G 20/20 meeting Brisbane 2014

Thyroid eye disease TED
What works, what doesn't

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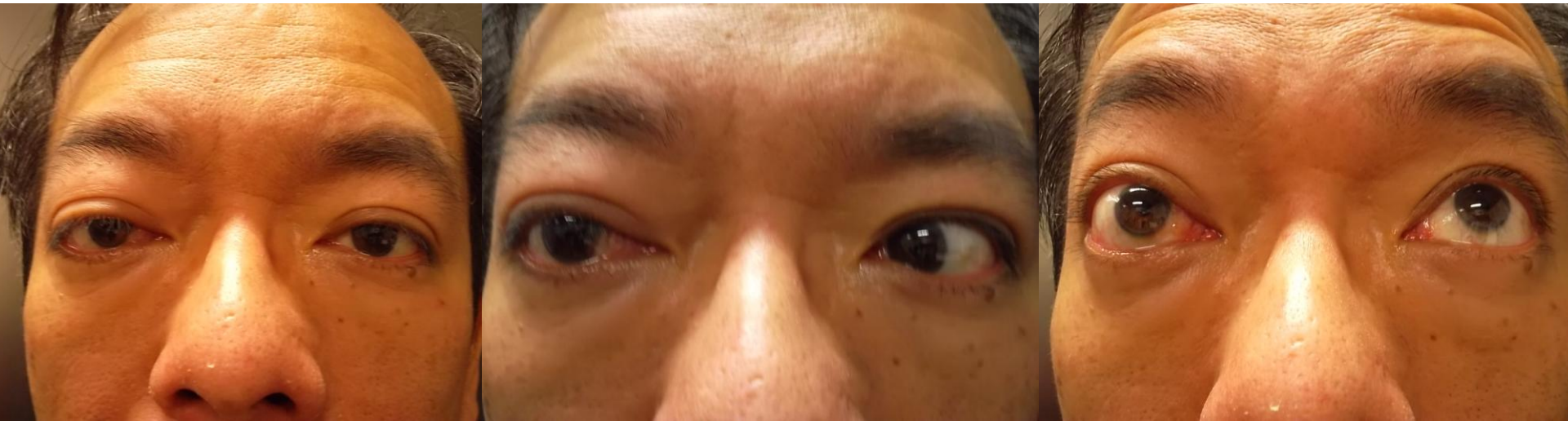
Summary

- TED can be very tough to treat
- Need effective staging strategies in each of inflammatory, congestive & fibrosis components
- Need better imaging [prob biochemical]
- Probably best managed in dedicated TED clinic manned by oculoplastics, strabismus, endocrine & addiction Drs [Σ Australia =1, @ RNS].

Pt 1.

- Constant diplopia since 4/13.
- 9/13: tight RMR, RIR
- Good vision / optic n function
- Multiple endocrinologists / ophthalmologists



He gets worse, has pulsed steroids : no better, possibly worse

Unstable biochem. High TSH Rc Abs. Constant diplopia.
Normal acuity, optic n function.

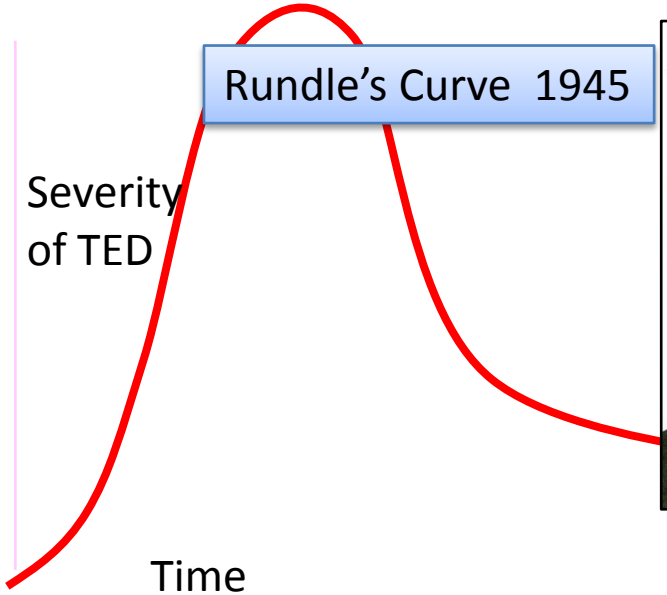
Next??

