Speeding the healing of corneal ulcers

IT was the end of a great meeting in Denmark. I had been lecturing to Danish veterinary ophthalmologists and enjoying their great hospitality too. But the best thing about such visits is the contacts made and the new ideas which make their mark.

A man I’d never come across before made his way to the front of the lecture theatre and produced from his pocket a tiny tube of clear gel (Figure 1). This, he told us, had been shown to speed the healing of corneal ulcers in a recent scientific study in rabbits, a copy of which he held in his other hand.

It was a polymethylated hyaluronic acid gel which formed a scaffold across the ocular surface, speeding the healing of epithelial and stromal ulcers. Had this been tried in a clinical setting I asked — and did he have any I could take and try? Only this one tube he said apologetically. Never mind — one was better than none, so I whipped it out of his hand and asked who had come up with the idea in the first place. A good end to an excellent weekend conference!

How ironic then that Monday morning brought a referral of a dog with a long-standing stromal ulcer which showed no signs of healing (Figure 2). My normal treatment would have been a surgical manoeuvre — a pedicle graft or a hood flap. But this elderly dog was not a good anaesthetic risk and hey — I had the answer in my pocket — or did I?

A drop of this gel twice daily should have a beneficial effect, I told the owner, but in these days of evidence-based medicine here was a treatment for which I really had no evidence at all, but for the rabbit paper I had printed out for myself by now. I kept in touch with the dog’s owner who said that the animal seemed more than happy to have the drop of soothing gel in his eye, and 10 days later I was delighted to see a healed cornea.

Granted, there was some corneal oedema and migrated pigment onto the surface but the dog had some vision in the eye and the owner was over the moon. In fact, he had only used half of the tiny tube and brought the rest back for my next case. Having had such success with his dog, he wanted to share the gel with another, knowing that it was the only tube I had!

And sure enough, the next week along came a cat with a similar non-healing stromal ulcer (Figure 3). Here the problem preventing us from going to surgery was a financial one: the owner had come to us through our RSPCA clinic run by the vet school to provide help for owners with insufficient funds for normal veterinary care and a wonderful supply of first opinion cases for the students.

In this little cat it was only seven days before the owner triumphantly brought the patient back just delighted with the result. A completely healed cornea with a tiny circle of opacity in place of what a week before had been one heck of a mess!

By now I had tracked down Richard Koehn of Sentrx Animal Health in Salt Lake City, Utah. I think he was somewhat surprised to hear me bouncing with excitement and enthusiasm about his new product, and asking for more so that we could perform a proper clinical study.

These two cases, with ulcers which hadn’t healed for 35 and 28 days but then resolved in 10 and seven days respectively, were almost statistically significantly different in healing time on their own at p=0.055 in a paired T test, but we clearly needed more cases to evaluate.

**Remarkable results**

Soon more tubes of gel were winging their way over the pond to me and our study could begin in earnest. The results were remarkable. In the first 15 cases, ulcers which had been referred after failing to heal for an average of 25 days only took 13 days, again on average, to heal. The statistical significance of this was really substantial.

We had started to call this gel DMD — David’s Magic Drops — as they seemed to have a completely novel effect on these ulcers, many of which would have gone to surgery for a conjunctival pedicle graft or similar in the past but now could just be treated with this gel. It is soon to be marketed by Bayer — not, sadly, as DMD but as Sentrx Remend, the name it comes with from its Salt Lake City originators.

“Wait a moment,” I hear other ophthalmologists saying. This sounds a bit dangerous. Isn’t it important for someone with experience to evaluate an ulcer, especially a deep one, to determine what is best to be done? You are risking a number of eyes perforating if they aren’t treated optimally.

And that certainly may be the case in many ulcers. Every ulcer needs a really careful assessment before treatment can be decided upon. First, what is the cause — is there an underlying infection or a dry eye which will need correcting before the ulcer will heal, however good the magic drops are? Secondly, is the ulcer healing?

A superficial ulcer with a devitalised epithelial edge where the basal cells are not adhering to the basal lamina could be expected to respond to this gel. If the ulcer had some proteoglycans left it could be deep and possibly perforating if it wasn’t treated. The next step is the ‘what’ or ‘why’ is it necessary to surgically correct the ulcer.

If the cause is a foreign body, for example, it will heal, however good the magic drops are! But if the cause is a conjunctival scar, for example, it may have to be removed.

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underlying basement membrane will not heal unless the dead tissue is removed, the remaining live tissue encouraged to heal and the area protected. In our study, these ulcers, not surprisingly, did not heal with Sentrx but only resolved after removal of the devitalised non-adherent epithelium and a stimulation of re-epithelialisation using a grid keratotomy or the newer diamond burr debriodement. More of that in a subsequent article, I think!

Back to the assessment of an ulcer. The other key feature of such a lesion is its depth. If Sentrx Remend fails to heal superficial non-adherent epithelial erosions, the ulcers it excels in are mid-stromal defects. It seems to be creating a matrix, a scaffold, into which the keratocytes can migrate and produce new collagen to repair the stromal defect.

The other ulcers where surgery is still required are those where the defect has progressed through almost every layer of the cornea, just leaving Descemet's membrane intact. This is the basement membrane of the corneal endothelium and as such is comprised of collagen type 4 and laminin.

“Does that really matter?” you may ask. Collagens normally have a glycine at every third amino acid, this allowing the tight alpha helical structure. Collagen type 4 lacks this regular glycine and so forms sheets which can expand since they are not regularly covalently linked together.

It is this chemistry which allows Descemet's membrane to expand, giving the classic descemecocoele (Figure 4) which signals a cornea ready to burst! Such a case calls for reconstructive surgery and not merely an eye drop. But for an ulcer extending into the stroma and without a predisposing cause such as dry eye, Sentrx Remend may be just the answer, especially in dogs which are not candidates for surgery.

But it’s not only ulcers. A gel formulation which produces a long-lasting scaffold across the ocular surface is an ideal option for animals with dry eye. Now again, the optimal treatment for keratoconjunctivitis sicca is topical cyclosporine in Optimmune, with the aim of increasing the eye’s production of its own tears.

But not every eye with KCS responds to the immunomodulatory effect of cyclosporine. It is in these cases where an effective tear replacement drop is required and Sentrx Remend fills this requirement admirably. We compared the cross-linked hyaluronic acid of Remend with a standard HA drop in 25 dogs with cyclosporine-resistant dry eye. Remend was significantly better than the standard HA tear replacement drop when we compared ocular redness, irritation and discharge after twice daily medication.

So when Bayer marketed Sentrx Remend in the UK, look out for David’s Magic Drops for corneal ulcers and dry eye in the canine eye and try them out for yourself!


David L. Williams, MA, VetMB, PhD, CertVOphthal, CertWEL, FHEA, FRCVS, graduated from Cambridge in 1988. He then worked at the Animal Health Trust before gaining his certificate in veterinary ophthalmology and moving to the RVC to undertake a PhD. After this he stayed at the RVC as resident in clinical pharmacology with a particular interest in ocular pharmacology. After two years he moved back to the AHT for a period as clinical investigative ophthalmologist before returning to Cambridge where he is now associate lecturer in veterinary ophthalmology, a position he combines with teaching at St John’s College, where he is director of studies in veterinary medicine and college lecturer in pathology.