Recurrent Corneal Erosion Syndrome

Synonyms: recurrent erosion syndrome

In recurrent corneal erosion syndrome (RCES) repeated episodes of breakdown of the corneal surface produce disabling eye symptoms and predispose the cornea to infection. Recurrent corneal erosions are common. They arise when damage to the cornea occurs; then, as healing begins, the new tissue is repeatedly stripped off by eyelid movement so that the epithelial layer fails to re-attach. The condition is very painful, as it leaves corneal nerve endings exposed. It may occur due to trauma but corneal dystrophy or other corneal disease may predispose.[1, 2]

Structure of the cornea

The cornea is a multilayered structure consisting of (from outside to inside):

- **Anterior corneal epithelium** a thin, multicellular epithelial tissue layer composed of around 6 layers of cells (non-keratinised stratified squamous epithelium) of rapidly regenerating cells kept moist by tears. the air/tearfilm interface is the most significant component of the total refractive power of the eye, so disruption of this surface can reduce acuity. The corneal epithelium is continuous with the conjunctival epithelium. It regenerates constantly, from the bottom layer.
- **Bowman’s layer** (also called the anterior limiting membrane): this is a protective acellular collagen layer.
- **Corneal stroma** (or substantia propria), a thicker, transparent layer of collagen and keratocytes which makes up around 90% of corneal thickness.
- **Descemet’s membrane** (posterior limiting membrane): a thin acellular layer which acts as the basement membrane to the corneal endothelium, and consisting mainly of collagen. There may be an even thinner protective membrane called Dua’s layer on its surface. This membrane was described in 2013 but its existence is a matter of dispute.
- **Corneal endothelium** a simple squamous monolayer of cells which regulate fluid and solute transport. These cells do not regenerate, but instead stretch to compensate for dead cells.

An ABCDE mnemonic is: **Anterior corneal epithelium**, **Bowman's membrane**, **Corneal stroma**, **Descemet's membrane**, **Endothelium**.
RCES occurs where there is disturbance of the epithelial basement membrane, resulting in defective adhesion of the epithelium to Bowman's membrane, causing recurring cycles of epithelial breakdown. Multiple recurrences are common because the basal epithelial cells require at least 8-12 weeks to regenerate or repair the epithelial basement membrane.

**Aetiology**[1, 3]

- The most common initiating factor is superficial trauma to the cornea (including micro-trauma caused by contact lens wear).
- The pathogenetic mechanism is related to poor adhesion of the corneal epithelium to the underlying stroma.
- A clean cut abrasion is more likely to cause the problem than a ragged abrasion. Other types of trauma may include alkali burns, foreign bodies and exposure keratopathy.
- Typically, RCES develops 3-10 days after the insult, although it can develop several months later.
- It may arise spontaneously.
- It is more likely to occur in the presence of risk factors relating to the cornea, such as corneal dystrophies (particularly epithelial basement membrane dystrophy), dry eye syndrome and exposure keratopathy.
- Epithelial, stromal and endothelial corneal dystrophies have all been described in association with RCES.
- Other causes that may lead to RCES include chemical and thermal injuries, herpetic keratitis, meibomian gland dysfunction, ocular rosacea, diabetes mellitus, Salzmann's nodular degeneration, band keratopathy, bacterial ulceration, kerato-conjunctivitis sicca and epidermolysis bullosa.
- Some more unusual trigger factors (all involving disruption of the epithelial basement membrane) are cataract surgery or refractive surgery.
- Other iatrogenic causes include vitrectomy (surgical removal of the vitreous) and photocoagulation.
- Systemic diseases which may predispose to this condition include:
  - Diabetes
  - Junctional epidermolysis bullosa
  - Alport's syndrome
  - Münchhausen's syndrome
  - Malnutrition
Drugs associated with the development of RCES include:
- Thiomersal (found in contact lens solutions).
- High-dose topical neomycin.
- Topical paromomycin.
- Topical diamidines and propamidine.
- All topical anaesthetic medication causes some degree of epithelial cell damage but this is most marked with cocaine, which is associated with RCES more than others.

A variety of RCES associated with autosomal dominant inheritance has been described but is rare.

Epidemiology
- There are no accurate statistics relating to the exact incidence and prevalence of this condition, as it often goes undiagnosed or misdiagnosed.
- One study suggested that the incidence of recurrence following traumatic abrasion was 1 in 150.\[^1\]
- It tends to occur slightly more commonly in females.
- RCES is generally seen in adulthood, usually from the fourth decade of life onwards, unless it is associated with one of the corneal dystrophies (eg, Reis-Bücklers dystrophy) or Alport's syndrome, in which case it can arise in children.

Presentation\[^2, 4\]
- RCES is characterised by repeated episodes of sudden onset of acute pain, usually at night or upon first awakening, accompanied by redness, photophobia and watering of the eyes. The symptoms are related to corneal de-epithelialisation and may relate to rapid eye movements during sleep.
- In its early stages, the condition may be asymptomatic.
- Individual episodes may vary in severity and duration.
- There is frequently a foreign body sensation.
- There may be an associated blepharospasm (inability to open the lids) and blurring of the vision.
- Some patients report glare and haloes around lights (this occurs if corneal oedema develops).
- The problem may be unilateral or bilateral.
- Corneal infiltrates may develop at the site of erosions.

Symptoms may gradually subside over the course of the day and then start all over again the next morning. The unpredictability of these episodes may lead to an associated anxiety.

