

Refractory Doesn't Mean Hopeless: A New Path With JETT

"The patient has tried everything. The ocular surface is still failing."

Richel Liu • Compex

Refractory dry eye disease (RDED) • drivers, subgroups and four illustrative cases



JETT Medical II system • console, handpiece and applicators

Why refractory dry eye is a different problem

Dry eye that persists after standard stepwise care has been properly delivered.

Stepwise treatment, in practice

- Guided by diagnosis, severity and previous response
- DEWS III replaces the severity-staged ladder with an aetiology-matched prescribing algorithm — interventions selected by driver, often concurrently
- So steps can be combined or skipped according to the dominant driver

Working definition used here

- Persistent symptoms and/or signs despite diagnosis-driven, adequately delivered stepwise care
- First confirm the diagnosis, then confirm delivery — dose, duration, adherence
- Severe is not refractory: severity is magnitude, refractoriness is failure to respond. DEWS III sets no refractory threshold, so state your failure definition in advance

Practical signals to re-phenotype — not diagnostic criteria.

- 01** Symptom–sign discordance, or pain / photophobia / wind sensitivity out of proportion to examination
- 03** Recurrent epithelial breakdown: filamentary keratitis, PED — or symptoms persisting > 6 months after ocular surgery

- 02** No meaningful response after ~3 months of adequate tears plus prescription therapy

- 04** High-risk context: GVHD / Sjögren / SJS, MMP-9 positive, or tear osmolarity ≥ 308 mOsm/L

Source: [TFOS DEWS III · Management and Therapy](#) · [TFOS DEWS III · Diagnostic Methodology](#) · [Vázquez 2022 · Ocul Surf](#) · [Iglesias / Galor 2018 · Cornea](#)

DEWS III changes the lens: from severity to drivers

What actually changes at the chair — and the two surface axes it puts in play.

01

Diagnosis: symptoms plus one sign

A symptomatic, multifactorial disease with loss of tear-film and/or ocular-surface homeostasis. OSDI-6 ≥ 4 plus at least one positive objective sign — symptoms are still required.

Guideline requirement.

02

Nerve dysfunction, operationalised

Neurosensory abnormality was already an aetiologic factor in DEWS II. What DEWS III adds is operational: nerve dysfunction appears inside the subclassification, not as an outlier.

Guideline requirement.

03

Goblet cell • mucin • glycocalyx

The surface-protection axis: goblet-cell loss, reduced MUC5AC and a degraded glycocalyx. Not a category DEWS III created, but an ocular-surface driver that becomes clinically decisive once management is matched to phenotype instead of a linear ladder.

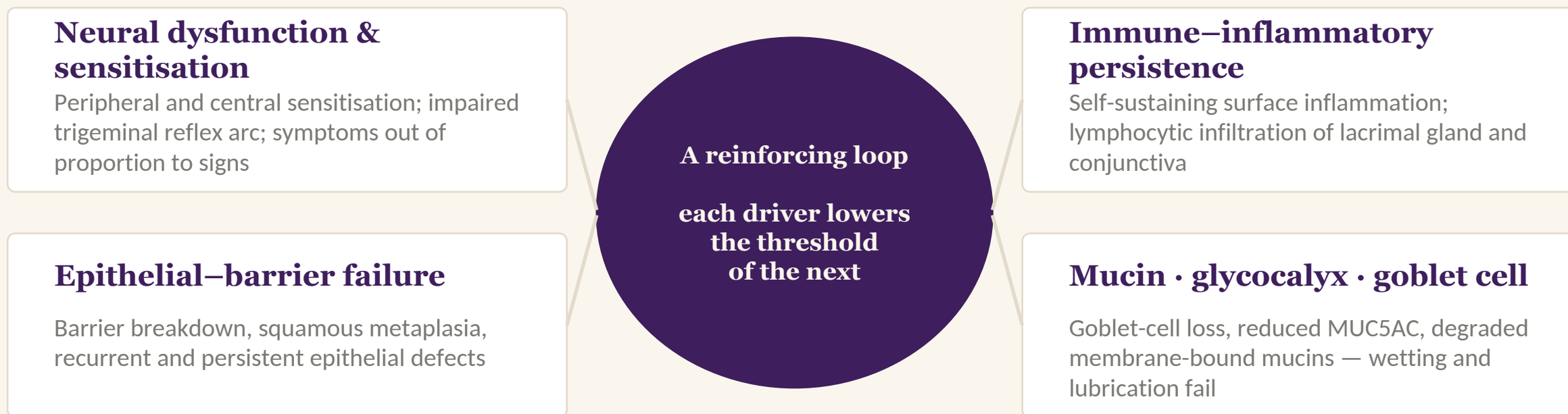
Ocular-surface biology.

