ROSACEA :

CLUES FOR IMPROVED CONTROL

Dr Scott Barker
Consultant Dermatologist
Wellington

ROSACEA SUMMARY

- Chronic Inflammatory skin condition
- Common
- Exact pathogenesis not known
  - Dysregulation of innate immune system
  - Overgrowth commensal organisms
  - Aberrant neurovascular signalling

- Features usually recognised on face
  - But I have seen features on scalp and chest and neck

- Diagnostic criteria for rosacea
  - Presence of at least 2 of the following primary features

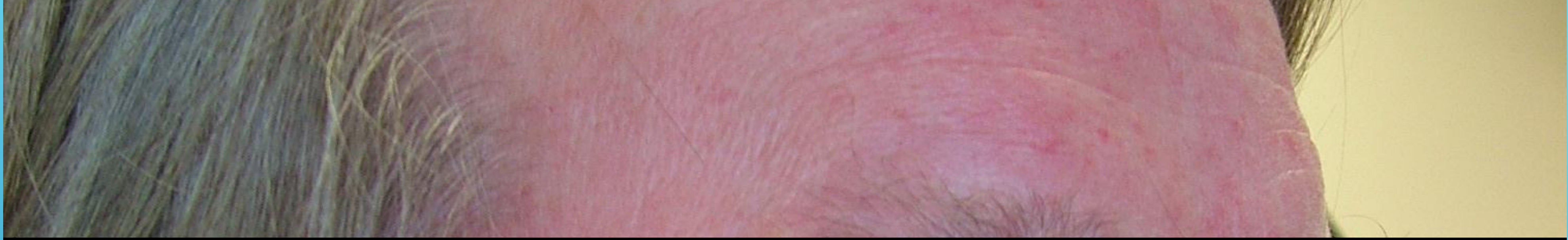
  - Flushing (transient erythema) ......usually first feature
  - Nontransient erythema
  - Papules and pustules
  - Telangiectases

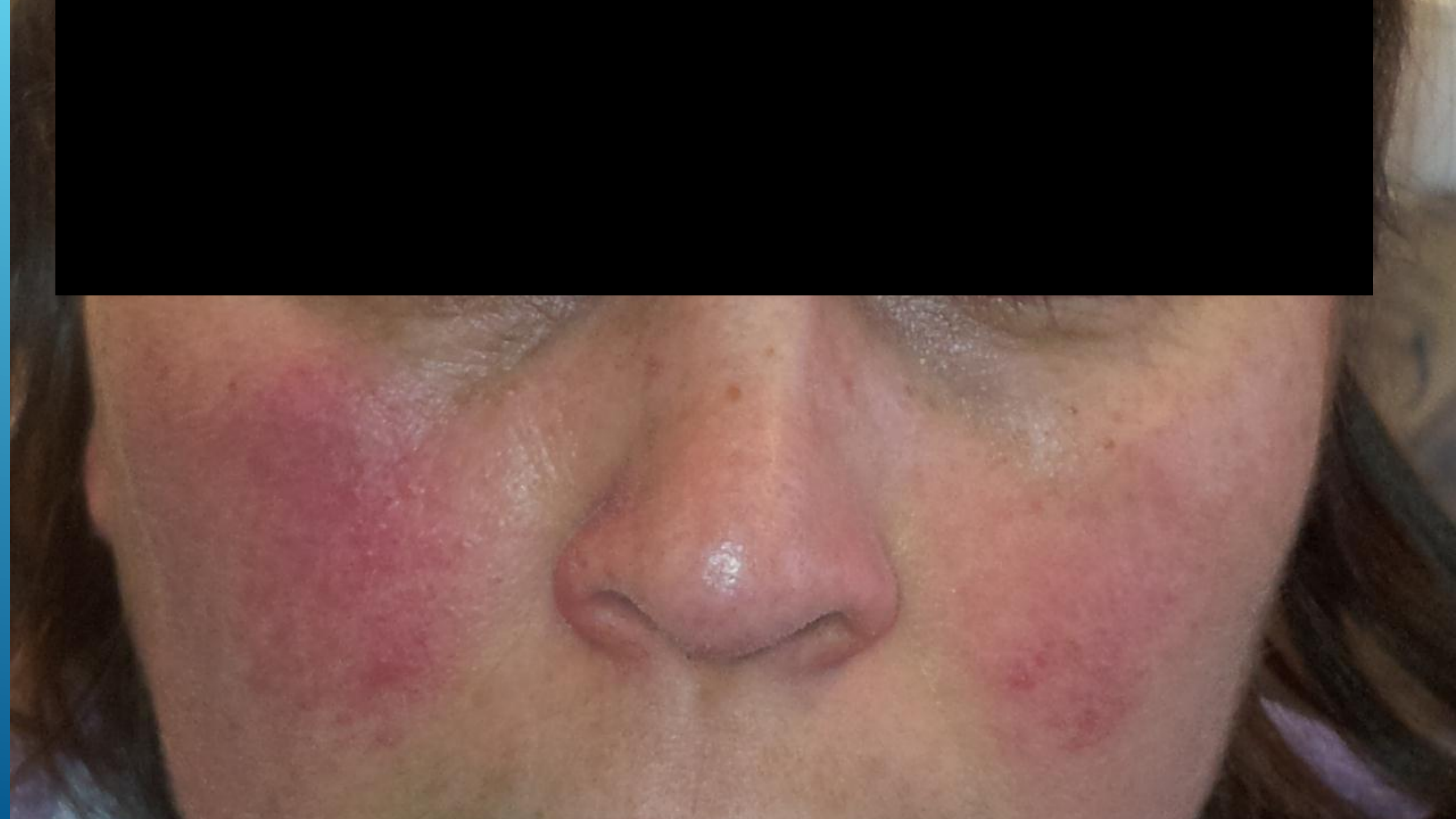
- May include the following secondary features
  - Burning or stinging
  - Dry appearance
  - Edema
  - Ocular manifestations
  - Peripheral location
  - Phymatous changes

DIAGNOSTIC CRITERIA

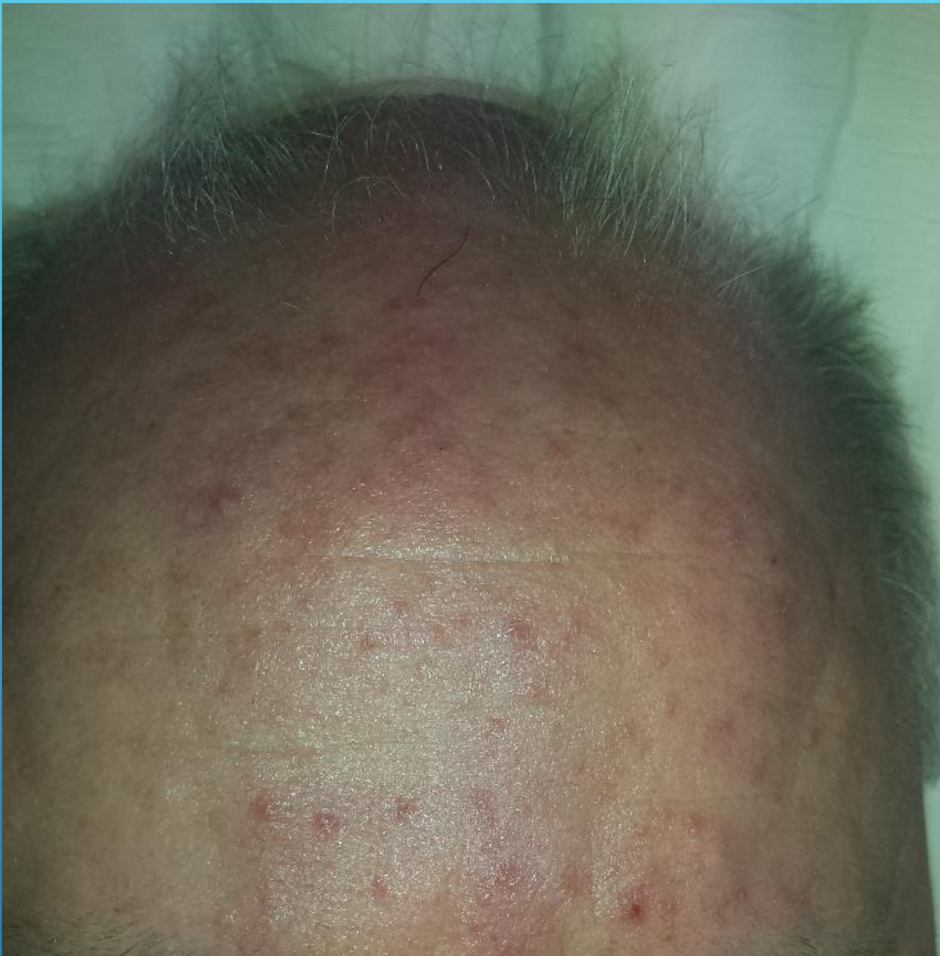
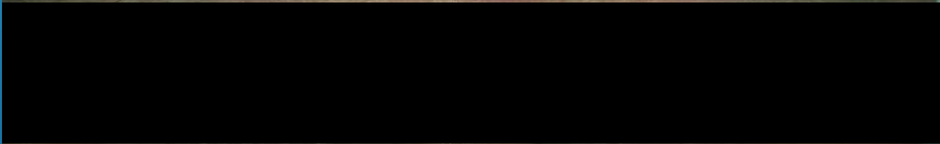
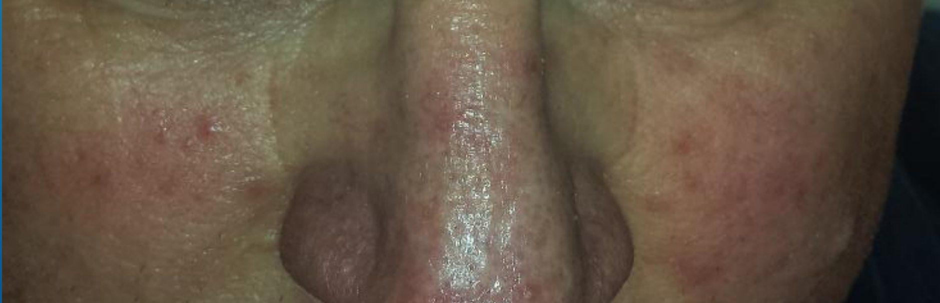
- Erythematotelangiectatic
- Papulopustular
- Phymatous
- Ocular

