, etc.), eye accidents, eye surgery, contacts, 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 the literature searches was conducted in July 2017 and observations from the update indicate the most commonly associated bacteria with eye infections/diseases were *Staphylococcus* sp., *Chlamydia* sp. and *Pseudomonas* sp. Also, the literature searches indicate the most commonly associated fungi with eye infections/diseases were *Fusarium* sp., *Aspergillus* sp. and *Candida* sp. A relative rank of occurrence of microorganisms associated with eye infections/disease in the literature citations was; *Staphylococcus aureus, Chlamydia trachomatis*, Cytomegalovirus, Herpes zoster virus, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Acanthamoeba* sp., *Fusarium* sp., *E. coli* and *Mycobacterium tuberculosis*. Literature searches for opportunistic microorganisms and emerging pathogens for this update identified several articles on fungi, *Bacillus* sp. (primarily *B. cereus*), *Haemophilus influenzae* and Human Papillomavirus (HPV) associated with eye infections/diseases. Although the literature searches focused on microorganisms, key eye diseases noted in the citations were keratitis, conjunctivitis, corneal ulcers, endophthalmitis and keratoconjunctivitis.

Ocular Pathogens, Eye Infections, and Cosmetics - Periodic Update (July 1, 2016 to June 30, 2017)

A PubMed literature search was conducted to support analyses and investigations of the relationship between microorganisms associated with human eye infections (including opportunistic pathogens) and cosmetics. Key search terms were identified by U.S. Food and Drug Administration, Center for Food Safety and Nutrition (CFSAN), Office of Cosmetics and Colors (OCAC) and Oak Ridge National Laboratory (ORNL) Human Health Risk and Environmental Analysis staff. The search terms included; microbial genera and species of interest (bacteria, viruses, fungi, protozoans, parasites), opportunistic pathogens, human eye disease and infection, human ocular infections, specific eye diseases (keratitis, conjunctivitis, etc.), eye accidents, eye surgery, contacts, 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 the 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 1643 articles), relevant citations and associated abstracts were cataloged and incorporated into a searchable MS Access information system. There are 1054 citations and associated abstracts added to the information system during this update. Results of the literature searches for this periodic update indicate the most commonly associated bacteria with eye infections/diseases are *Staphylococcus* sp., *Chlamydia* sp., and *Pseudomonas* sp. 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 eye 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* sp. and *Chlamydia* sp. ranked first and second respectively when compared to all key microorganisms from the literature searches. Results from literature searches of opportunistic microorganisms for this update identified several articles on fungi, *Bacillus* sp. (primarily *B. cereus*), *Haemophilus influenzae* and Human Papillomavirus (HPV) associated with eye infections.
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 eye infections. Results of the literature searches indicate the most commonly associated fungi with eye infections/diseases are *Fusarium* sp., *Aspergillus* sp. and *Candida* sp. 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, *Fusarium* sp. ranks #8 and *Candida* sp.is #13.

Table 3 lists the key virus, protozoa, and parasites identified in the literature searches. A relative rank of occurrence with respect to other microorganisms associated with eye infections indicates the most common viruses associated with eye infections are Cytomegalovirus and Herpes zoster virus. *Acanthamoeba* sp. and *Onchocerca* sp. were commonly associated with eye infections as well as the parasite *Toxoplasma gondii* which was the fourth most commonly identified in this group. When

compared to all key microorganisms from the literature searches, Cytomegalovirus ranks #3, Herpes zoster virus is #4, *Acanthamoeba* sp. is #7, and *Toxoplasma gondii* is #11 in association with eye infections.

Table 1. Summary of key bacteria identified in literature searches of PubMed from July 1, 2016 to June 30, 2017 for microorganisms associated with eye 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 sp.	14	19
Alcaligenes faecalis	20	36
Bacillus		
B. cereus	7	14
B. subtilis	19	33
Chlamydia trachomatis	2	2
Corynebacterium	9	15
E. coli	5	9
Klebsiella sp.	8	12
Moraxella sp.	17	26
Mycobacterium tuberculosis	6	10
Neisseria gonorrhea	10	17
Proteus mirabilis	13	20
Pseudomonas aeruginosa	3	5
Serratia marcescens	12	18
Staphylococcus		
S. aureus	1	1
S. epidermidis	4	6
S. haemolyticus	18	32
Streptococcus		
S. pneumonia	16	27
S. pyogenes	15	25
Treponema pallidum	11	21

Table 2. Summary of key fungi identified in literature searches of PubMed from July 1, 2016 to June 30, 2017 for microorganisms associated with eye infections. Relative rank of each fungus 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	7	28
Ascomycota	5	23
Aspergillus		
A. fumigatus	4	24
A. flavus	2	16
A. niger	9	31
Candida albicans	3	13
Cladosporium	10	34
Curvularia	6	30
Fusarium sp.	1	8
Penicillium	8	29

Table 3. Summary of other key microorganisms identified in literature searches of PubMed from July 1, 2016 to June 30, 2017 for microorganisms associated with eye 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
Acanthamoeba sp.	3	7
Cytomegalovirus	1	3
Herpes zoster virus	2	4
Leishmania sp.	6	35
Onchocerca sp.	5	22
Spirometra sp. (previously *Sparganum* sp.)	7	37
Toxoplasma gondii	4	11

In addition, Table 4 lists the top 10 microorganisms identified in this update literature search 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 PubMed for microorganisms associated with eye infections.