Classify the dominant drivers before escalating treatment.

Source: [TFOS DEWS III • Diagnostic Methodology](#) • [TFOS DEWS III • Executive Summary](#) • [Argüeso 2002](#) • [IOVS \(MUC5AC in dry eye\)](#) • [Goblet cells & ocular surface mucins • review](#)

Why single-target escalation plateaus

Four drivers, one surface — they reinforce each other, so treating one layer moves the phenotype, not the disease.



One dominant driver can hide another. Discordance is information, not noise.

Disease biology, synthesised by the author from: [Stern 1998 · Cornea \(lacrimal functional unit\)](#) · [Vázquez 2022 · Ocul Surf](#) · [Argüeso 2002 · IOVS](#) · [Goblet cells & ocular surface mucins · review](#)

Immune-mediated RDED

oGVHD, Sjögren and SJS/TEN fail on several of these drivers at once.

Ocular GVHD

CD4+ lymphocytic infiltration and fibrosis of conjunctiva and lacrimal gland. Mixed aqueous-deficient dry eye plus MGD, with recurrent epithelial defects.

Prevalence: oGVHD in 37.8% after allogeneic HSCT (95% CI 29.4–46.3).

Sjögren syndrome

Lymphocytic infiltration of the lacrimal gland, producing aqueous-deficient, hyperosmolar disease with a high symptom burden.

Sjögren cohort (n = 49): tear osmolarity 314.5 ± 22.2 mOsm/L, OSDI 37.5 ± 24.0 .

SJS / TEN sequelae

Cicatricial conjunctivitis, meibomian gland scarring, marked goblet-cell loss and limbal stem-cell deficiency.

Deepest end of the refractory spectrum; often needs surface reconstruction.

Current approach: control inflammation • biologic tear replacement • barrier protection and surface reconstruction.

Source: [Wang 2025 • PLoS One \(oGVHD meta-analysis\)](#) • [Chen 2011 • IOVS \(tear osmolarity in Sjögren\)](#) • [Front Med 2025 • chronic SJS](#)

Iatrogenic and neurotrophic RDED

Persistent symptoms after ocular surgery may reflect interacting surface injury, altered corneal innervation and pre-existing dry-eye drivers.

Post-LASIK / refractive

The flap cuts the subbasal nerve plexus, reducing reflex tearing and blink drive.

Subbasal nerve density down 51% / 35% / 34% at 1 / 2 / 3 years.

Post-cataract / IOL

Incisional nerve transection on top of pre-existing surface disease. Persistent ocular-surface symptoms can undermine postoperative visual satisfaction (author's clinical view).

32% report dry-eye-like symptoms 6 months after cataract surgery; 10% severe (DEQ-5 $\geq$ 12).

Neurotrophic keratopathy

Partial or complete loss of the corneal trigeminal reflex arc — diabetes, herpes zoster, cranial surgery, chemical injury.

Cenegermin: FDA-approved for neurotrophic keratitis; EU-authorised in adults with moderate persistent epithelial defect or severe corneal ulcer. Local availability varies.

Optimising the surface before and after surgery is a mechanistic rationale for protecting the visual result — not an outcome claim.

Source: [Erie 2005 • Am J Ophthalmol](#) • [Iglesias / Galor 2018 • Cornea](#) • [FDA OXERVATE approval package](#) • [EMA OXERVATE • EPAR](#)

A new path with JETT

One reflex arc, one hub, three effector areas — the lacrimal functional unit treated as a system.

NEURAL REFLEX ARC

Trigeminal afferent input → **reflex / central integration** → **parasympathetic efferent output** →
ocular-surface effectors

JETT

designed as a whole-LFU, multi-axis intervention for refractory and complex dry eye

Lacrimal output	Lacrimal output may be supported through local stimulation of accessory lacrimal tissue and through trigeminal-parasympathetic reflex pathways.
Goblet cells • mucin–glycocalyx	The surface-protection axis behind wetting and lubrication, which volume replacement alone does not restore.
Lid & meibomian apparatus	Lid and lid-margin treatment where the evaporative component dominates the phenotype.

These are proposed JETT mechanisms; clinical outcomes and molecular target engagement should be evaluated as separate evidence layers. Clinical response is tracked across symptoms, tear-film signs and mechanism-relevant biomarkers.

Biological rationale, not JETT-specific mechanism evidence: [Stern 1998 • Cornea \(lacrimal functional unit\)](#) • [LFU definition](#) • [DEWS 2007 • Ocul Surf](#) • [Argüeso 2002 • IOVS \(MUC5AC in dry eye\)](#)

Refractory MGD after IPL and gland probing

Symptoms and tear-film measures were still below expectations after four months of targeted gland treatment.

