Moraxella

Moraxella, down but not out—the eye bug that won't go away

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Neisseria→Branhamella→Moraxella→???

Ocular infections caused by *Moraxella* sp have an interesting social history, often with somewhat unsavoury associations. To begin with, *Moraxella* is a true ophthalmic pathogen, an “eye bug” par excellence that can occasionally be found colonising the nasopharynx and on other mucous membranes,¹ although rarely causing infections in other parts of the body. Originally isolated by Morax² and Axenfeld³ in 1896 and 1897, respectively, from patients with angular blepharitis, the organism was at first called the diplobacillus of Morax–Axenfeld, and later came to be known as *M lacunata*. In 1899, Petit⁴ isolated a similar organism from a central corneal ulcer that he called, not surprisingly, the diplobacillus of Petit. This organism was later renamed *M liquefaciens*. A third species was also isolated, *M nonliquefaciens*, which was felt to be more benign, rarely causing keratitis or severe ocular infections. These rather arbitrary divisions into different species were based on the degree of liquefaction produced by the organisms when they were inoculated on to coagulated human serum, known as Loeffler's medium.

In 1900, *Moraxella* sp was reported by several authors to be the most common cause of conjunctivitis in Europe.⁵ But by the middle of the century, Thygeson and Kimura,⁶ Jones *et al*⁷ and others reported that the organism could be cultured in ≤1% of all cases of conjunctivitis, an apparent dramatic decline in the prevalence of *Moraxella* ocular infections in the population. The organism was down but still not out. A common view at the time was that different species of the organism selectively grew only in specific areas of the external eye. Angular blepharitis was thought to be caused by *M lacunata*, whereas corneal ulcers were said to be almost always caused by *M liquefaciens*.⁸ This view persisted until 1980, when Baum *et al*⁹ reported 20 cases of *Moraxella* keratitis in 19 patients from a derelict population in New York city. *M lacunata* was grown from the ulcers of only two of the patients, whereas *M liquefaciens* was cultured from seven, *M nonliquefaciens*

from eight and mima *Moraxella* from three. In effect, Baum showed that the species of the organism causing corneal ulceration was irrelevant. What mattered clinically was that the bacteria produced destructive proteases and endotoxins, and this ability was exhibited by all of the species in question.

Baum *et al* also reiterated what was believed to be one of the more unsavoury characteristics of *Moraxella* organisms, their apparent predilection for colonising alcoholics and derelicts and causing corneal ulceration almost exclusively in these patients. We now know that this is not necessarily the case. *Moraxella* can cause keratitis in any compromised host, including those dependent on alcohol, but normal people can be infected as well, especially if they have a persistent corneal epithelial defect or corneal pathology that enhances their susceptibility. *Moraxella* is an opportunist. It can be cultured from many sites in the body, but it rarely causes clinical disease unless it infects the eye—its preferred host.

The organism is amazingly indolent from the laboratory point of view. Most biochemical tests performed on the bacterium are negative; however, it does share one positive test in common with its more virulent relatives. Similar to *Pseudomonas* sp, *Neisseria meningitidis* and *N gonorrhoeae*, the *Moraxella* genus is oxidase positive. Like them it is also Gram negative, and sometimes its large pink diplobacilli, which have been described as looking like big box cars, are so pleomorphic that it is possible for a microbiologist to confuse the morphology with that of *Neisseria* sp. This raises an interesting question about how closely these organisms are actually related.

A case in point is the curious family history of *N catarrhalis*. The runt of the *Neisseria* genus from birth, *N catarrhalis* never felt at home. His big pushy sisters, *N gonorrhoeae* and *N meningitidis*, produced their own diseases and occasionally even thumbed their noses at antibiotic treatment. To be sure, *N catarrhalis* was oxidase positive and liked to grow on chocolate agar, but he could never figure out how to use

sucrose, not to mention dextrose or maltose; and he had no disease that he could call his own except for the occasional opportunist eye infection. This sad state of affairs was finally set right by a kindly well-meaning taxonomist,⁹ whose breed should be recognised as the social workers of microbiology. *N catarrhalis* was moved to the *Branhamella* genus and rechristened *B catarrhalis*. For awhile things went well, but unfortunately *B catarrhalis* just never fitted in with the kindly *Branhamella* clan. There was no excitement at all compared with his boisterous *Neisseria* family, and *B catarrhalis* slowly languished as runts and misfits often do. To remedy this unhappy situation the taxonomists moved him once more, this time to the *Moraxella* genus. He was christened yet again (one would hope for the last time) as *M catarrhalis*, and there he remains in the *Moraxella* family to this day. Admittedly, it's a boring existence, causing only the occasional acute or chronic catarrhal conjunctivitis, the odd opportunist corneal ulcer and the rare pseudo membrane.⁸ It's not much of a life, but it may be all that a bug like *M catarrhalis* can ever expect as a temporary guest in the *Moraxella* clan. Of course, the issue of his true paternity is still not decided, even though it is now possible to determine it with DNA testing. When that occurs, and the genetically related relatives of *M catarrhalis* are finally tracked down, it is very likely that he may have to pack up and move again. C'est la vie. It is a bug-eat-bug world out there.