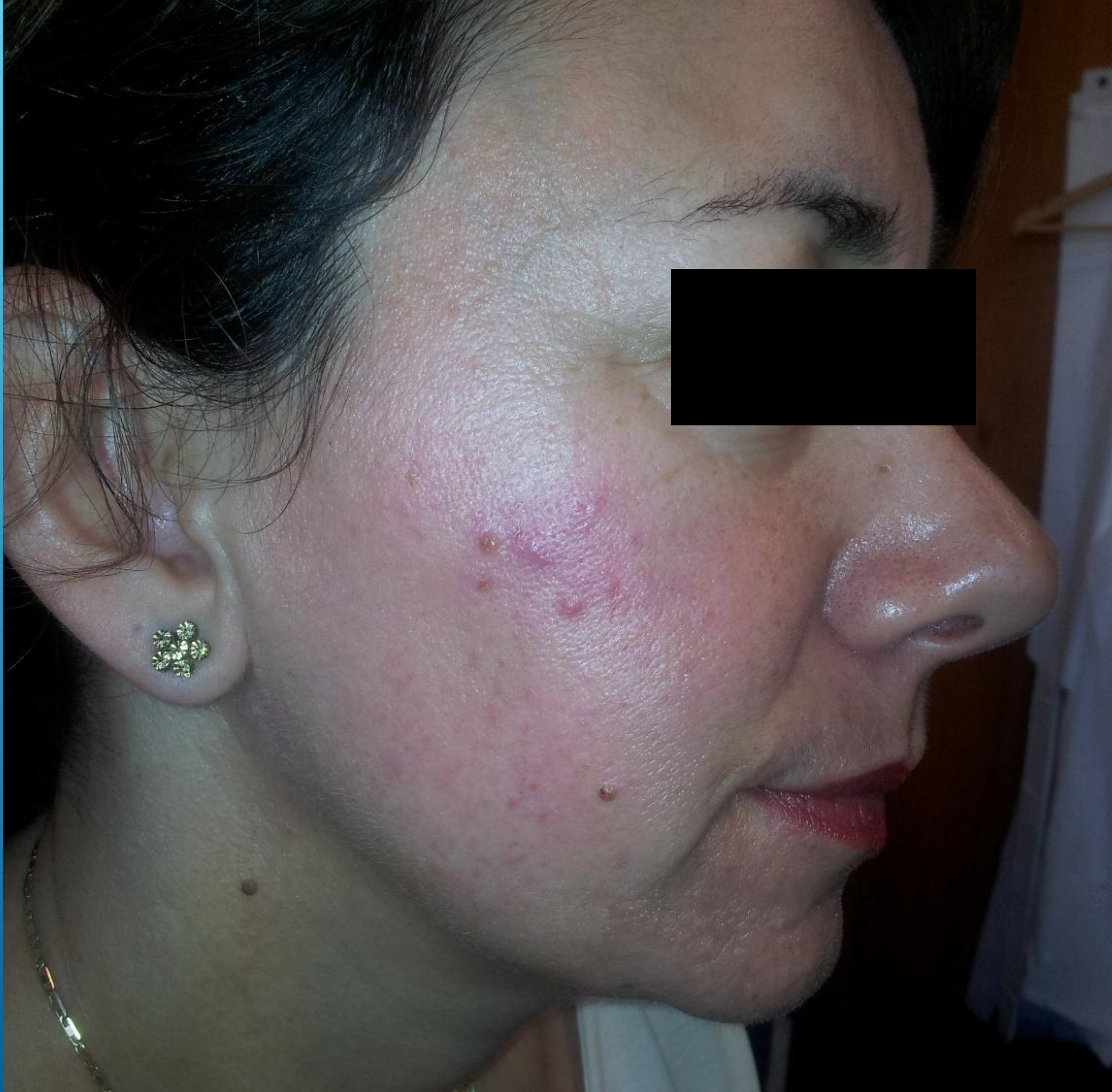
- Episodes of flushing
- Persistent central facial erythema
- Periocular skin usually spared
- Telangiectasis common





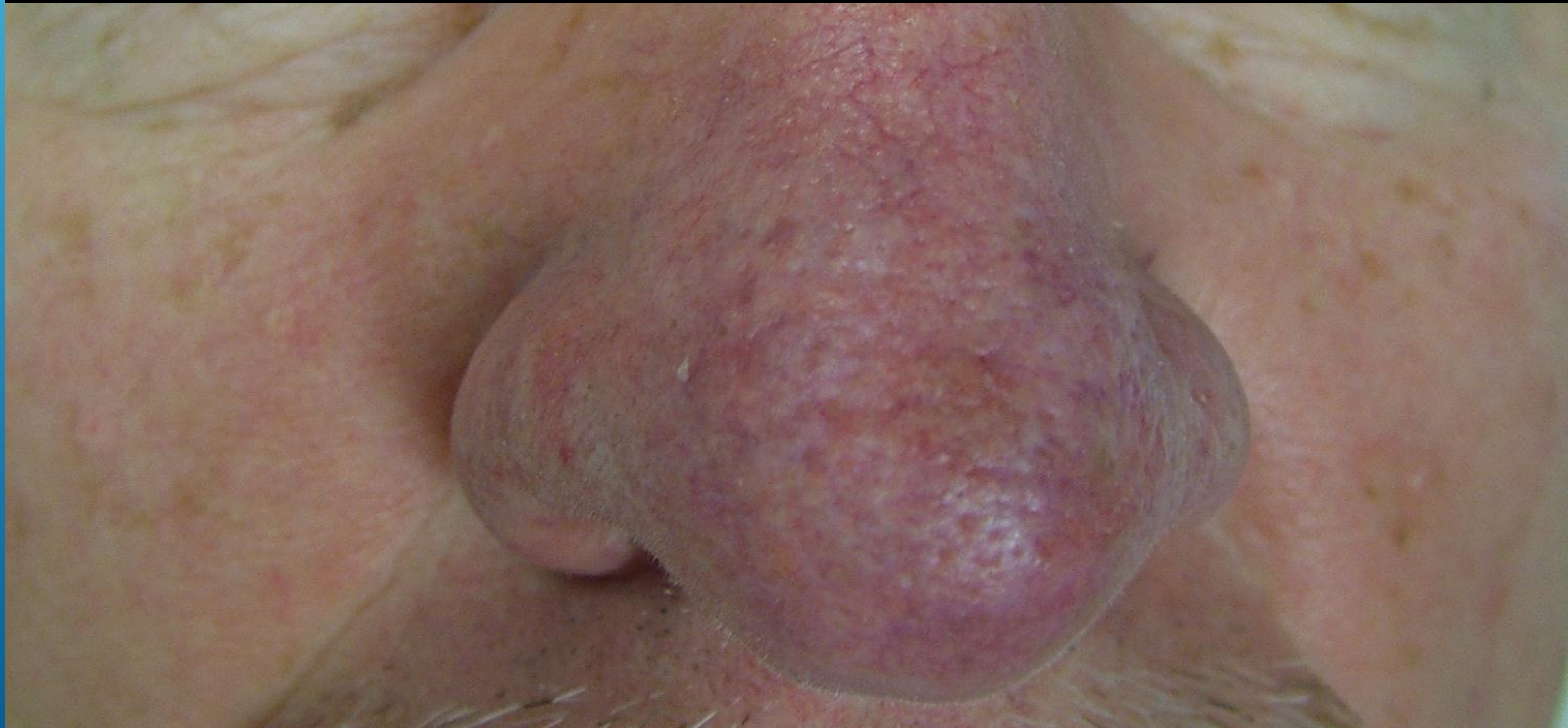
- Features of flushing and erythema
- Transient papules / pustules
- Facial oedema

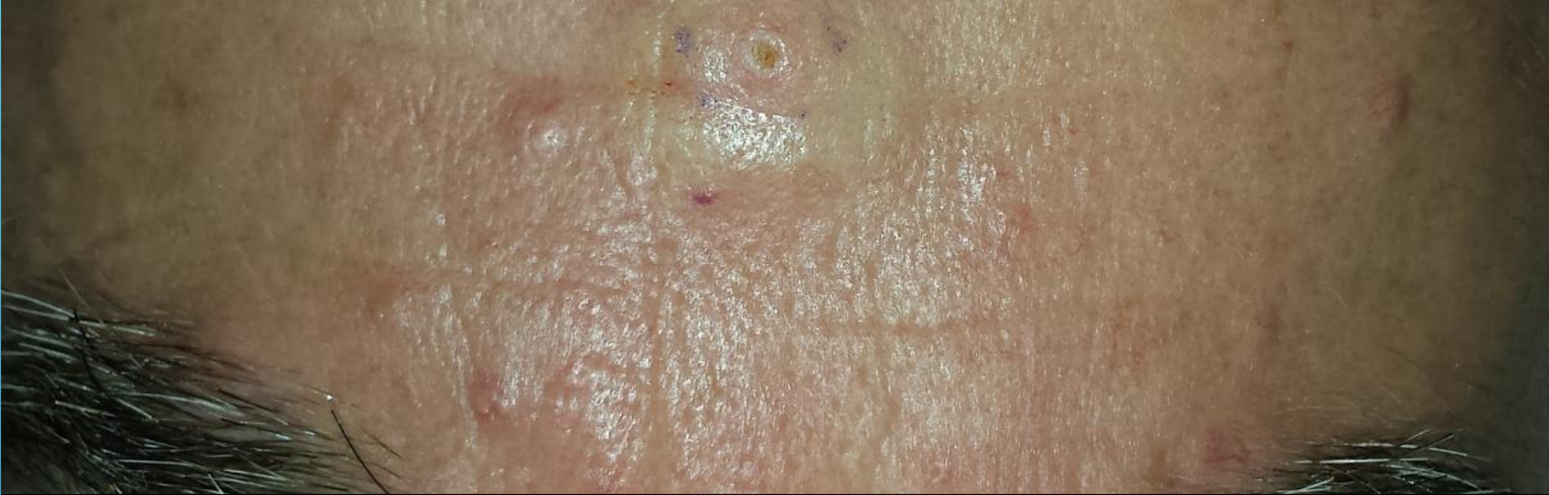
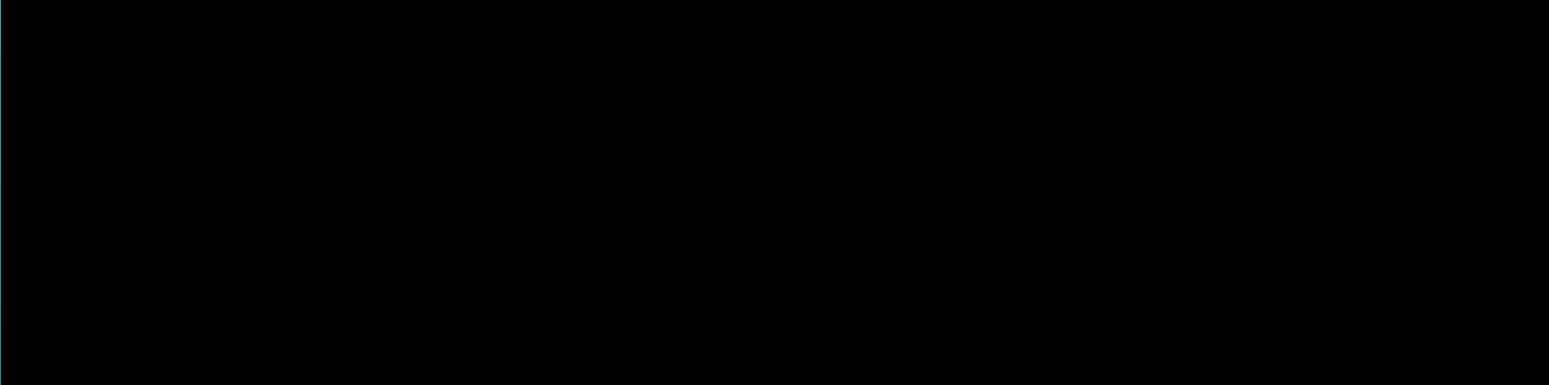
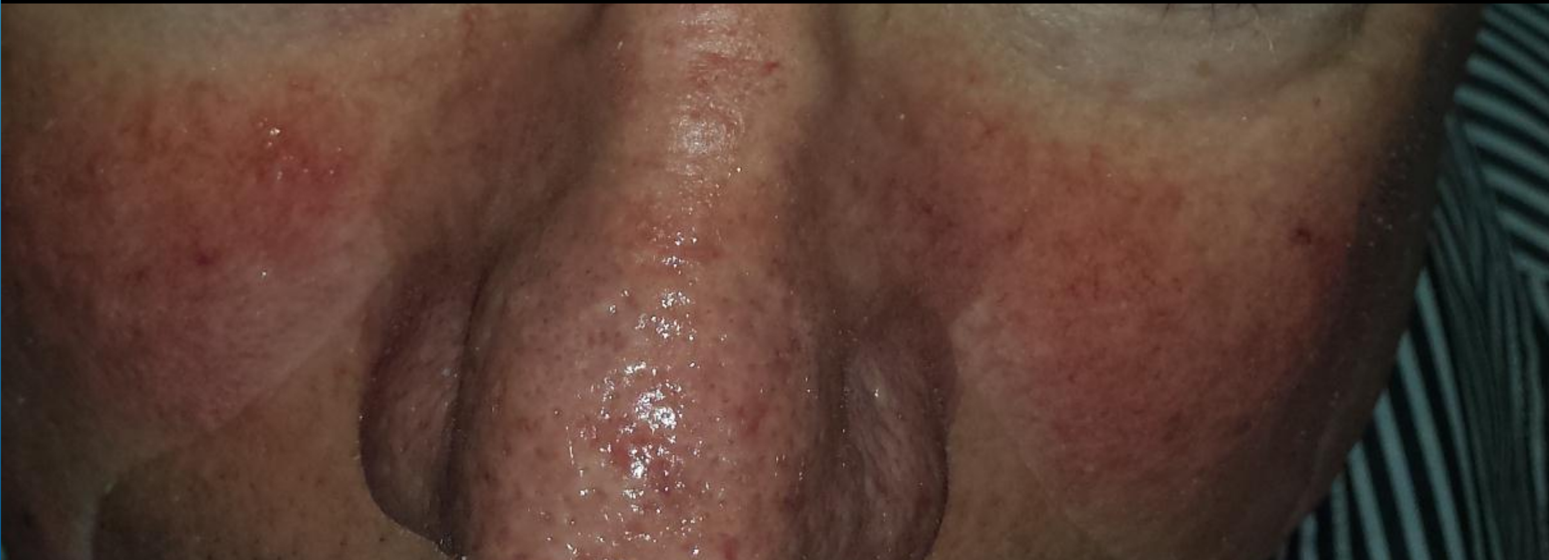
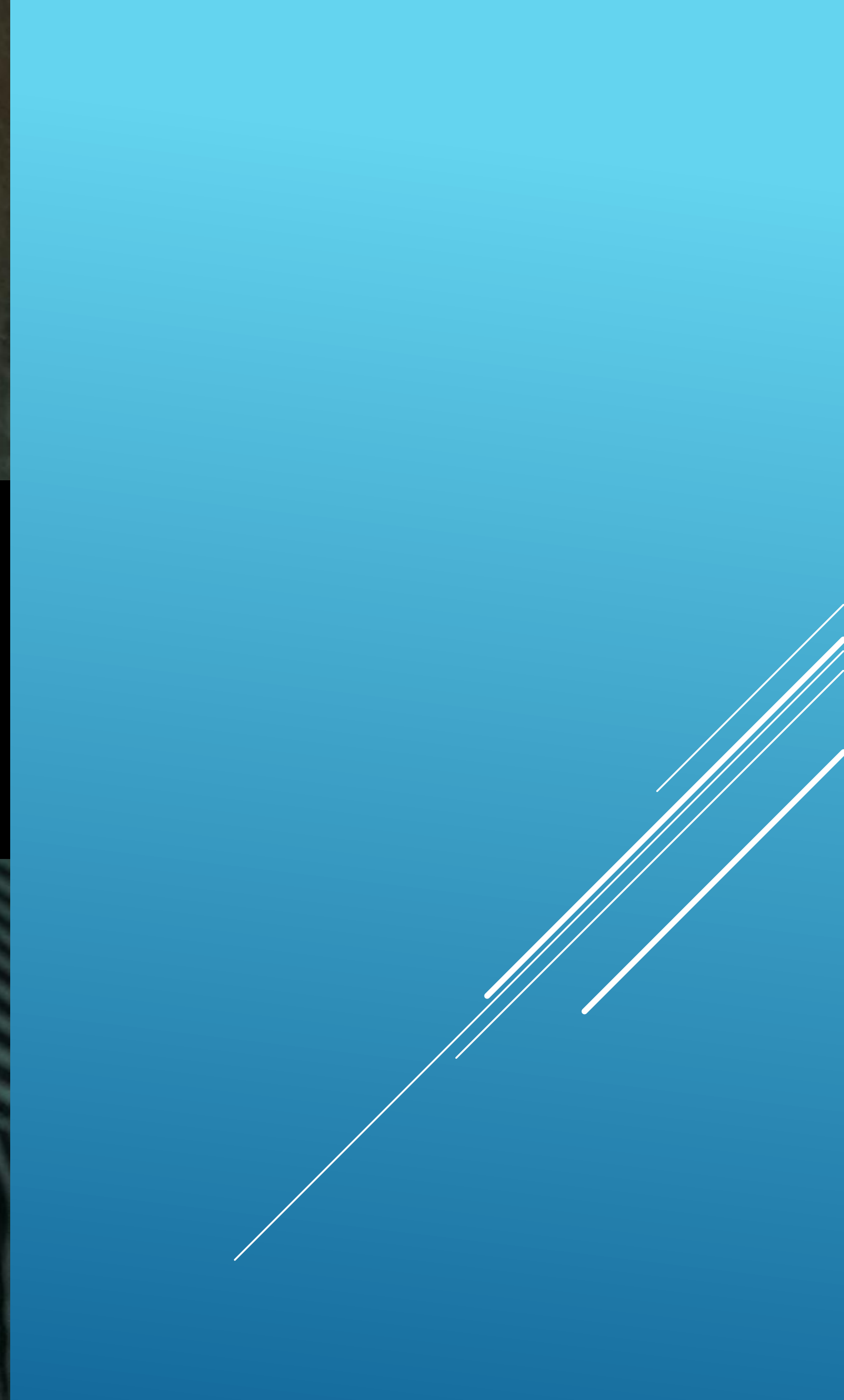




