The red face—an overview and delineation of the MARSH syndrome

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Summary

The problem of the red face in females is reviewed. After excluding common causes such as contact dermatitis, seborrhoeic eczema and photodermatitis the diseases affecting the remaining patients fall into three groups: marked erythema with no feeling of heat or sensitivity, usually erythromelanosis faciei; marked flushing and burning with intense sensitivity for which the term facial erythrodysaesthesia is proposed; the so-called MARSH syndrome in which an overlap of androgen-dominant symptoms occurs – melasma, acne, rosacea, seborrhoeic eczema, and hirsutism. The latter group may respond best to low dose oral isotretinoin.

There are few patients who present the dermatologist with more problems of management than the red-faced woman. and this problem is much more common than in males, although the occasional man may also be considerably disturbed by the disorder.

Some of the many causes of such redness are listed in Table 1 and for the purposes of this report, I assume that its more obvious causes have been eliminated either by a fortunate discovery in the history taking, such as of the use of a new cosmetic or hair dye, or of flushing appearing after a meal,[1–4] while the examination may , on the other hand, reveal an obvious classical dermatosis[5] (Figs 1, 2 and 3); investigation is sometimes needed to exclude contact or photocontact factors. However, we are often left with a patient in whom there is uncertainty as to what is happening until it rapidly becomes clear that the patient has already seen numerous colleagues, is at the end of his or her tether and cannot tolerate any medication whatsoever on the face. The condition is then often described very graphically: 'I cannot tolerate make-up or even tap water. My whole skin goes very dry and very red and my face feels as if a flame thrower has been on it. Lights make it worse but this is not the cause.' (Attempts at self-diagnosis are often offered, and another patient spent the whole period during which she was being investigated in hospital with the curtains drawn round her bed plying a battery operated fan on to her face.)

My interest in this situation goes back a number of years and I have worked closely, during that time, with a dermatologist whose primary interest is in the cutaneous circulation and another interested in psychodermatoses. Although a definitive answer to the problem cannot be given here I hope that this article, in which I share with you some thoughts which have formed my personal approach to the matter, will prove stimulating and provocative. Thus, over the last 10 years I have kept a file on all those patients whose red face was so severe as to cause a major psychiatric disturbance, 14 females and four males. The diagnosis, in each case, was difficult to identify with any degree of certainty but in the females there were five with predominantly rosacea symptoms and signs, four with mainly flushing, three with a predominantly seborrhoeic pattern, and two with erythromelanosis faciei which is discussed below. In this sample, the females developed psychiatric problems associated with their red face approximately four times more commonly than the males, while erythromelanosis, although seen frequently, gave profound psychological problems only rarely.

After exclusion of the more easily defined causes of red

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Table 1 Some causes of facial erythema.

Atopic eczema
Seborrhoeic eczema
Sebopsoriasis
Allergic contact dermatitis
Irritant dermatitis
Photocontact dermatitis
Rosacea
Lichen planus
Lichen planus actinicus
Carcinoid
Glutamate sensitivity
Diabetic rubeosis
Topical steroids
Alcohol flush
'Weather beating'
Mitral stenosis
Poikiloderma Rothmund–Thomsen
Sarcoid
Lupus erythematosus
Dermatomyositis
Pemphigus foliaceus
Erysipelas
Hansenosis
Lymphoma
Haemangioendothelioma
Keratosis rubra faciei of Brocq
Ulerythema ophryogenes
Erythrose peribuccale of Brocq
Riehl's melanosis
Perioral dermatitis
Erythromelanosis faciei et colli

face mentioned above the disorders affecting the patients can be grouped into three classes on the basis of the predominating symptoms:

- marked erythema with or without a feeling of heat in the skin;
- marked flushing and sensitivity or a feeling of burning, and intolerance of almost any topical application. Sometimes this sensation may be described as severe pain in the skin. Such flushing without sweating suggests direct vasodilator activity and the carcinoid syndrome should therefore be excluded;
- a combination or overlap of seborrhoeic eczema, rosacea and acne, together with several other findings, which I have designated the MARSH syndrome.

The first group above is characterized by the condition termed Erythromelanosis follicularis faciei et colli which was first described by Kitamura *et al.*[6] in 1960 (Fig. 4). These authors described six males aged between 17 and 22 years with durations of disease of 1–4 years. They noted in particular, that the skin appeared 'reddish brown, in some areas blotchy, with discolouration which involved symmetrically the pre-auricular and

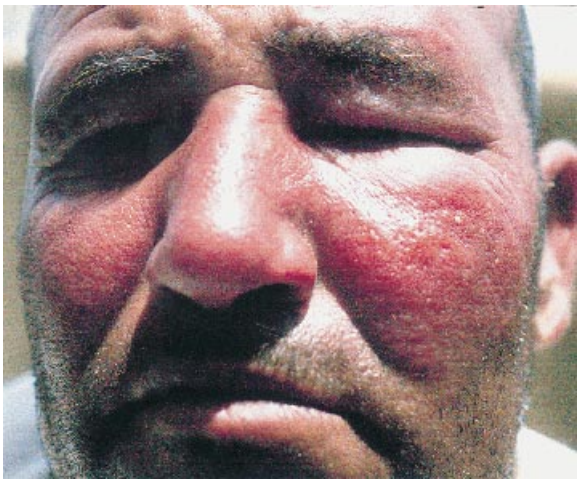

Figure 1 Erysipelas.