My apologies for the frivolity of this digression and any microbiological disrespect it might imply, but the point is to illustrate how the association of an apparently docile bacterium with truly pathological relatives may explain how that organism can produce a virulent clinical infection. In the case of corneal ulcers caused by *Moraxella* sp, even though the organism is described as being clinically indolent it can also be extremely destructive to corneal tissue. The keratitis it produces usually deepens rather than spreading peripherally, and the associated inflammatory response can be so hyperacute that a hyphema forms within a hypopyon—a clinical feature that is usually seen in ulcers infected with much more virulent bacteria. *Moraxella* is also paradoxically sensitive to most antibiotics, and resistant strains rarely develop. Yet the clinical course of a *Moraxella* corneal ulcer can be uncommonly protracted and fraught with many complications. Even though the ulcer is almost always rapidly sterilised in the first few days of treatment, the destruction of the corneal tissue continues unabated, sometimes

for weeks, requiring the addition of topical corticosteroids and other adjunctive therapeutic agents to prevent severe corneal necrosis and perforation. Even in its response to treatment it can be said that a *Moraxella* corneal ulcer often appears to be down but it is never out. Once the diagnosis is confirmed with positive corneal scrapings and cultures, the truly difficult part begins: the battle to limit the necrosis of the corneal tissue that ultimately leads to scarring and visual disability. In this sense *Moraxella* can truly become the bug from hell.

My congratulations to Das *et al*¹⁰ for providing in this issue of the *British Journal of Ophthalmology* (see p 1236) an excellent analysis of 95 cases of culture-proved *Moraxella* keratitis. The authors have shown that multiple local ocular risk factors predispose a person to *Moraxella* keratitis. This was the case in 78 of the 95 eyes (table 1 in Das *et al*¹⁰). Systemic risk factors such as diabetes, rheumatoid arthritis and leprosy were also mentioned in 13 patients (table 2 in Das *et al*¹⁰). It is of interest that terms

such as alcoholic and derelict were not mentioned even once in this article as predisposing a person to *Moraxella* keratitis. This series of patients appears to finally put to rest the myth that *Moraxella* keratitis is a disease seen only in those who are alcoholic, derelict, or down and out. It is obvious from this excellent study that the organism is merely an opportunist looking for a compromised host, and its preferred host can be any cornea that is locally compromised for any number of reasons.

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ILM peeling

Relationship between macular hole size and the potential benefit of internal limiting membrane peeling

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Macular hole size is a predictor for anatomical closure. Holes >400 µm in aperture size on an OCT scan are more likely to close when ILM is peeled

The development of surgical repair for macular hole surely ranks among the most important advances in vitreoretinal surgery over the past 15 years. Since the seminal report of Kelly and Wendel¹ in 1991, we have witnessed a remarkable evolution of surgical techniques, resulting in improved anatomical success, such that we can now confidently inform our patients that they have at least a 90% chance of anatomical closure of the macular hole. Despite this progress, two major challenges remain: firstly, to safely refine our surgical technique to allow anatomical closure of all holes and secondly, to improve the visual outcomes that all too often do not replicate the anatomical results. The resolution of

these challenges constitutes the future of further advances in macular hole surgery. Various surgical techniques have been used to try to increase the rate of macular hole closure, including biological adjuncts such as serum, platelet extracts and growth factors.^{2–4} More recently, surgical dissection of the internal limiting membrane (ILM) or “ILM peeling” has been introduced. The role of ILM peeling is now at the epicentre of the most important controversies in macular hole surgery.^{5–6} Although several reports suggest that ILM peeling increases the rate of anatomical closure in selected patients, other reports disclose high closure rates without ILM peeling.^{7–10} The mechanism by which ILM peeling facilitates macular hole

closure is unknown, but may include the release of residual tangential traction on the edges of the macular hole or stimulation of a glial healing response. Some authors suggest that ILM peeling adversely affects visual outcome despite anatomical closure.^{11–12} Others believe that ILM peeling may minimise or even eliminate the need for postoperative facedown (prone) positioning.¹³ However, there is increasing evidence that the risks of ILM peeling are technique dependent. The use of indocyanine green (ICG) to stain the ILM has been reported to cause decreased vision and visual field defects.^{14–17} Therefore, the issue is not only when but also how to peel the ILM. In this issue of the journal, Tadayoni *et al*¹⁸ (see p 1239) provide information on the relationship between macular hole size as measured by ocular coherence tomography (OCT) and the benefits of ICG-assisted ILM peeling. As with previous reports, they found that hole size is a predictor for anatomical closure.^{19–20} More importantly, they determined that holes >400 µm in “aperture size” on OCT were more likely to close when the ILM was peeled (73% closure without ILM peeling compared with 100% closure with ILM peeling). For macular holes <400 µm in size, there was 100% anatomical closure regardless of whether or not ILM peeling was carried out. The authors conclude that ILM peeling should be reserved for larger holes. This information is useful to