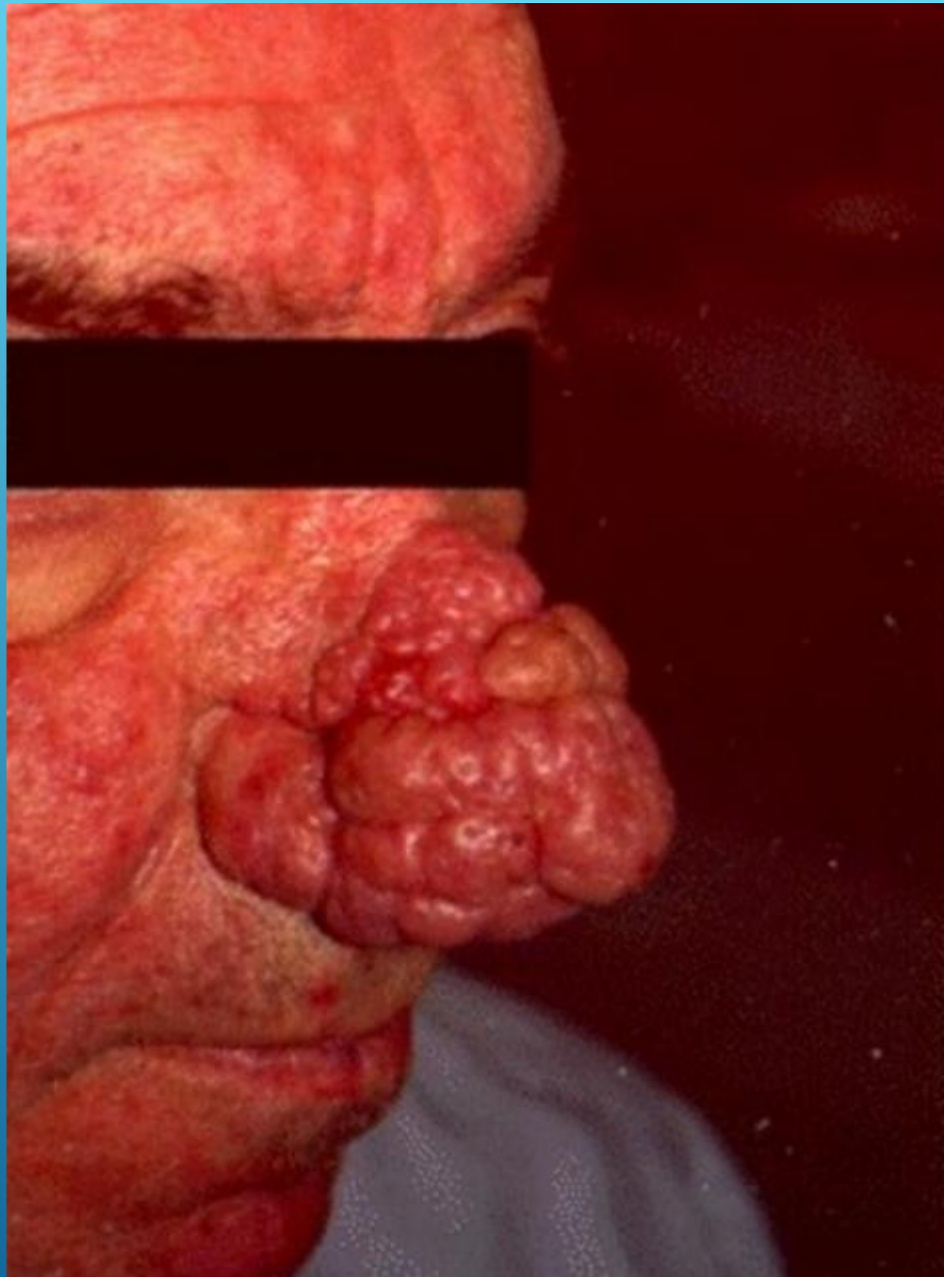
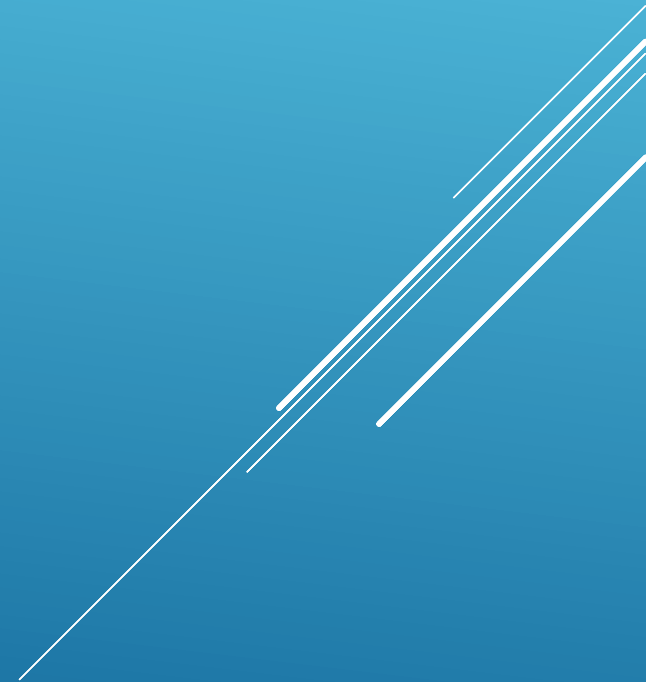


- Thickened skin
- Surface nodularity
- Nose especially

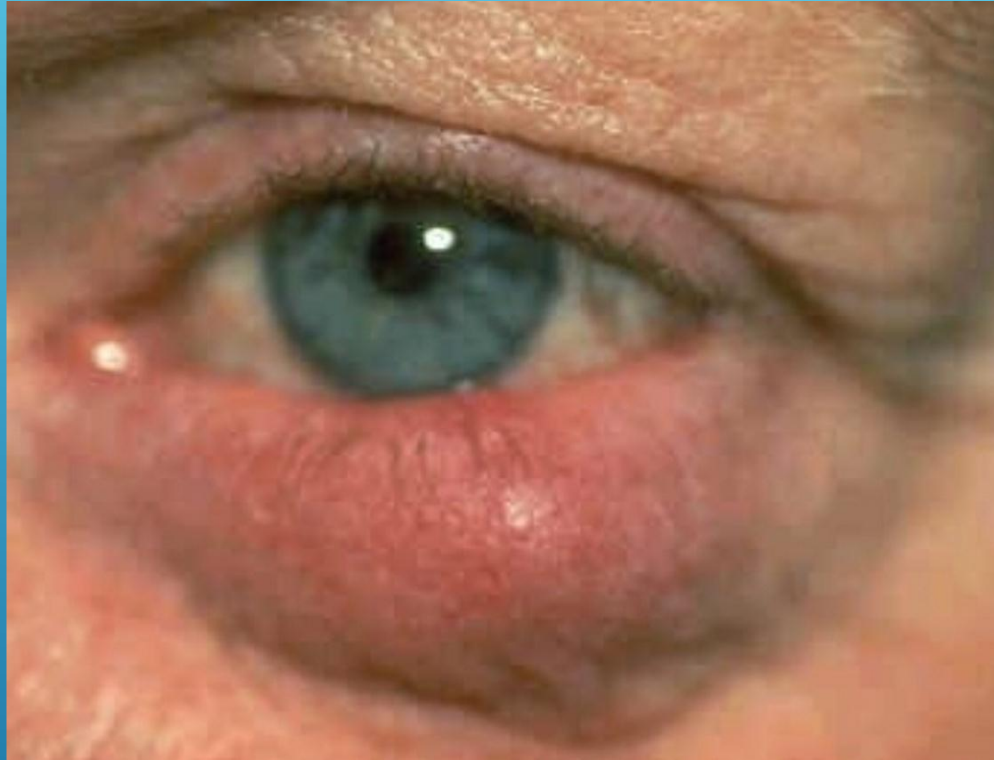
PHYMATOUS



- Watery / bloodshot appearance
- Foreign body sensation
- Burning or stinging
- Dryness
- Itching
- Light sensitivity