maxillary segments of the cheeks. The affected skin is covered with a dense crop of pinhead sized hyperkeratotic papules. These impart a fine granular appearance to the involved skin. Keratosis pilaris was present in 2

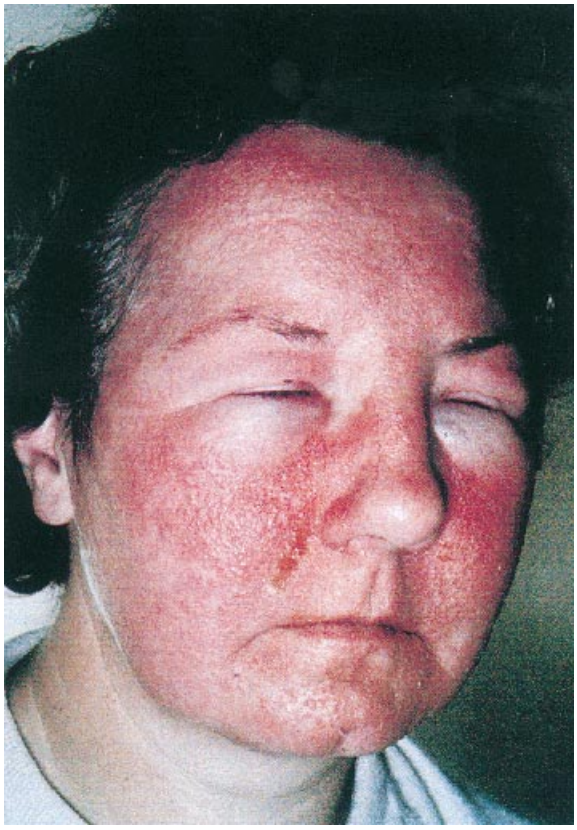

Figure 2 Contact dermatitis – chloramphenicol eye-drops.

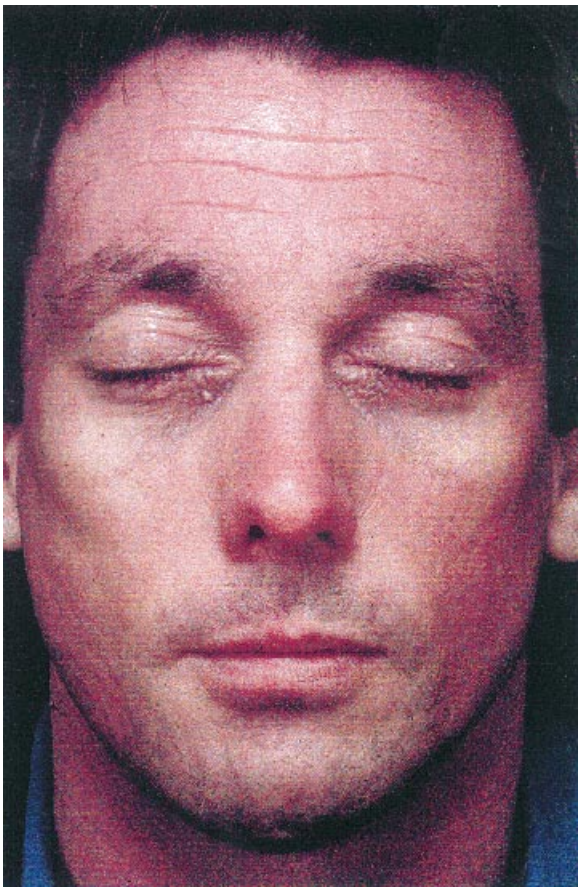

Figure 3 Atopic dermatitis.

patients, whereas 5 of 6 siblings of another patient presented KP only'.

In the 30 patients seen at St John's in my clinic, keratosis pilaris (KP) was nearly always present, a family history of erythromelanosis and/or keratosis pilaris was common, males and females were both affected and the histopathology showed KP, or KP with folliculitis, occasionally reported in the literature as specific to the disorder. Furthermore, in the Year Book review of Kitamura's article, a footnote records that 'Dr Kitamura, in a letter to the editors, pointed out that, in the opinion of the late Dr Hashimoto, erythromelanosis follicularis is the same as keratose pilaire rouge of the French schools'.[7]

With respect to KP, in a monumental study in three parts totalling 67 pages Brocq observed 'lesions that are pink, bright red or bluish red. These colourations are almost always much more marked than the cutaneous lesions which we describe at length. This is in our view keratose pilaire rouge'.[8] He also referred to previous