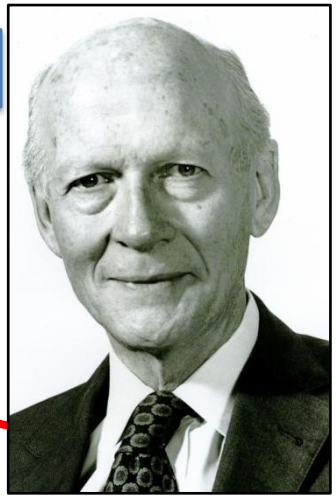
How to assess the stage of TED

3 overlapping phases / pathologies:

- Inflammation
- Venous congestion
- Fibrosis

Another way to assess & predict clinical activity and course in TED





Fibrosed? Inflamed? Congested? **Confused?**

- *In TED, the clinical pictures of inflammation, venous congestion & fibrosis overlap and* ***cannot be reliably distinguished***
- 'Orbital inflammation' can be relieved by orbital decompression
- It is fibrosis that probably makes strabismus worse

Graefe's Arch Clin Exp Ophthalmol (1996)
234:331–336 © Springer-Verlag 1996

LABORATORY INVESTIGATION

SEMINAL PAPER

Essam Saber
Jan McDonnell
Kerry M. Zimmermann
Javier E. Yugar
Steven E. Feldon

Extraocular muscle changes in experimental orbital venous stasis: some similarities to graves' orbitopathy

- …. animal model of orbital venous obstruction by ligating the…ophthalmic veins of the eye of 4 cats.. **there was .. marked proptosis, chemosis, exotropia & histology typical of TED**.

Without evoking a primary orbital inflammation or inducing a systemic autoimmune disease, an animal model of venous stasis has been developed that closely mimics many of the advanced clinical and histologic changes that occur in TED

Graefe's arch clin exp ophthalmol 1996

What usually works in TED

- Generous decompression

Optic n compression, uncosmetic proptosis, makes strabismus surgery more effective, reduces ‘inflammation’ & ‘congestion’

- Lid surgery

Selection bias – I don’t see pts with solely oculoplastic problems

- Strabismus surgery for diplopia

Success per surgery >50% for ‘old’ diplopia, ~ 50% when ‘hot’

- Strabismus for bad abn head posture
- Glasses for acquired astigmatism

Strabismus surgery for abn head posture

What sometimes works in TED

- Doing nothing – it gets better
- Botox for lid retraction
- Botox for diplopia
- Celebrex for orbit pain
- Guanethidine eye drops for lid retraction [made by Leiter's pharmacy; TGA paperwork]

Treatments with a good reputation for safety & effectiveness

- Orbital radiotherapy
- Steroids – oral
- Steroids – pulsed
- Glaucoma drops to lower high IOP

Treatments with a good reputation for safety &effectiveness -

Orbital radiotherapy

- Mayo 2001 & 2002

*In this group of patients, representative of those for whom radiotherapy is frequently recommended, we were **unable to demonstrate any beneficial therapeutic effect.***

*Because it is**neither effective nor innocuous**, radiotherapy does not seem to be indicated for treatment of mild-moderate ophthalmopathy.*

- American Academy Ophthalmology meta-analysis 2008

*Level I evidence indicates that **proptosis, eyelid retraction, and soft tissue changes do not improve** with radiation treatment*

- Cochrane 2012

some effect in mild - moderate TED

XRT better if combined with steroids

One study: effect of XRT = steroids

Treatments with a good reputation for safety & effectiveness:

Steroids

- Often over- used and wrongly used
- Pulsed better than oral steroids

Real morbidity

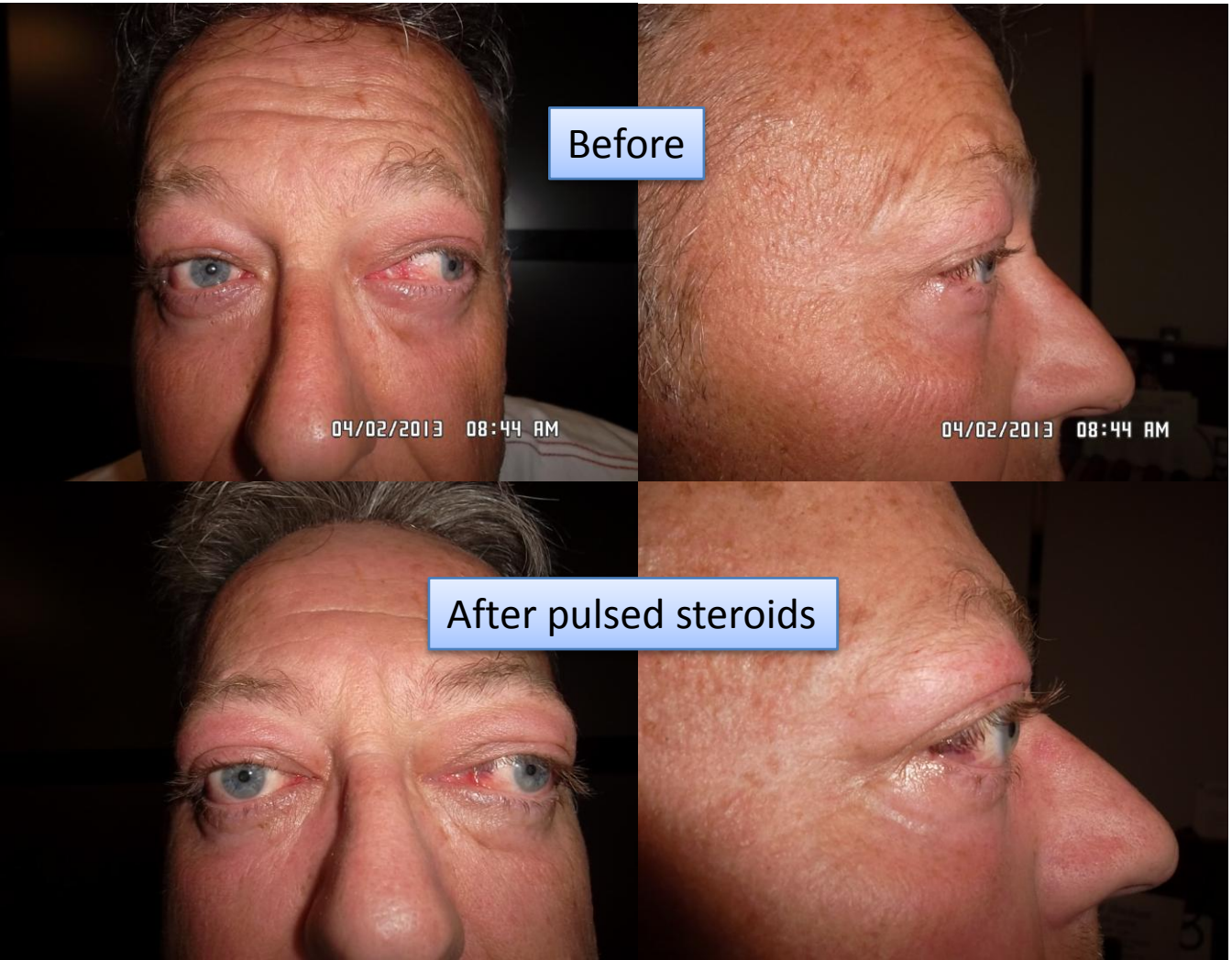
- Can be dramatically effective
- **Can be dramatically ineffective**

I see this regularly - ?selection bias in diplopia population

- Needs a prospective study

High +. ET surgeries: consecutive L XT. L amblyopia 6/18.