- **Dysregulation of the innate immune system**
- **Microorganisms**
  - Demodex folliculorum,
  - Stap epidermidis
  - H pylori
  - Bacillus oleronius
- **Neurogenic Dysregulation**
- **UV radiation**
- **Abnormal Barrier function**

PATHOGENESIS

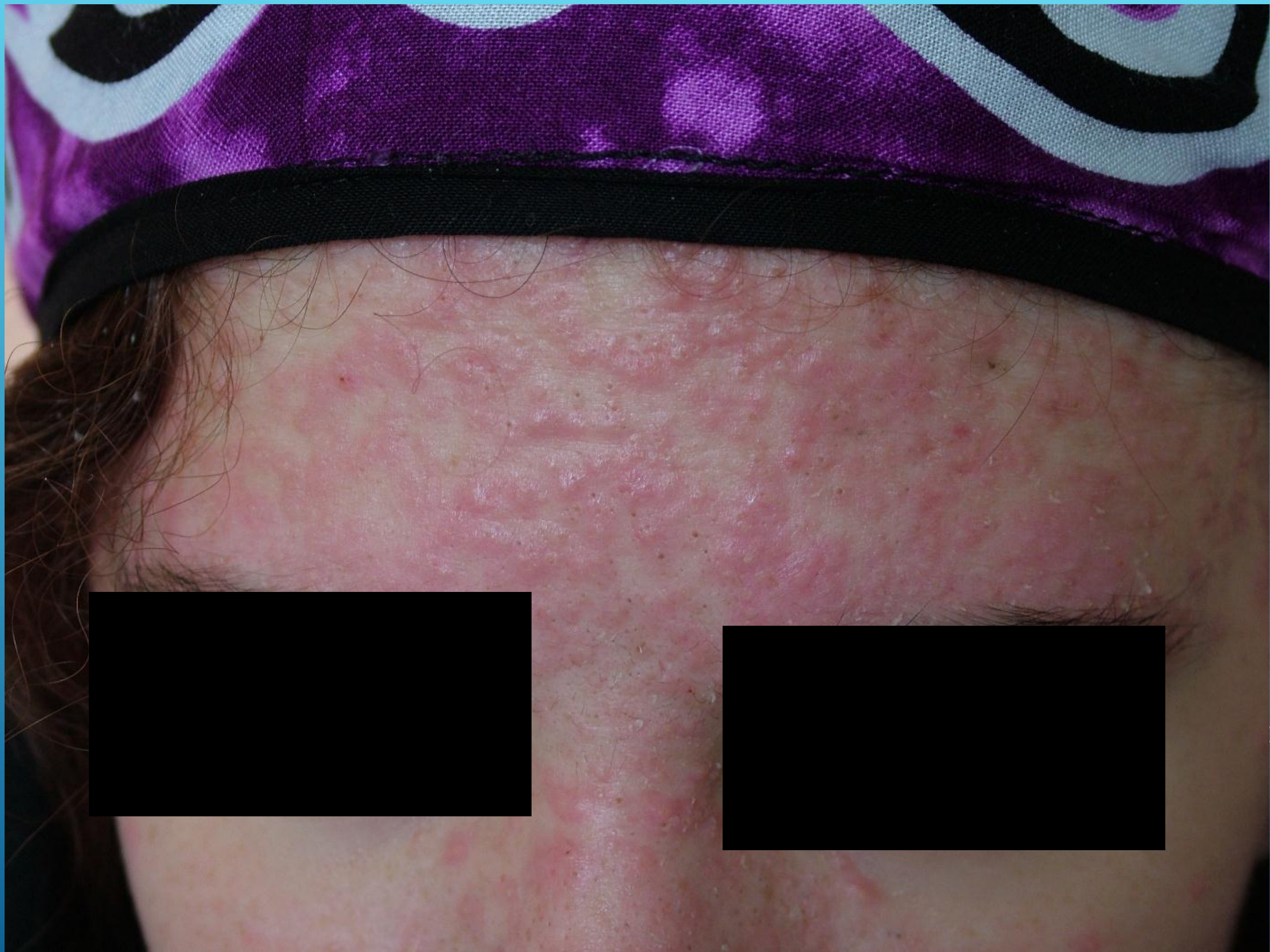
- Stress (emotional / physical)
- Temperature change
- Hot drinks
- Alcohol
- UV light
- Thick creams / Fragrances
- Steroids
- Spicy food

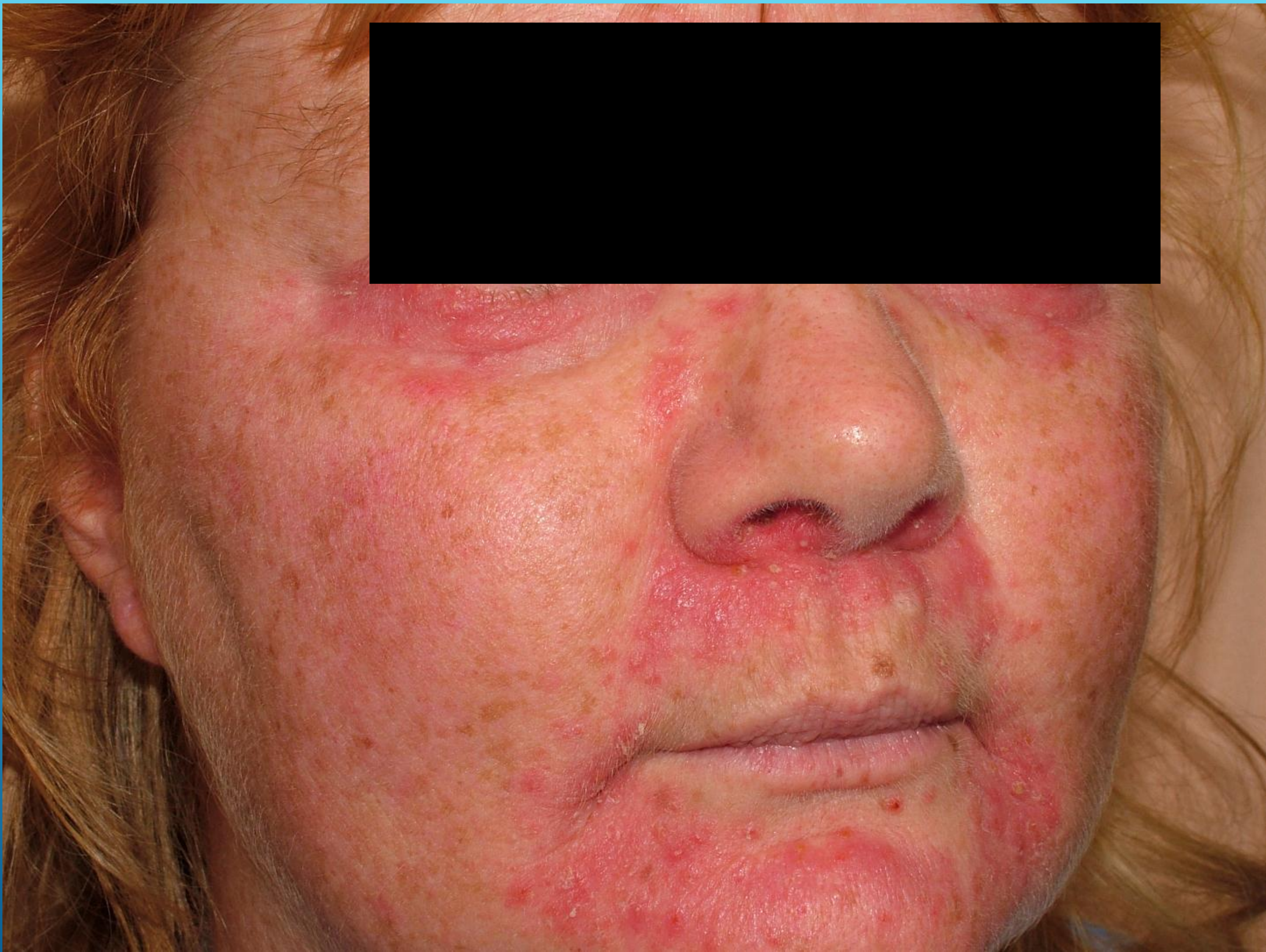
- Acne
- Seb Derm
- Perioral dermatitis
- Steroid acne
- Lupus
- Carcinoid syndrome
- Dermatitis
- .... and many more ....