Assessment\[^1\]
- Visual acuity should be checked (local anaesthetic may be needed to relieve the pain and associated blepharospasm).
- Examine as much of the anterior segment of both eyes (even if symptoms are unilateral) as possible. This includes fluorescein staining of the cornea in order to rule out other differential diagnoses (see list below).
- If RCES is suspected the patient should be referred to ophthalmology: the urgency depends on the degree of pain the patient is in. Same day referral is required for an acute attack.
- In the ophthalmology clinic, the anterior segment of the eye should be assessed with particular attention to the epithelium. Findings may include:
  - Macroerosions, microerosions or a roughening of the corneal surface.
  - Associated oedema or disruption at deeper levels of the cornea. The degree and location of the disruption will affect the visual acuity.
  - Evidence of corneal dystrophy/other predisposing factors in the fellow eye.
  - In mild cases, as the epithelium can heal within a few hours and findings may be normal: diagnosis may be made on history alone.
  - Severe cases can cause marked corneal changes quantifiable by corneal topography (a 3-dimensional mapping of the corneal surfaces giving gradients at each point).

Differential diagnosis
- Corneal abrasion.
- Corneal foreign body.
- Contact lens-related problem.
Dry eye syndrome.
- One of a variety of corneal dystrophies.
- Floppy eyelid syndrome.
- Herpes simplex keratitis.
- Other types of keratitis.

RCES can also occur following prolonged eye patching.

Investigations[1]
- Diagnosis is made on history and examination.
- Severe cases may require corneal topography (see 'Assessment', above) to outline the degree of corneal damage or help in the diagnosis of a corneal dystrophy.
- The depth of corneal involvement dictates treatment options and prognosis.

Management[1, 3, 4]
RCES is a chronic relapsing disease, which means it can be a frustrating disorder to treat and to experience. Most acute episodes are managed by patching, and cycloplegic and topical antibiotic ointment, with prophylactic application of gels during daytime and ointment at night. In a minority of cases these measures are insufficient and alternative treatments are needed. There is insufficient evidence to inform definitive management guidelines. A recent Cochrane review concluded that more evidence is required.

Primary care
- The best time to see patients is first thing in the morning, as in mild cases signs will have resolved within a few hours.
- Patients should be referred to the local ophthalmology unit. The degree of urgency depends on the severity of pain.
- Topical anaesthetic agents should NOT be used in the meantime, as these disrupt epithelial healing and aggravate the problem. Topical lubricants and oral analgesia are an appropriate initial plan.
- Avoid pressure patches until the patient has been assessed in the eye clinic. Once there, most patients respond to simple measures such as padding and antibiotic ointment.
- In some patients, RCES can be a recurring problem. If symptoms do not settle or they recur then re-referral is appropriate.
Specialist interventions
The aim of treatment is to encourage proper formation of adhesion complexes between the epithelium and the stroma. In resistant cases more complex treatment may be needed. Many of these are techniques which aim to promote epithelial adherence.

- Anterior stromal puncture with insulin needles or neodymium may enhance the epithelial adhesion to the basement membrane by scar formation - success rates of up to 80% have been reported in the treatment of recalcitrant RCES. Numerous tiny punctures are made away from the central visual axis, which induces cicatrization and promotes permanent epithelial adherence. It may be performed using Nd:YAG laser. [5]
- Alcohol delamination has shown good efficacy and safety. [6]
- Keratectomy is reserved for severe and difficult cases (usually in patients with associated corneal dystrophies). [4] The entire epithelium is removed and allowed to regrow from new over the following 5-7 days. Excimer laser photo-therapeutic keratectomy (PTK) is now a well-established treatment modality for RCES. Partial ablation of Bowman's layer with PTK gives a smooth surface for the newly generating epithelium to form adhesion complexes. It can be carried out more than once if the problem recurs. Long-term data suggest that most patients treated with PTK do not develop recurrences and that side effects from PTK are minimal. [7]
- The use of extended wear contact lenses, autologous serum eye drops, botulinum toxin, induced ptosis, oral matrix metalloproteinase (MMP) inhibitors, and diamond burr polishing of Bowman's membrane has been reported with varying degrees of success.
- Treatment of RCES with the combination of oral doxycycline and topical corticosteroid has been found to be effective in one study - 71% had no recurrence by 12 months. Both have been shown to inhibit key metalloproteinases important to disease pathogenesis. This treatment may help patients with RCES for whom other forms of treatment have failed. [8]

Complications
- Infectious keratitis.
- Corneal scarring.
- Decreased visual acuity (due to either of the above).

Prognosis
This is generally good, as long as any underlying conditions are diagnosed and managed appropriately. Most patients respond well to topical treatment; few patients will have their vision permanently affected.

Prevention [2]
- Prophylaxis with long-term lubrication (eg, night-time lubricating ointment for three months) may help prevent recurrence. The success of this approach depends on the patient understanding the importance of continuing the treatment in the absence of symptoms. However, there is some suggestion that a lubricant may actually increase the risk of recurrence - further research is required. [9]
- More severe cases may require a protective bandage contact lens.
- Some evidence suggests that a 12-week course of systemic tetracyclines (eg, oxytetracycline 250 mg bd) may be beneficial (these promote epithelial stability). [4]

Other general preventative measures include:
- Avoiding dry/irritating environments (eg, cigarette smoke).
- Wearing protective glasses, especially where exposure might risk abrasion (eg, gardening, painting).
- Keeping well hydrated.
- Avoid rubbing the eyes
- Applying long-lasting lubricating ointments last thing at night.
- Avoiding sleeping in late.
- Learning to wake with eyes closed and still (and having lubricant within reach by the bedside).
Further reading & references

- Clinical Ophthalmology: A Systematic Approach
- Recurrent corneal abrasions/erosion; Good Hope Eye Clinic
- Recurrent corneal erosion syndrome - Accident and Emergency; Moorfields Eye Hospital Patient Information


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