TED onset late 2012. Pulsed steroids May-July 2013: developed choroidal folds, VA R 6/24. Orbital decompression Aug 13. Choroidal folds improved, VA did not. Biochem labile. Thyroidectomy 4/14.



Lots of steroid side effects

- Peri-menopausal women: osteoporosis
- Weight gain
- Cataract

European Journal of Endocrinology (2012) 166 247–253 ISSN 0804-4643

9 deaths reported
7 from IV, 2 from oral steroid
32 non-fatal events reported

CLINICAL STUDY

Fatal and non-fatal adverse events of glucocorticoid therapy for Graves' orbitopathy: a questionnaire survey among members of the European Thyroid Association

Claudio Marcocci, Torquil Watt[1], Maria Antonietta Altea, Ase Krogh Rasmussen[1], Ulla Feldt-Rasmussen[1], Jacques Orgiazzi[2], Luigi Bartalena[3] and for the European Group of Graves' Orbitopathy (EUGOGO)

Department of Endocrinology and Metabolism, University of Pisa, Via Paradisa 2, 56124 Pisa, Italy, [1]Department of Medical Endocrinology, Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark, [2]Department of Endocrinology and Metabolism, Hopital Lyon Sud, and Claude Bernard University, Lyon, France, and [3]Department of Clinical Medicine, University of Insubria, Varese, Italy

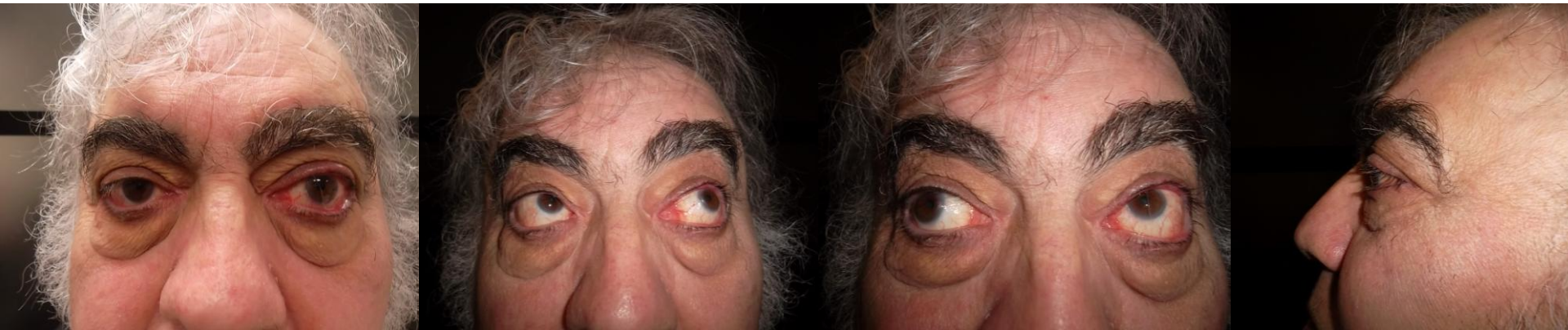
AJ, dob 1949

Constant diplopia since onset TED in 11/2011; needs chin up.

I^{131} in 10/2012. Oral steroids since.

40 Kg weight gain. Osteoporosis, AMI.

Little/ no change to diplopia.



What usually doesn’t work

- Low dose steroids eg 10-20 mgm /d
- Selenium
- Strabismus surgery to expand a modest field of single vision

Sexy expensive new treatments

- Biologicals [Enbrel etc], Actemra, Rituximab, ….***all*** potentially exciting, ***all*** awaiting good trials – NO place in treatment of your next pt. There will be pressure to use the biosimilars that are about to hit the market.

We fail our patients

- I can prescribe $x000s of drugs.
- Smoking is the most important risk factor for occurrence & progression of TED, and for lower & slower response to any treatment
- We have alcohol, ice and narcotic facilities. There is no smoking cessation facility in Melbourne

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