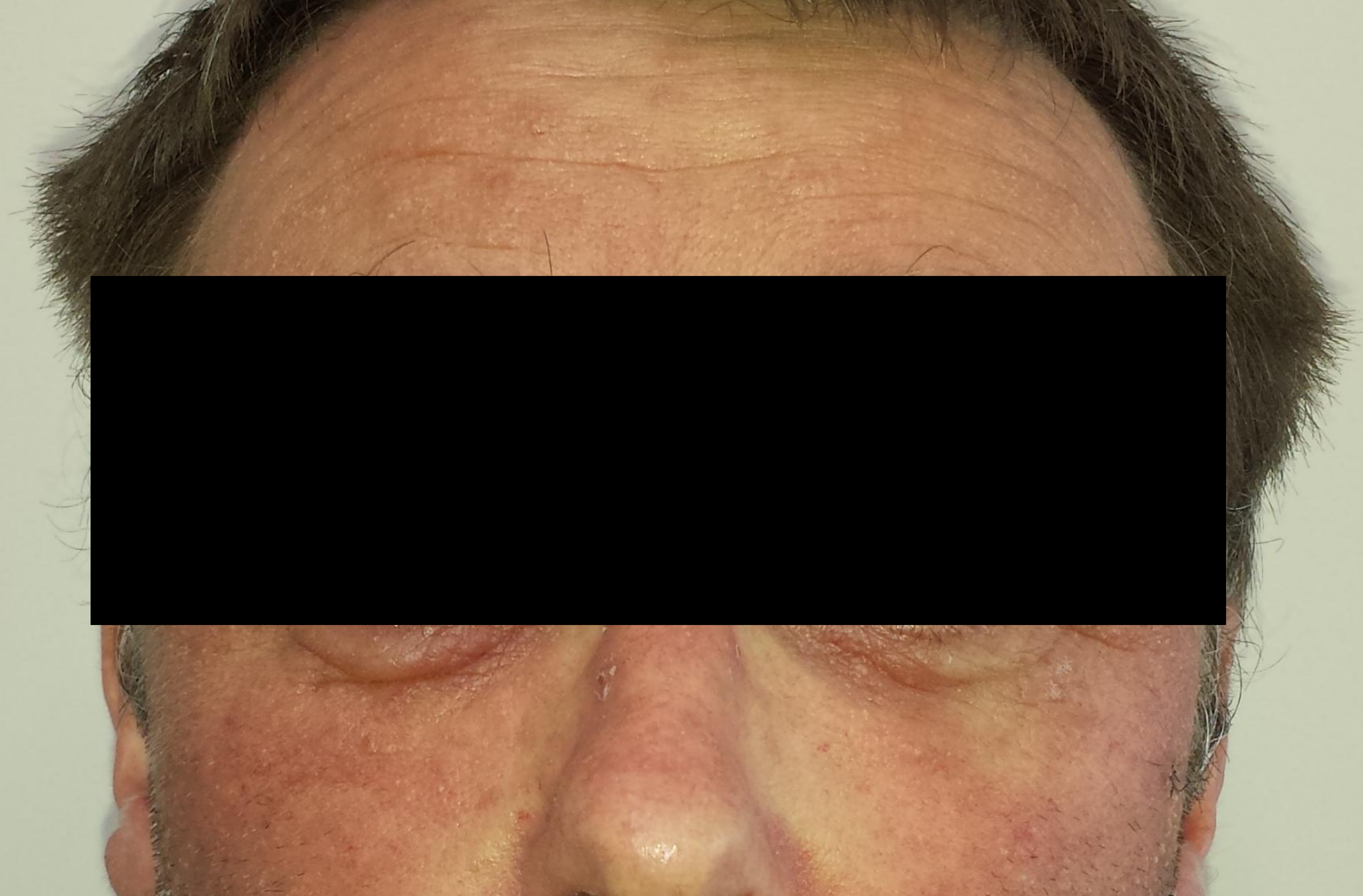
DIFFERENTIAL DIAGNOSIS

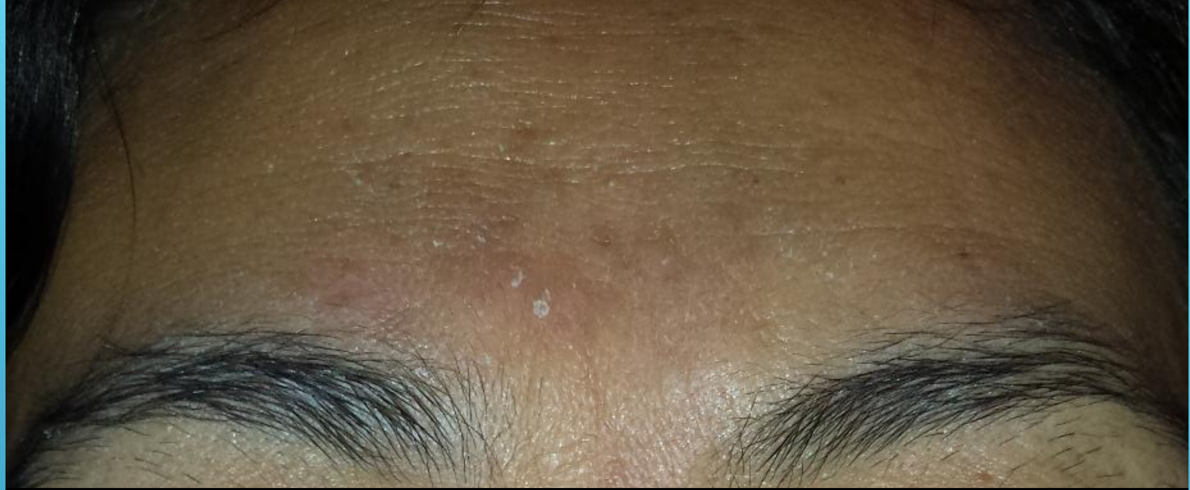
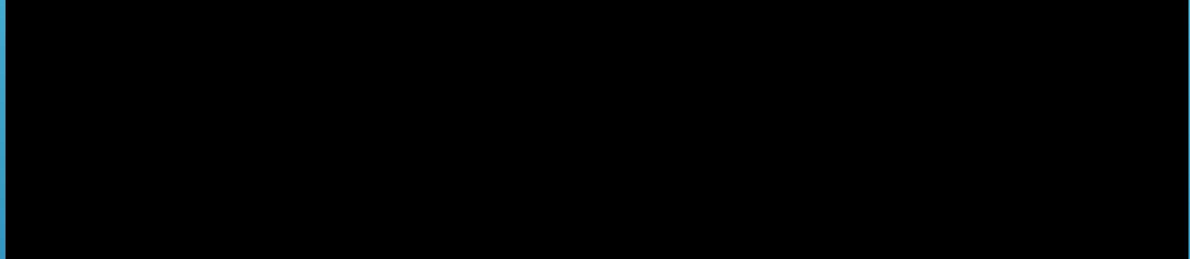
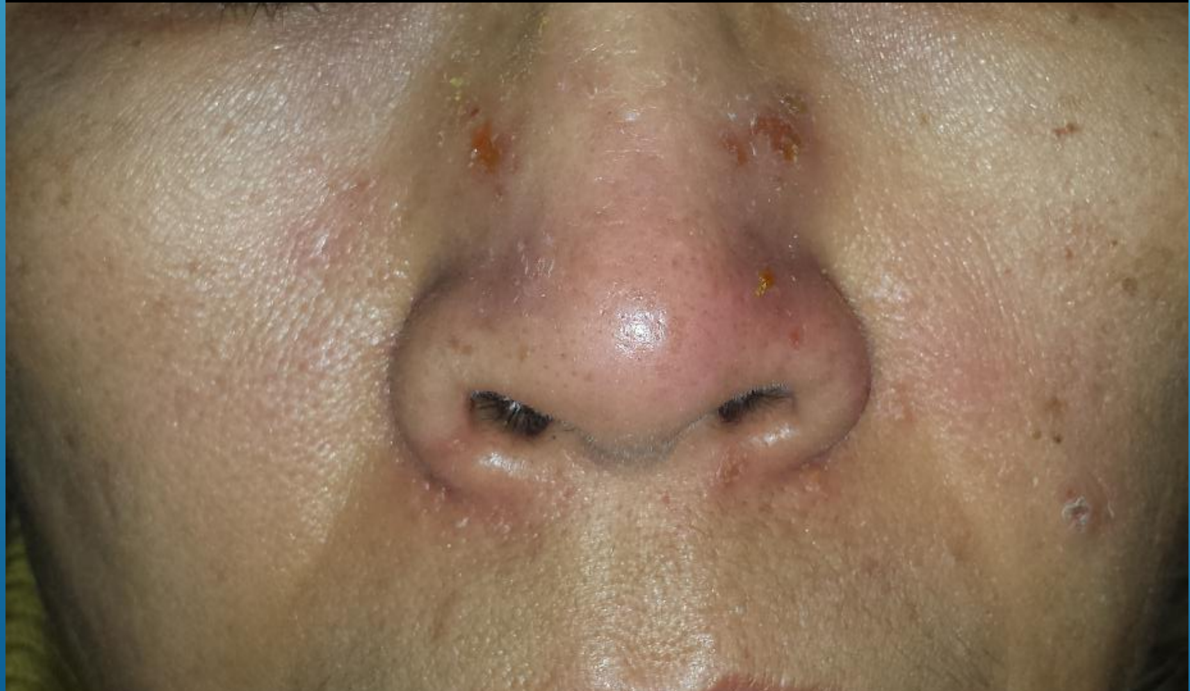
DIFFERENTIAL DIAGNOSIS

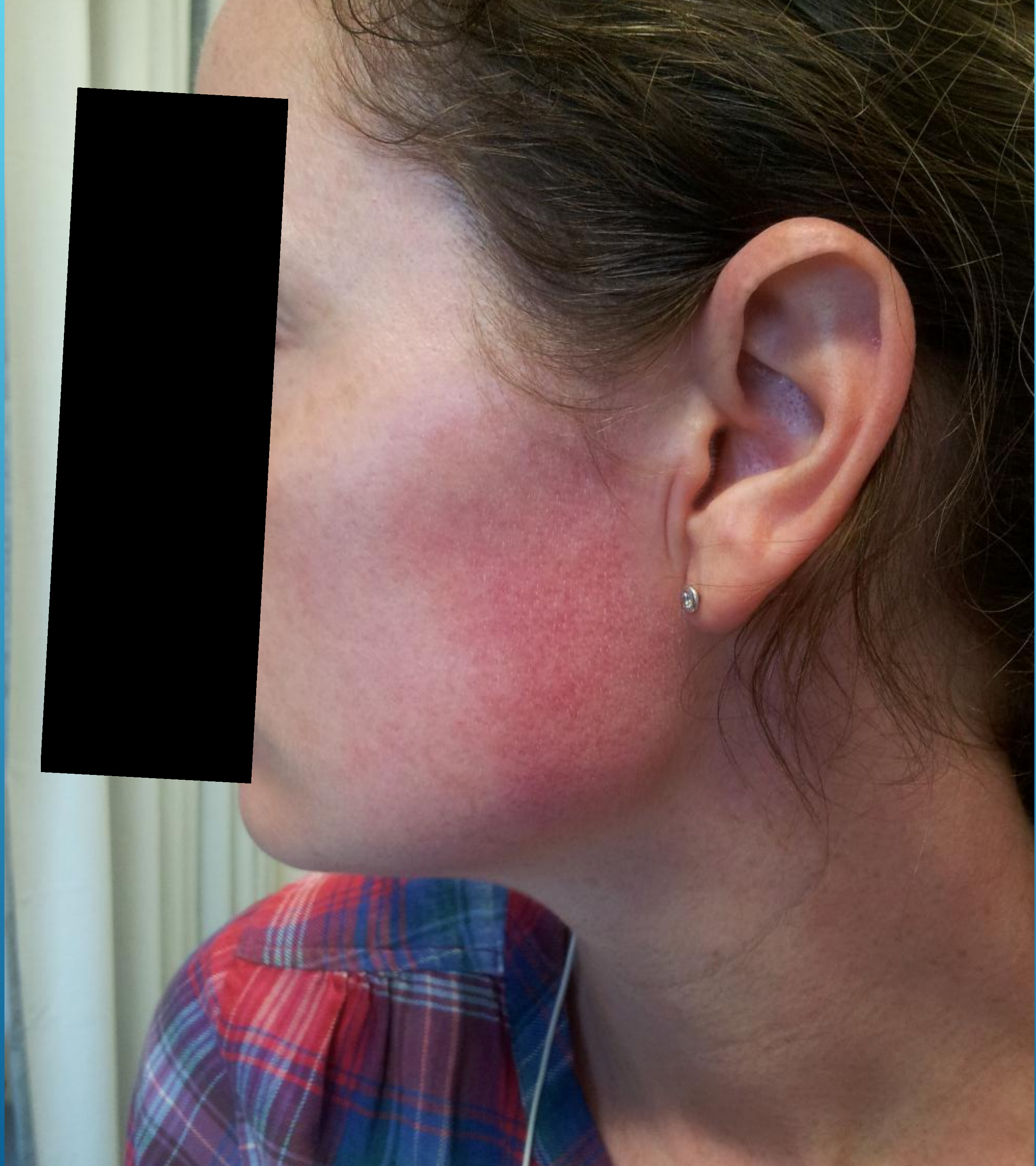
- Acne
  - Teens
  - Papules
  - Pustules
  - **Comedones**
  - No erythema
  - No telangiectasias
- Rosacea
  - Adults
  - Papules
  - Pustules
  - **No Comedones**
  - Erythema
  - Telangiectasias

