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Eye infection

Polymicrobial infection and the eye

S Tuft

Has important management implications

Treatment for infection is typically determined following an assessment of the clinical features of the disease, the likely causative pathogen, and the spectrum of activity of the available drugs. This treatment can be modified subsequently when the results of clinical investigations are available. It would simplify management if each infection were caused by a single pathogen that was amenable to treatment with one antimicrobial agent. Unfortunately, multiple pathogens may be present and they may interact to confuse the clinical picture. Simultaneous or sequential polymicrobial infection can occur, both with similar organisms (for example, different species of bacteria) and with organisms from completely separate kingdoms (for example, bacteria, fungi, acanthamoeba) or non-living viruses.[1] The presence of a polymicrobial infection has important management implications because it will modify the clinical course of the disease and the anticipated response to treatment. With the exception of topically applied antiseptics, the antimicrobials used in ophthalmology do not have a significant activity across groups of potential pathogens. Polymicrobial infection may be missed unless specific investigations are performed to identify all potential participants in the disease process, and protocols may need to be developed for effective treatment. Although polymicrobial infection in ophthalmology has been reported previously the clinical impact has received little attention (table 1).

The reported incidence of ocular polymicrobial infection varies widely. In part this is a result of differences in the criteria used to define an organism identified by microscopy or in culture as either a pathogen or a contaminant. Polymicrobial isolates from cases of suppurative keratitis are reported in up to a third of cases, the majority due to multiple bacterial species.[2] Polymicrobial isolates have also been reported from 33% of scleral explants removed for suspected infection.[3] Abscesses potentially contain anaerobic conditions and they typically yield a variety of the organisms found on skin or mucous membranes,[4] with polymicrobial infection reported from 45% of cases of dacryocystitis[5] and sub-periosteal abscess.[6] In this issue of the *BJO* Pate *et al* (p 289) report that 20% of positive cultures from cases with fungal keratitis were co-infected with bacteria. There was a propensity for this to occur with candida isolates co-infected with staphylococcal bacteria, with a risk of polymicrobial infection that was approximately three times greater than with infection with filamentous fungi. They suggest that this may be because the bacteria are protected within the biofilm produced by the candida.[7] Whether this synergism contributes to the generally poor prognosis for fungal keratitis is unknown. In their laboratory they have also established criteria based on multiple identification by microscopy or culture to try to define whether an isolate is likely to be a pathogen. These criteria reflect the bacterial load in the wound but do not give any weight to the virulence of the organism, despite the fact that the presence of some types of organisms is usually considered significant if identified by any means.[8 9] Their results also confirm that the use of multiple investigational techniques and media may be required to identify all possible pathogens.[1]

Polymicrobial infections can become established by various means. When multiple organisms are present in the environment, trauma can result in inoculation and simultaneous (parallel) infections. In contrast, sequential or super-infection with a second organism may occur in an eye that has been put at risk by another pathogen. For example, a herpetic corneal ulcer can allow microbial adherence by bacteria or fungi that can then also cause infection, particularly if the local immune response has been inhibited with topical steroid. In this situation the opportunistic infection may be with an unusual

Table 1 Principal polymicrobial infections and ocular disease

	Causal agent	Association	Disease
Simultaneous infection	*Acanthamoeba*	Bacteria	Keratitis
	Fungi	Bacteria	Keratitis
Sequential infection	HTLV-I, II, III	Herpes virus, bacteria, fungi	Keratitis
		Cytomegalovirus	Retinitis
		Toxoplasmosis	Retinitis
		Cryptococcus	Retinitis, uveitis
		Pneumocystosis	Retinitis, uveitis
		Microsporidium	Keratitis
	Herpes simplex virus	Bacteria, fungi	Keratitis
	Herpes zoster virus	*Strep pyogenes* (Gp A)	Invasive skin necrosis (necrotising fasciitis)
	Measles virus	Herpes simplex	Keratitis
Synergistic infection	*Onchocerca volvulus*	*Wolbachia* spp	Onchocerciasis
Associated infection	*Chlamydia*	*Gonococcus, Treponema*	Conjunctivitis
Microbial interference	None identified to date		

organism.[10] Systemic immunosuppression by drugs or as the result of virus induced immunosuppression by the human T lymphotropic virus or the measles virus can also allow opportunistic infections to become established at the ocular surface and in the retina.[11–13]

In polymicrobial infection several distinct interactions between organisms can result in synergy of effect. The primary organism can create a ''niche'' for a second organism that either predisposes the host to further infection or enables a normally non-pathogenic organism to cause disease. Alternatively, the primary organism may cause tissue necrosis, provide a sequestered environment, or supply specific metabolic needs such as tissue hypoxia or immunosuppression.[8] Finally, interactions within a biofilm may permit persistent infection in the presence of a foreign body such as explant or contact lens.[3 7 14] The adverse effect of polymicrobial infection is illustrated by the increased risk of vascularisation and prolonged healing if acanthamoeba keratitis is associated with bacterial co-infection.[15]

Although there are numerous examples of amplification of disease and synergy as a result of polymicrobial infection, examples of symbiosis are rare in both general microbiology and ocular disease. Non-streptococcal necrotising fasciitis of the ocular adnexa is probably a synergistic infection.[16] In onchocerciasis it is now recognised that a rickettsiaceae (*Wolbachia* spp) lives symbiotically within the microfilaria filarial worm *Onchocerca volvulus*.[17] The presence of the bacterium is important for the fertility of the female filarial worm, and treatment of *Wolbachia* with doxycycline offers an indirect target for treatment of onchocerciasis. Microbial interference, in which colonisation by one organism prevents colonisation by a second organism,[18] is rare and has not been described in ophthalmology.

Although it is not a true polymicrobial infection the presence of some groups or organisms may be linked by common exposure, such that the isolation of one of the group should prompt active investigation for other commonly associated organisms at the same site or at a remote site. For example, isolation of *Chlamydia* from patients with follicular conjunctivitis should trigger investigated for the carriage of *Neisseria gonorrhoeae* and *Treponema pallidum*, and both hepatitis B and C are commonly present with HTLV in patients with HIV-AIDS.

There are numerous practical implications of polymicrobial infection. If treatment is targeted at the first pathogen identified, and if a polymicrobial infection is not considered or is missed, the outcome may be adversely affected. One should have a high index of suspicion for possible polymicrobial infection, particularly if the clinical course of the disease is unusual, and ensure that the initial investigation is appropriate to identify all clinically relevant potential pathogens. If there is deterioration after an early period of improvement a polymicrobial infection should also be considered and treatment modified appropriately. One should ensure that the spectrum of activity of the selected treatment covers all the likely pathogens, and consider adding specific antimicrobial agents if necessary. For some polymicrobial infections, especially those associated with HIV-AIDS, treatment of the primary infection will aid resolution of the opportunistic infection and improve the prognosis.

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