Microorganisms	Relative Rank among all Microorganisms
Staphylococcus aureus	1
Chlamydia trachomatis	2
Herpes zoster virus	4
Cytomegalovirus	3
Pseudomonas aeruginosa	5
Staphylococcus epidermidis	6
Acanthamoeba sp.	7
Toxoplasma gondii	8
Fusarium sp.	9
E. coli	10

Several observations from this update of the literature search indicate prevalence of fungal related eye infections in citations when compared to previous updates. Emerging microbes of interest based on more prevalence in citations were *Bacillus* sp. (primarily *B. cereus*), *Enterobacteriaceae* (*Enterobacter gergoviae*), HPV and *Haemophilus influenzae*. Based on the citations from this literature search update, the occurrence of these microbes with eye infections is noteworthy.

Although the literature searches focused on microorganisms, information on eye diseases was also compiled. Table 5 lists the key eye diseases identified in the literature searches and the ranking of occurrence indicates keratitis is most commonly associated with microorganisms. Keratitis, conjunctivitis, corneal ulcers, endophthalmitis and keratoconjunctivitis round out the top five eye diseases in rank order that are associated with eye infections.

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

Search Term (Diseases)	Relative Rank to other Diseases
Anterior Uveitis	7
Blebitis	11
Blepharoconjuctivitis	15
Conjunctivitis	2
Corneal Erosion	12
Corneal Ulcers	3
Endophthalmitis	4
Iritis	9
Keratitis	1
Keratoconjunctivitis	5
Keratomycosis	8
Ocular Rosacea	10

Orbital Cellulitis	6
Preseptal Cellulitis	14
Scleritis	13

Microbial/Eye Infection Literature Information System

To support analyses and investigations of the relationship between microorganisms associated with human eye infections (including opportunistic pathogens) and cosmetics, the citations and abstracts from the PubMed literature searches described above were assimilated in a literature inventory. Journal citations and abstracts from the PubMed literature searches were cataloged and entered into a MS Access database to support queries and additional analyses to investigate the relationships between human eye 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 eye infection occurrence and clinical information on pathogenicity.

Version 5 of the Microbial/Eye Infection information system (MS Access database) was delivered to FDA OCAC on September 25, 2017 via ftp. Version 5 contains 11,883 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. Quick turnaround literature searches for opportunistic microbial pathogens that are not currently included in the Microbial/Eye Infection information system will be added as requested by FDA OCAC.

Appendix A.

Listing of microorganisms identified in literature searches from PubMed for microorganisms associated with eye infections by rank order of occurrence in the literature citations for the periodic searches.

Microorganism	Relative Rank to all other Microorganisms			
	March 31, 2015	October 31, 2015	June 30, 2016	June 30, 2017
Chlamydia trachomatis	1	1	1	2
Staphylococcus aureus	2	2	2	1
Herpes zoster virus	3	3	3	4
Pseudomonas aeruginosa	4	4	5	5
Staphylococcus epidermidis	5	5	6	6
Toxoplasma gondii	6	6	8	11
Cytomegalovirus	7	7	4	3
Acanthamoeba sp.	8	8	7	7
Onchocerca sp.	9	10	17	22
Fusarium sp.	10	9	9	8
Candida albicans	11	11	20	13
E. coli	12	13	12	9
Klebsiella sp.	13	12	10	12
Mycobacterium tuberculosis	14	14	13	10
Bacillus cereus	15	15	11	14
Aspergillus fumigatus	16	16	22	24
Corynebacterium	17	17	14	15
Moraxella sp.	18	18	27	26
Serratia marcescens	19	19	16	18
Streptococcus pyogenes	20	20	26	25
Proteus mirabilis	21	21	18	20
Neisseria gonorrhea	22	22	15	17
Ascomycota	23	23	23	23
Aspergillus flavus	24	24	21	16
Curvularia	25	25	28	30
Alternaria	26	26	29	28
Penicillium	27	27	30	29
Treponema pallidum	28	29	24	21
Acinetobacter sp.	29	28	19	19
Aspergillus niger	30	30	31	31
Streptococcus pneumonia	31	31	25	27
Staphylococcus haemolyticus	32	32	32	32
Leishmania sp.	33	33	34	35
Cladosporium	34	34	35	34
Spirometra sp. (previously *Sparganum* sp.)	35	35	36	37
Bacillus subtilis	36	36	33	33
Alcaligenes faecalis	37	37	37	36

*Highlighted cells indicate major differences from previous rankings.