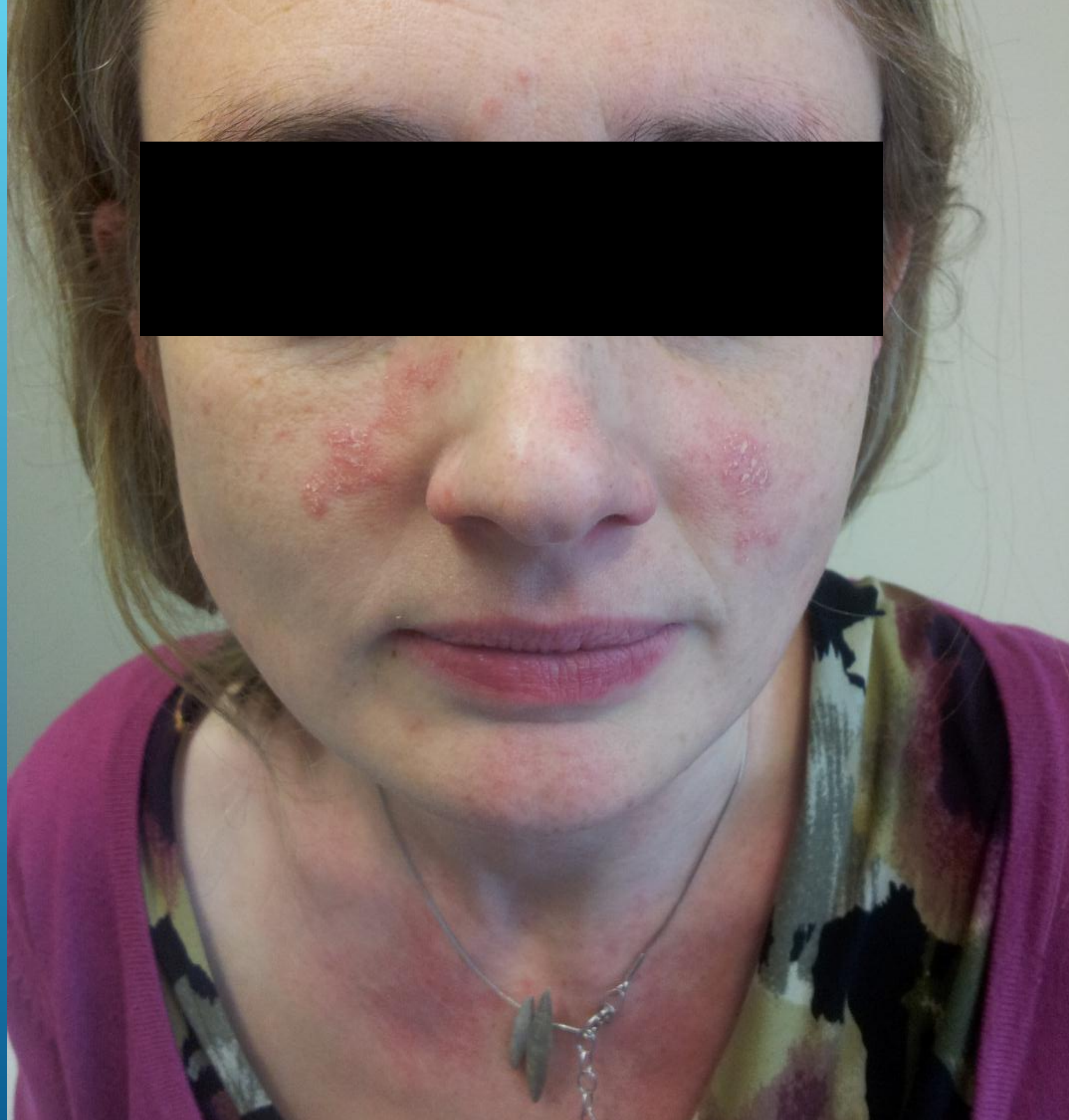


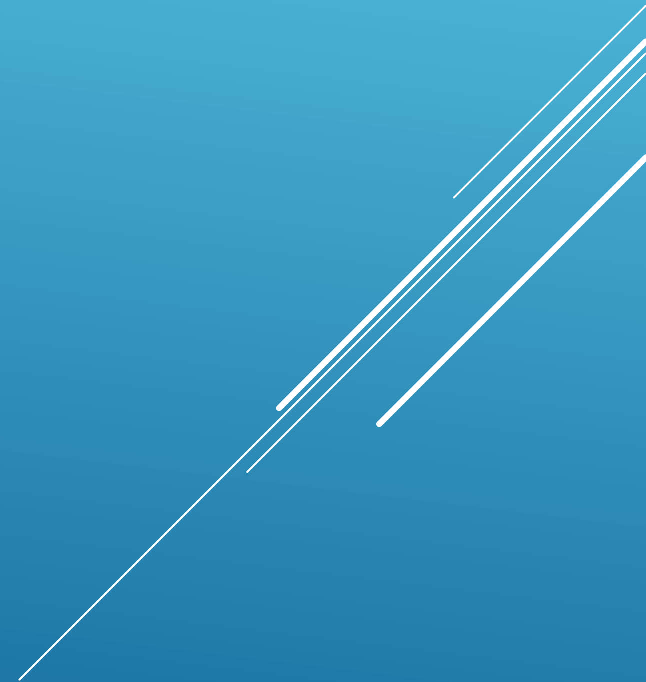


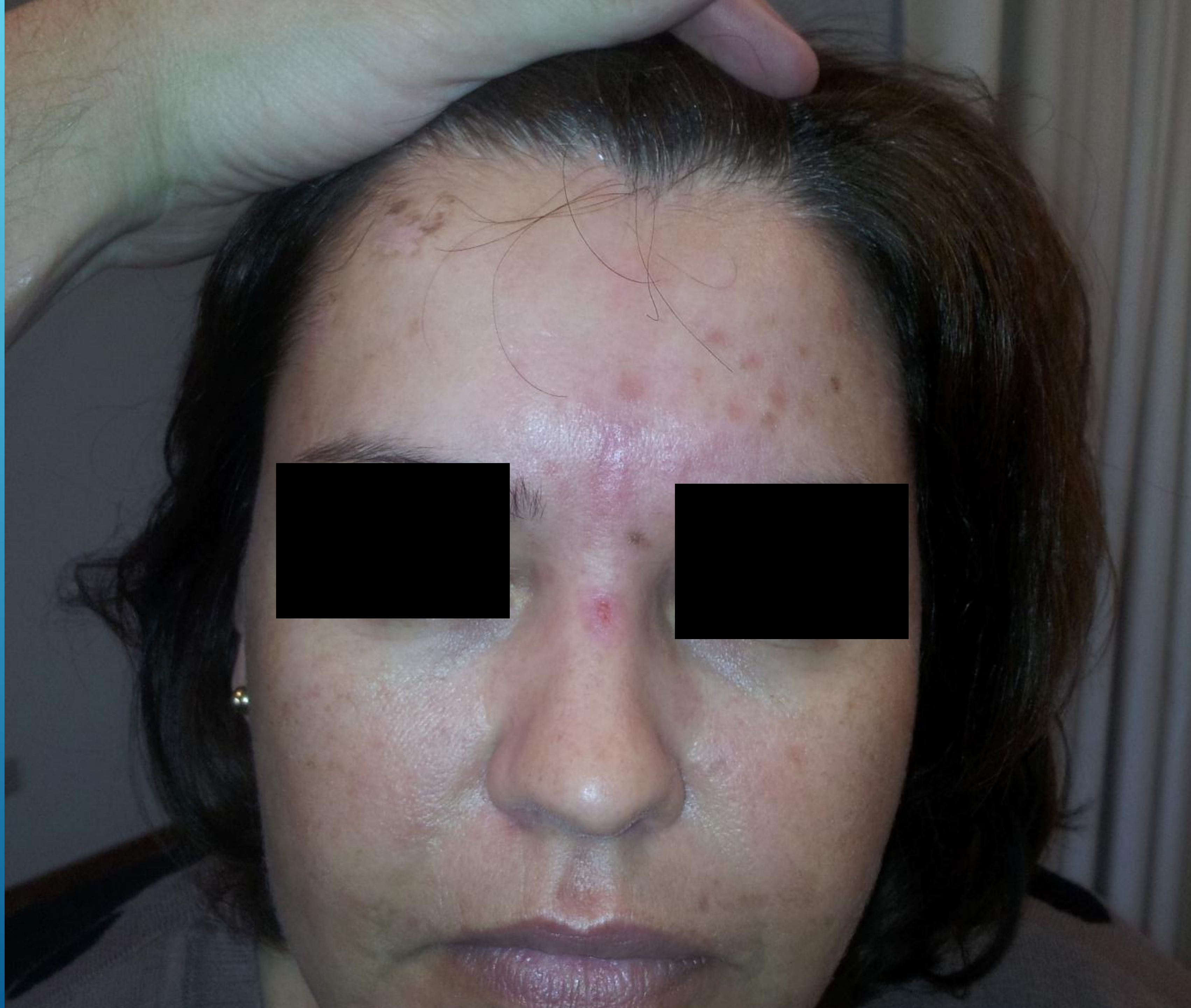


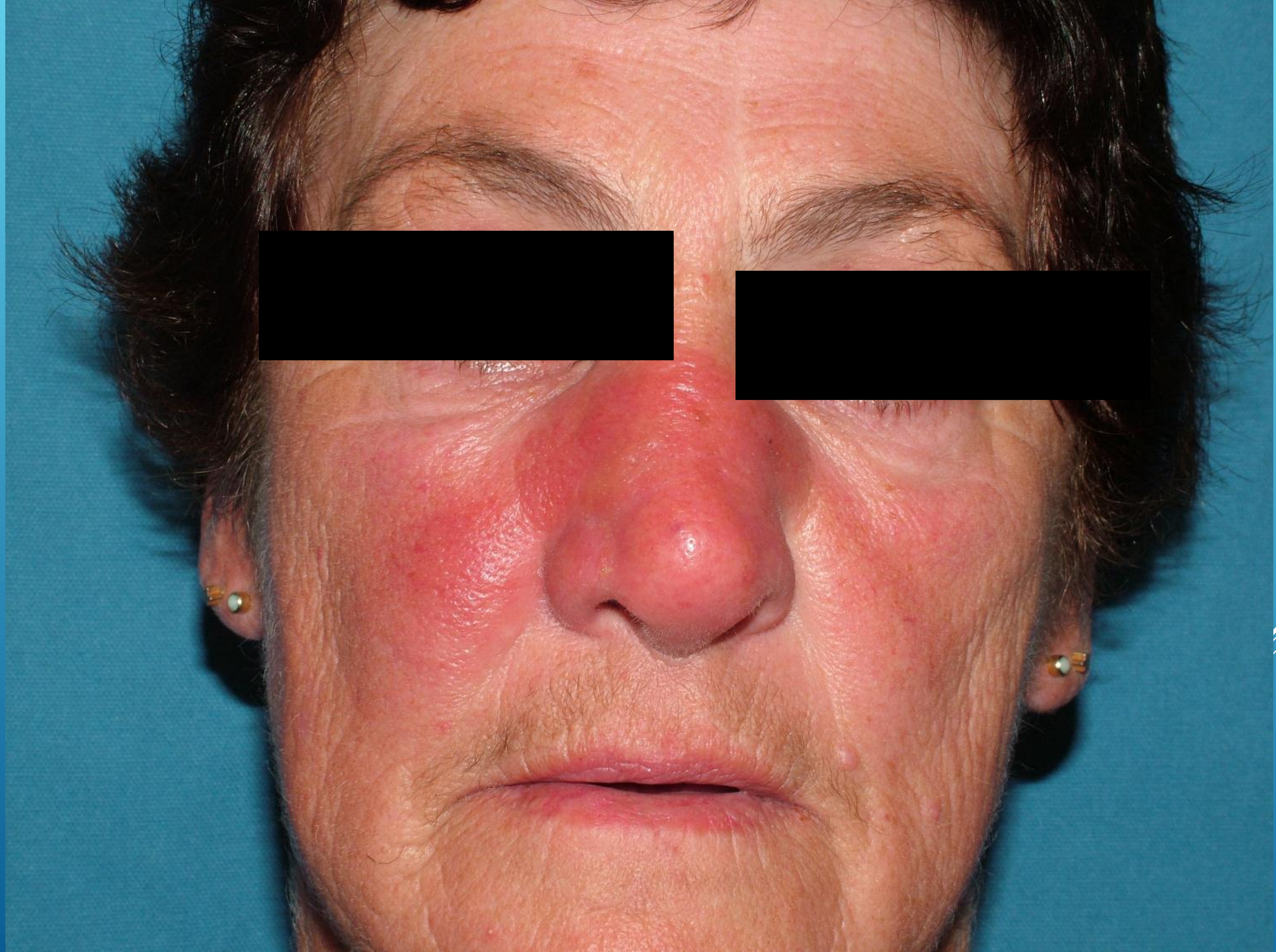




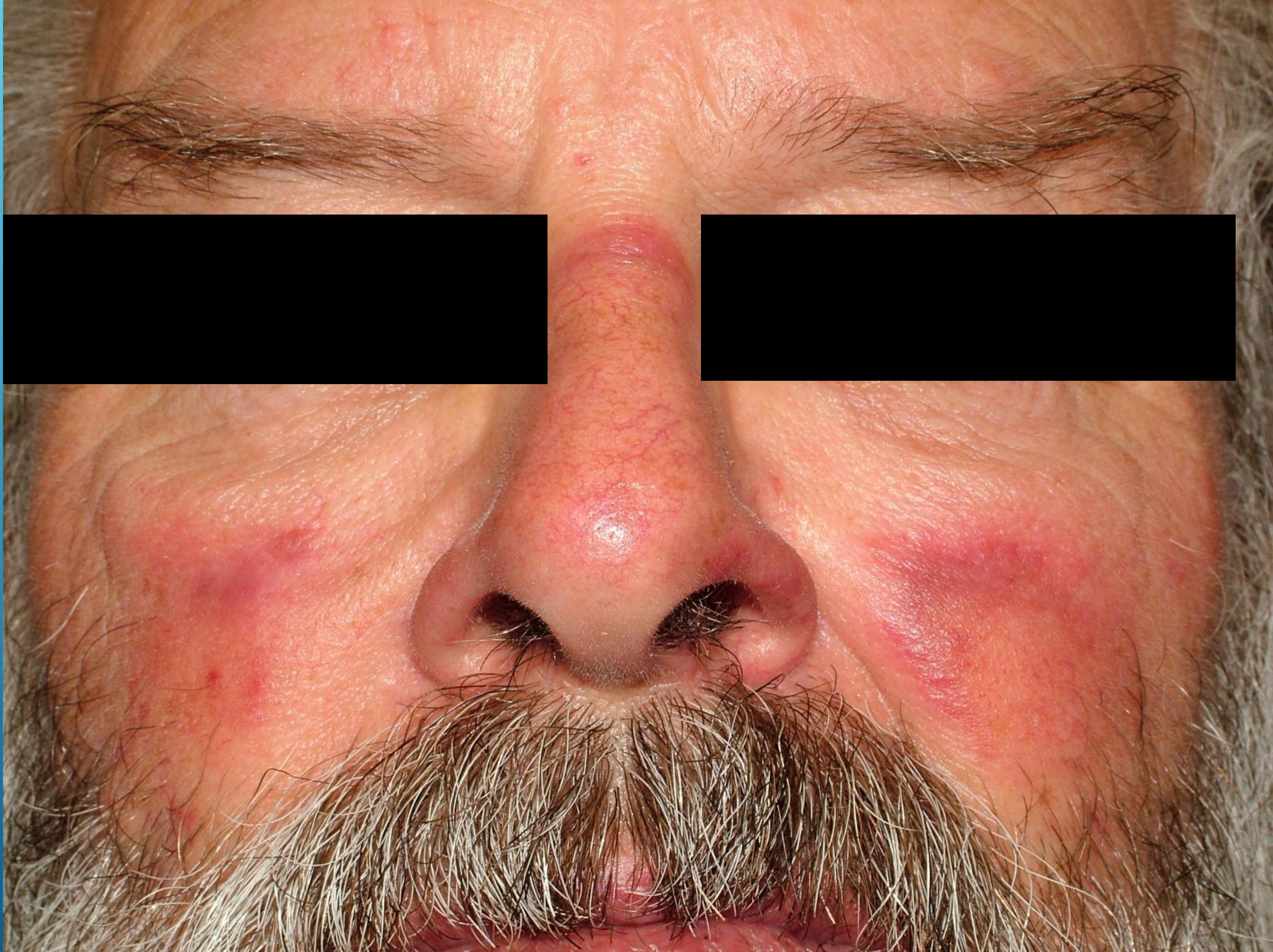


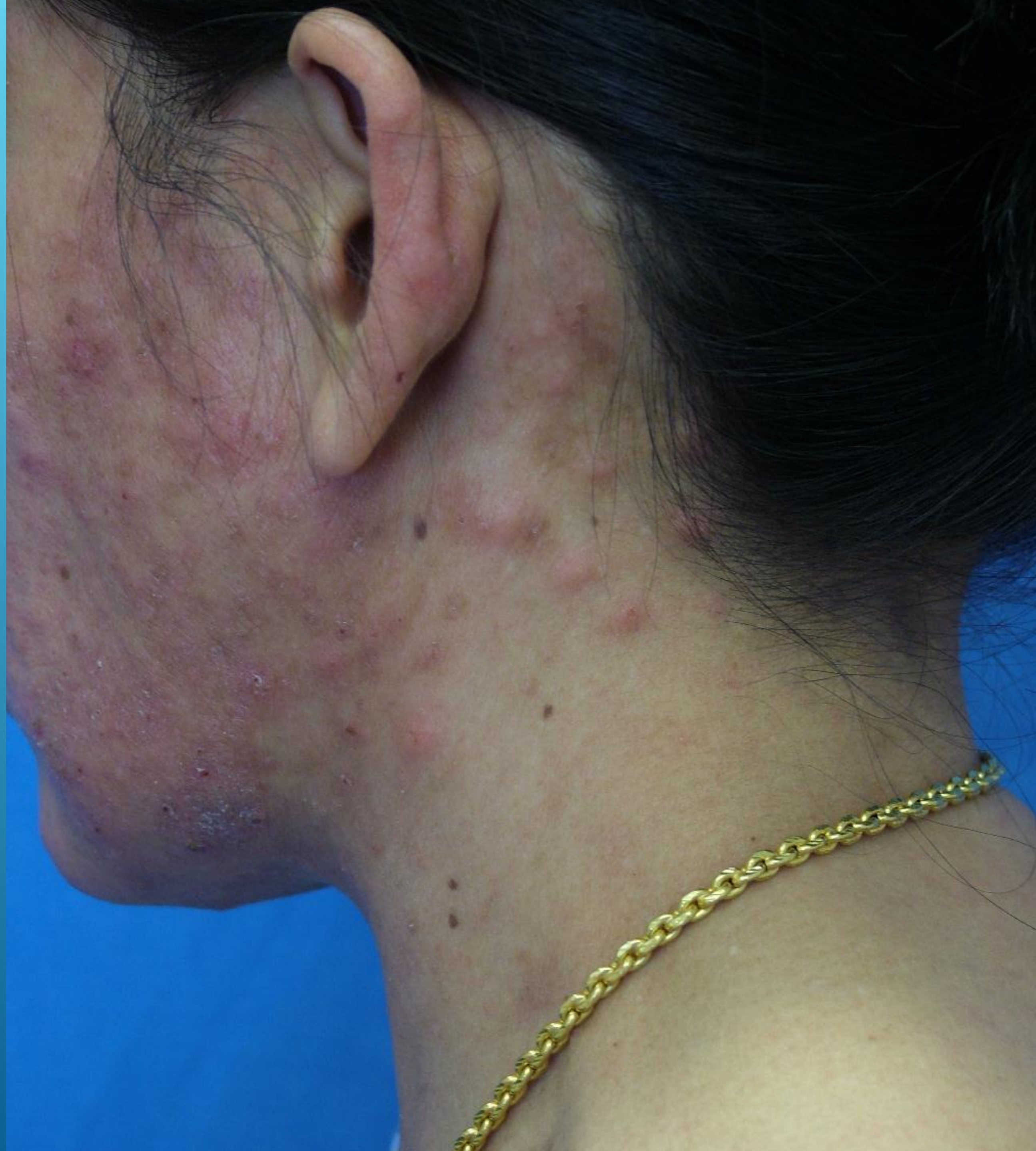












- Explain no cure
  - Treatment focused on control
- Many treatment options because none universally work
  - I show the list of options

- Focus on
  - Patient education
  - Skin Care
  - Pharmacologic / Procedural interventions

TREATMENT : PATIENT EXPECTATIONS

…une response) directly promotes further production of cathlecidin and …ates the cycle of activity (and resulting inflammation, vascular permeability and dilatation)

… **acid** is a naturally occurring dicarboxylic acid and aside from being …terial, reduces vasodilatation through the inactivation of cathlecidin and is …mmatory from blocking reactive oxygen species produced by neutrophils

…einhoff M, Schauber J, Leyden JJ. 2013 'New insights into rosacea pathophysiology: A review of recent findings' American … Dermatology pp 515-526 http://dx.doi.org/10.1016/j.jaad.2013.04.045

the heterogeneous nature of this condition

- Considering rosacea as … localised dysregulation of innate imm… into new treatment… …dities.
- Both existing and e… exert maximum clinical effect whe… specific clinical mani… …ase

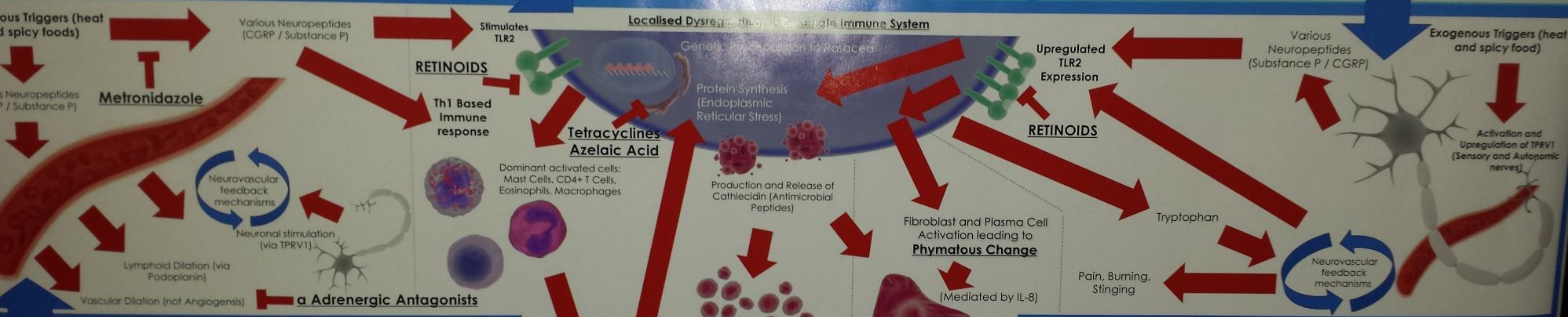
receptor on post capillary venules

•The upregulation of TPRV1 positive nerve fibres in the skin in susceptible individuals results in long-term and persistent erythema and dysethesia (burning and stinging pa… and sometimes itch

•Production of neuropeptides pituitary adenylate cyclase-activating polypeptide (PACAP) and vasoactive intestinal peptide (VIP) has also been shown to cause marked vasodilation and an increase in vascular permeability

Reference: Piccolo V, Ruocco V, Russo T, Ruotolo V, Piccolo S, Baroni A 2013, 'Unilateral rosacea in patients with facial nerve palsy: A … example of immunocompromised district', Japanese Dermatological Association – The Journal of Dermatology December 2013, p 850

Reference: Schwab VD, Sulk M, Seeliger S, et al 2011, ' Neurovascular and Neuroimmune Aspects in the Pathophysiology of Rosacea' Investig Dermatol Symp Proc December 2011; 15(1) pp53-62



Vascular Permeability and Dilatation

Triggers of vascular changes in rosacea: UV light, exposure to hot and cold temperature changes, strong emotional responses, ingestion of alcohol or spicy foods and chemical irritation

Vasodilation is widely recognised, however angiogenesis and lymphangiogenesis has only been implicated in the pathogenesis of Phyatous Rosacea

•Overexpression and dysregulation of TRPV1 receptor in susceptible individuals causes exogenus stimulants (heat / spicy foods) to cause prolonged vascular flushing and pain from extensive vasodilation after neuropeptide release (Substance P / CGRP)