PATIENT

Adult, IT occupation. Severe bilateral MGD for more than 2 years; long-standing conjunctival hyperaemia, dryness and foreign-body sensation.

PRIOR CARE

IPL — no meaningful self-reported benefit. Meibomian gland probing every 2 weeks through the first 4 months of 2026, with artificial tears and cyclosporine — still below expectations.

JETT COURSE

21 May – 6 August 2026, 8 sessions. Lids, lid margin, upper fornix and lid skin.

BREAK-UP TIME (s)

OD 3.25 → 12.90
OS 4.32 → 13.47

TEAR MENISCUS (mm)

OD 0.07 → 0.12
OS 0.09 → 0.15

OSDI

25 → 2

SANDE

65 → 12

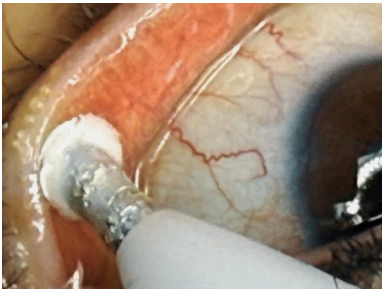
Tear-film measures baseline → session 4; OSDI and SANDE session 5 → session 8 — first recorded at session 5, so the session-5 score is not a baseline. Break-up time from the source chart labelled TBUT (Oculus measurement).

SERIAL MEIBUM EXPRESSION • descriptive serial images from an uncontrolled case; they do not independently establish causality

21 May • session 1 — ocular redness and inflammation; no meibum expressed



11 June • session 3 — toothpaste-like meibum expressed



23 July • session 7 — clearer lipid expressed from gland orifices



Illustrative internal case • uncontrolled longitudinal observation • ongoing therapy as documented • no causal inference • congress use subject to confirmation of patient consent.

Source: Internal case documentation, 2026.

SJS ocular surface disease with severe MGD

Immune-mediated, multi-compartment disease on ongoing full topical therapy.

PATIENT

32-year-old woman. SJS-associated ocular surface disease; bilateral blepharitis; severe dry eye; MGD. History of left chalazion and drug-induced dermatitis.

ONGOING TOPICAL THERAPY

Tacrolimus, levofloxacin, sodium hyaluronate, fluorometholone and perfluorohexyloctane eye drops, as listed. Regimen changes during the JETT course not documented.

JETT COURSE

Five sessions at 2-week intervals; data shown through session 4.

Measured change

TEAR MENISCUS HEIGHT (mm) • BASELINE → SESSION 4

OD 0.10 → 0.30 • OS 0.01 → 0.30

BREAK-UP TIME • BASELINE → SESSION 4

OD 2 → 9 s • OS 2 → 6 s

OSDI • BASELINE → SESSION 4

79 → 42

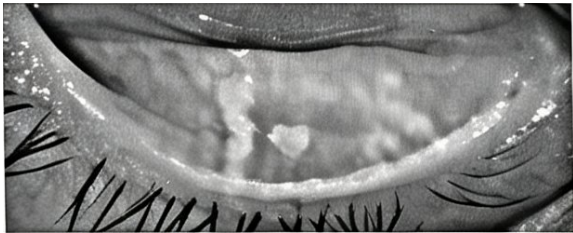
SANDE • BASELINE → SESSION 2

100 → 63

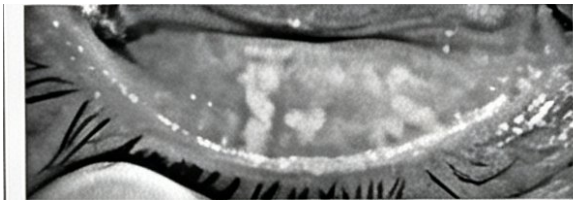
SANDE shown through session 2; OS baseline TMH recorded as 0.01 mm — at or below the limit of measurement. Break-up time from the source chart labelled TBUT (Oculus).

MEIBOGRAPHY

Baseline • OD lower lid



After session 4



Near-complete atrophy at baseline. Descriptive only; no gland recovery claimed.

Illustrative internal case • uncontrolled longitudinal observation • ongoing therapy as documented • no causal inference • congress use subject to confirmation of patient consent.

Source: Internal case documentation, 2026.

Neurotrophic and diabetic keratopathy

Symptoms improved while epithelial healing diverged between the two eyes — a documented clinical course without image records.