•Blood and lymph vessel vasodilatation causes plasma extravasation and resulting oedema which is clinically apparent

•The cycle of vasodilatation continues as a final pathway of dysregulation of innate immune system and neurogenic stimulation (from increased production of PACAP / VIP and the interaction between cathlecidin and Karikrellin-5)

Retinoids(chemical compounds of Vitamin A) are known to decrease the expression of TLR2 which may halt a dysregulated immune response, and reduces the size and number of sebaceous glands which has clinical implications for Phymatous Rosacea

Reference: Steinhoff M, Buddenkotte J, Aubert J, Sulk M, et al, 'Clinical Cellular and Molecular Aspects in the Pathophysiology of Rosacea' 2011, Journal of Investigative Dermatology Symposium Proceedings (2011) Vol 15 pp 2-11

Alterations in the Cutaneous Microbiome

•The cause and effect relationship of microbiome production and the clinical manifestation of rosacea is not well understood

•Infectious microbes implicated in rosacea: Demodex folliculorum, Bacillus oleronius, Helicobacter Pylori, Staphylococcus epidermidis, Chlamydophila pneumoniae

•Microbial colonisation may be enhanced in individuals with an altered innate immune system and influence disease progression

•An upregulation of alarmins (including cathlecidin) has been described in all subtypes of rosacea and stimulates an innate immune response

•The adaptive immune response (involving Th2 B cell and IL-8 activation) is more prominent in later subtypes of rosacea. IL-8 activity has been linked to increased fibroblast and plasma cell activity resulting in early phymatous change

Tetracyclines are often used to treat acne, but even at sub-antimicrobial doses have anti-inflammatory properties from causing a downregulation of proinflammatory cytokines and upregulatinon of anti-inflammatory cytokines. It also has anti-angiogeneic effects through the inhibition of matrix metalloproteinases which may counteract vasodilation and increased vascular permeability.

Reference: Holmes, AD 2013, 'Potential role of microorganisms in the pathogenesis of rosacea', American Academy of Dermatology pp 1025-1032 http://dx.doi.org/10.1016/j.jaad.2013.08.006

TREATMENT

- Patient Education
  - **Triggers**
  - Avoiding topical steroids
- Skin Care
  - Very **gentle cleansers**.
  - Moisturisers. Rosacea has increased transepidermal water loss.
  - A study of metronidazole gel 0.75% alone vs with **cetaphil** cream showed improved dryness, roughness, desquamation and skin sensitivity.
  - **Sunscreen**. At least SPF 30. No specific sunscreen product been found to be most beneficial. Find one that is tolerable, probably best titanium / zinc.

- Topical **Metronidazole**
  - Been used since 1950's
  - Decreases ROS
  - Decreases erythema , papules, pustules when applied daily.

- Topical **Azelaic Acid** BD
  - Decreases Kallikrein 5 and Canthelicidin
  - Changes microbiome
  - 70 – 80% patients get some improvement
  - Generally well tolerated.
  - Build up to twice a day

- Very good for acne also. Sometimes useful to put people on after finish isotretinoin.
- Very good for erythrasma.
- Possible modest depigmentation effect for melasma.

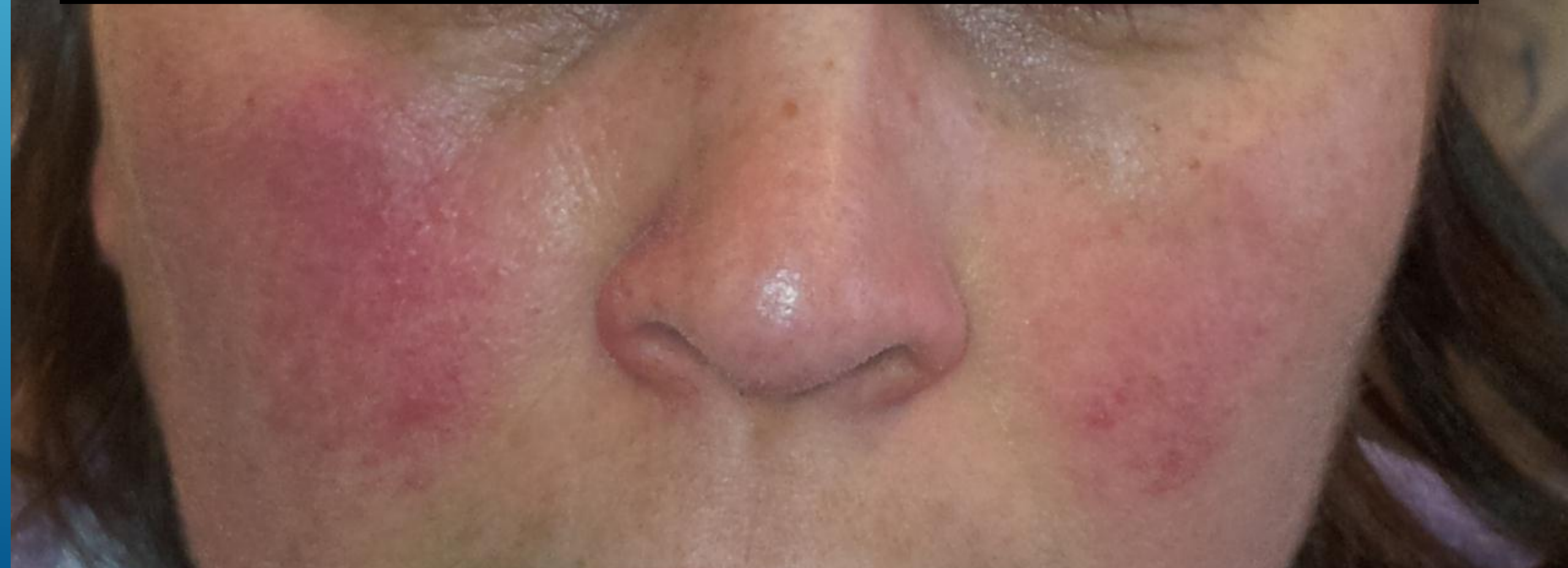
TREATMENT PHARMACOLOGICAL

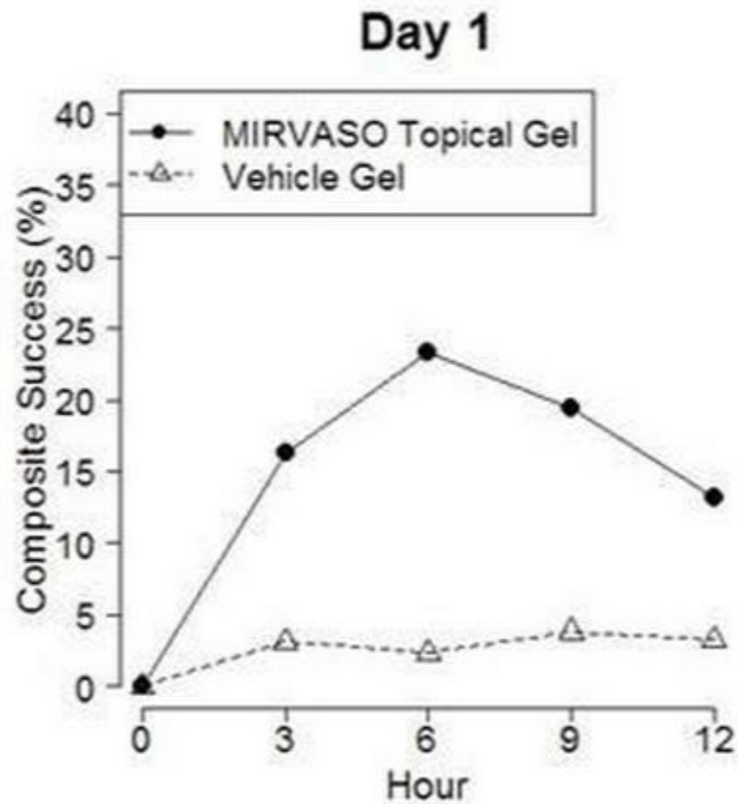
- Topical **Brimonidine 0.5% gel**
  - Alpha-adrenergic receptor agonist, works on smooth muscle cells around dermal plexuses.
  - Temporary reduction in facial redness
  - May be very marked.
  - Some patients love it "miracle cream"
  - Beware 10% have rebound erythema. Online profile.
  - Not useful for the large calibre telangiectasis without smooth muscle.

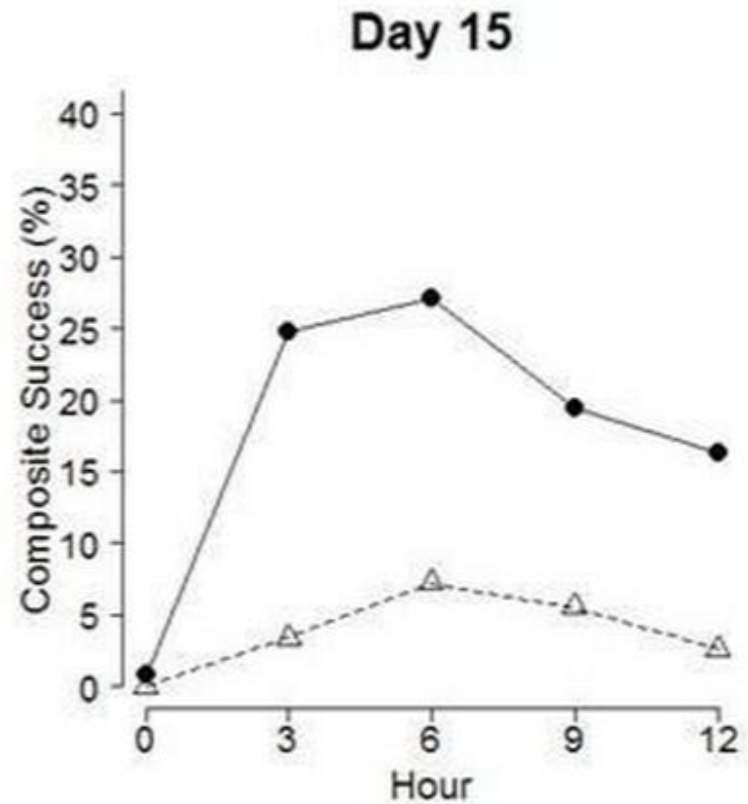
  - **I have found best when used with Azelaic acid.**

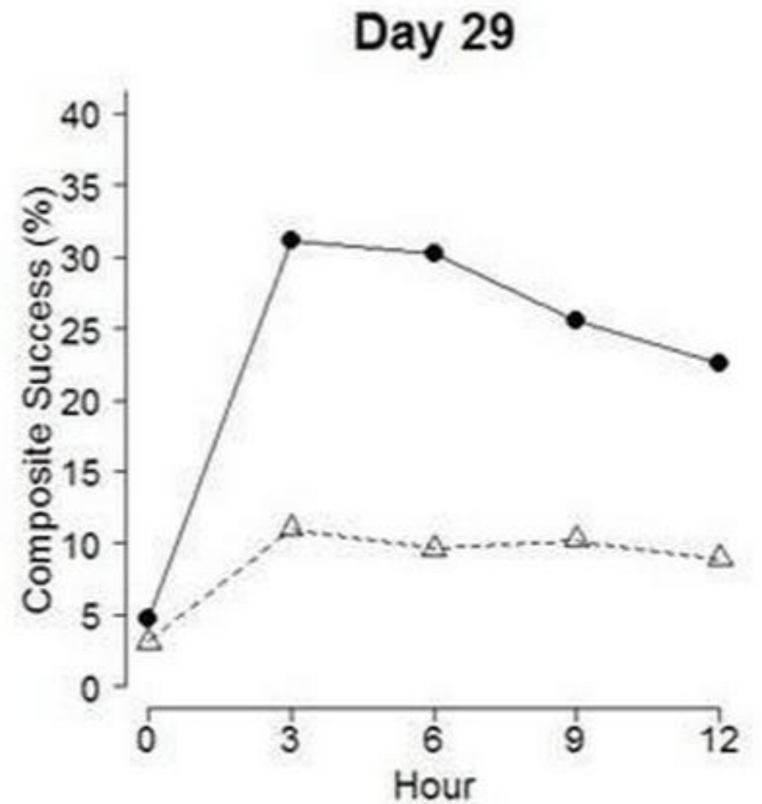
TREATMENT PHARMACOLOGICAL

Brimonidine gel









TREATMENT PHARMACOLOGICAL

TREATMENT PHARMACOLOGICAL

- **Topical retinoids**. Retrieve cream.
  - Helps dermal remodelling and possibly helps repair UV induced damage
  - Particularly good at reducing pustules, papules.
  - Not as well studied in rosacea. Not my first line.

- Topical **Calcineurin inhibitors : Pimecrolimus**
  - Inhibit T cell activation, reduces inflammation.
  - Mixed results in studies but well worth a go in conjunction with orals in refractory cases.
  - **Best I think if there is rosacea and dermatitis.**

TREATMENT PHARMACOLOGICAL

- **Permethrin Cream 5%**
  - Theoretically to lower demodex
  - Similar efficacy to metronidazole gel for erythema and papules.
- **Ivermectin cream 1 %**
  - I've not used yet. Very good results in recent trials FDA approved recently.
  - "Soolantra"   Cost ?

TREATMENT PHARMACOLOGICAL

- **Tetracyclines**
  - Doxycycline, Lymecycline , Minocyline
    - Antiinflammatory (lower ROS, inhibit nitric oxide, decrease MMP)
  - I like to use with Azelaic acid and then after a few months try just on the Azelaic acid.
  - If have to stay on long term then rotate including with erythromycin

TREATMENT : SYSTEMIC

- Isotretinoin
  - Low dose long term isotretinoin for papulopustular rosacea or phymatous.
  - Less likely to have a such a definite end point as when treating acne.
  - Warn re risk of increased erythema.

TREATMENT : SYSTEMIC

- For **Fulminant rosacea / pyoderma faciale ……**

  - **Prednisone** tapering over 4 – 6 weeks
  - PLUS **erythromycin** 400mg PO bd
  - PLUS **Azelaic acid**.

TREATMENT : SYSTEMIC

TREATMENT : PROCEDURAL

- Laser / IPL
  - Only option for telangiectasia
  - Can help general erythema
  - Several safety issues and patient expectation issues that need to go over.

- Pyoderma Faciale
- Unsatisfied patient
- Diagnostic uncertainty

WHEN TO REFER

- Avoid triggers …. advise keep a diary
- Ice in mouth prior to flushing triggers
- Sunscreen zinc oxide / titanium dioxide
- Soft scarf over face if in wind
- Avoid lots of “skin care” creams, fewer products the better
- Don’t do ANA with every red face
- Try and get control with systemics & creams then withdraw systemics
- Avoid rubbing / scrubbing face
- Avoid hairspray
- Elidel
- Triamcinlone injection. Risks.
- Beware efudix
- Watch out for hidden tumours

TIPS