PATIENT

54-year-old man. Type 2 diabetes for more than 10 years; bilateral IOL; previous viral keratitis with corneal endothelial decompensation; bilateral epithelial defects: OD central 3 × 3 mm; second corneal defect 1 × 1 mm (laterality not specified in source record).

ONGOING TOPICAL THERAPY

Gatifloxacin, deproteinised calf-blood extract, prednisolone acetate, sodium hyaluronate and autologous serum, as listed. Regimen changes during the JETT course not documented.

JETT COURSE

5 sessions completed (weekly, sessions 1–4). Lids, lid margin, upper fornix and lid skin.

Documented clinical response

SYMPTOM SCORES • BASELINE → SESSION 4

OSDI

77 → 34

SANDE

65 → 16

CLINICAL INTERPRETATION

Symptoms improved, but symptom response did not predict identical epithelial healing.

EPITHELIAL OUTCOME • SLIT-LAMP RECORD • AFTER 3RD SESSION

OS

Defect closed

Documented structural closure

OD

Central defect persisted

Inferior epithelial growth was observed, but closure was not documented.

No clinical images were recorded; outcomes are transcribed from contemporaneous case documentation.

Illustrative internal case • uncontrolled longitudinal observation • ongoing therapy as documented • no causal inference • congress use subject to confirmation of patient consent.

Source: Internal case documentation, 2026.

Chronic SJS — left eye treated only

The instructive case: tear-film and symptom change occurred while gland morphology stayed unchanged.

PATIENT & HISTORY

61-year-old man, post bone-marrow transplant, amoxicillin allergy. Chronic severe SJS with neurotrophic keratoconjunctivitis: palpebral conjunctival keratinisation, lower-lid distichiasis, conjunctival telangiectasia, corneal thinning and opacity.

EYES

Left eye treated (VA 0.06). Right eye no light perception — not treated.

ONGOING TOPICAL THERAPY

Sodium hyaluronate, tobramycin/dexamethasone, perfluorohexyloctane, calf-blood extract, as listed. Regimen changes not documented.

Measured change

TEAR MENISCUS • LEFT EYE

0.18 → 0.22 mm

BREAK-UP TIME • LEFT EYE

Not measurable → < 5 s

OSDI • BASELINE → SESSION 3

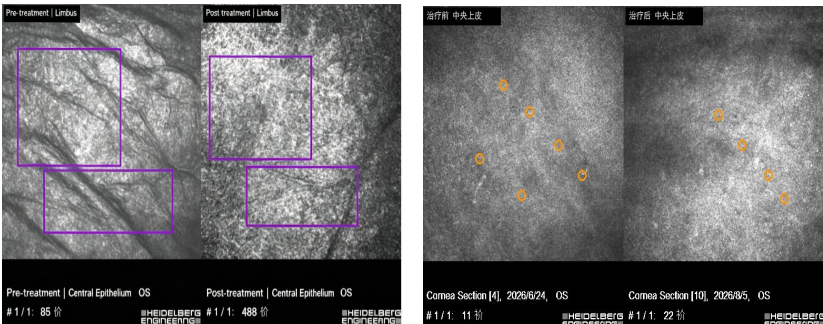
56 → 43

SANDE • BASELINE → SESSION 3

34 → 4

Glands fully atrophied at baseline and after session 4 — no meibographic improvement. Tear-film measures were repeated at session 4; questionnaires were last recorded at session 3. 6 sessions completed, left eye only.

OS • LIMBUS AND EPITHELIUM HIGH-REFLECTIVITY ANNOTATION



Purple boxes mark focal abnormal high-reflectivity and structural heterogeneity zones — before vs after.

LIMBUS • OS • 24 JUN → 05 AUG

Orange circles mark candidate granular-like high-reflectivity foci — morphological hints only.

CENTRAL EPITHELIUM • OS • 24 JUN → 05 AUG

Limbus. Sine-like / lattice-like structures persist after treatment; focal abnormal high-reflectivity and structural heterogeneity are reduced compared with baseline.
Epithelium. Reflectivity homogeneity and cellular regularity of the central epithelium are improved relative to baseline, with reduced granular-like high-reflectivity.

Illustrative internal case • uncontrolled longitudinal observation • ongoing therapy as documented • no causal inference • presented with patient consent.

Source: Internal case documentation, 2026.



RDED is a failure of driver matching across the lacrimal functional unit.

Re-phenotype

before escalating



Re-target

interacting drivers



Re-open the path

across the whole LFU

Refractory doesn't mean hopeless.

JETT may offer a whole-LFU, multi-axis path forward when conventional care reaches its limits.

Framework: [TFOS DEWS III Management](#) · [Diagnostic Methodology](#) · Mechanism-led clinical rationale.