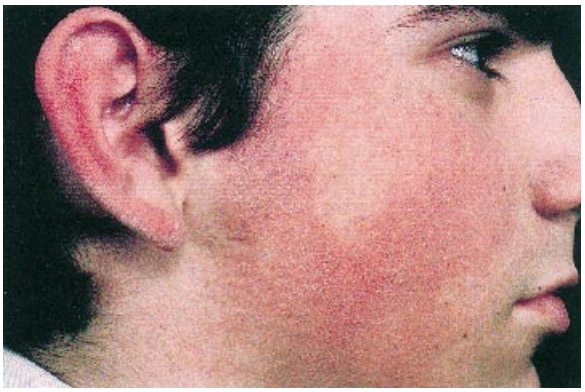

Figure 4 Erythromelanosis faciei.

descriptions by Erasmus Wilson and Tilbury Fox amongst others, one example is taken from the paper by Tilbury Fox: 'On the lateral parts of the cheeks are found tiny circumpilar elevations, very numerous, packed one against the other, distributed over two broad symmetrical zones occupying the whole extent of the lateral parts of the cheeks: but the redness of the affected regions is much brighter than on the forehead, and shows fine telangiectasia. . . On the face it is almost impossible to clearly appreciate the colour of the papules apart from the colour of the interfollicular skin because of the confluence of the lesions. . . In KP there is a definite tendency to atrophy of the hair follicle'.[9]

Such clinical findings may be attributed to the anatomical arrangement of follicles on the face. Thus, on the leg where there are about 40 follicles per square centimetre, the erythema is clearly perifollicular, whereas on the face where the density rises to 300 per square centimetre the still perifollicular erythema appears confluent. Nevertheless on palpation or stretching of the skin the eruption can be felt or seen to be finely granular – exactly the same changes as described in erythromelanosis follicularis faciei et colli. The two disorders therefore appear to be variations of the same condition.

Almost contemporaneously Taenzer described ulerythema ophryogenes which '. . . begins in early childhood with reddening of the eyebrows spreading locally and to the cheeks, the scalp and rarely the upper arms'. Taenzer reported six cases and emphasized follicular atrophy and scarring of the scalp.[10] There was also often a positive family history of a similar affliction or of eczema.

I believe that Brocq, Taenzer and Kitamura were describing the same phenomenon each with the emphasis on different aspects.

It is doubtful, however, if other conditions such as

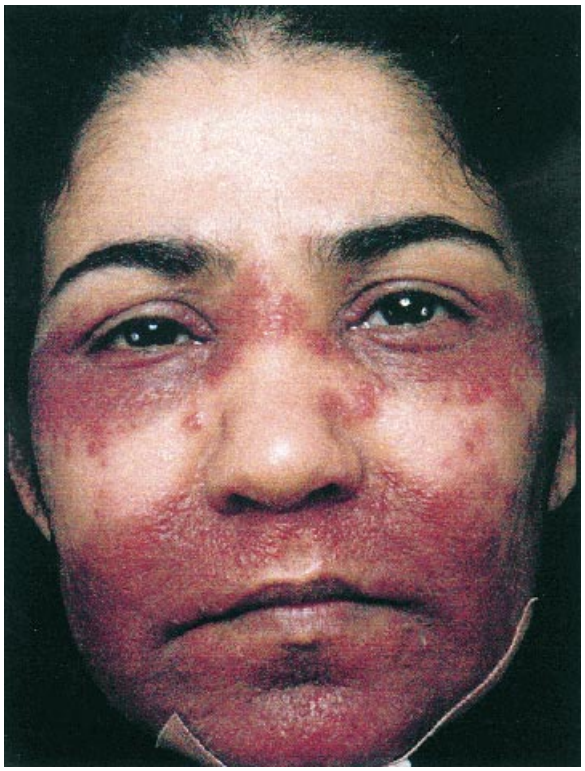

Figure 5 Erythrose peribuccale of Brocq.

atrophoderma vermiculatum or honeycomb atrophy of the face, should be included in the same spectrum. This condition is exceedingly rare and was best described by McKee and Parounagian 70 years ago in one male and one female:[11] 'Numerous closely crowded, small areas of atrophy separated by narrow ridges. This produced a reticulated, honeycomb or network appearance ... on close inspection with a lens, small follicular horny plugs were noted... the entire affected area was erythematous'. Also to be considered, on the other hand, is erythrose pigmentaire peribuccale of Brocq, which is a disorder of uncertain nature, but which could be a variety of perioral dermatitis as considered below[12,13] (Fig. 5). Further, poikiloderma of Civatte[14] is a different condition again. that shows fixed telangiectases on the face and sides of the neck often associated with blotchy hyperpigmentation. It is also known in Britain as Berkshire neck, after a study by the Berkshire dermatologist Hugh Calvert. Finally, Riehl's Melanosis[15] is another facial condition in which both sexes are affected. In Riehl's words 'Dark brown over the whole face, most marked on the forehead, malar region, and temporal region. In most cases the lateral parts of the face are more affected than the central. A floury scaling and on the forehead, cheeks and ears widened hair follicles with follicular plugging. Almost no erythema. Two of our patients also had generalized ichthyosis'. Many dermatologists consider this condition to be a form of photodermatitis with marked post inflammatory pigmentation, while exposure to cutting oils has also been incriminated.

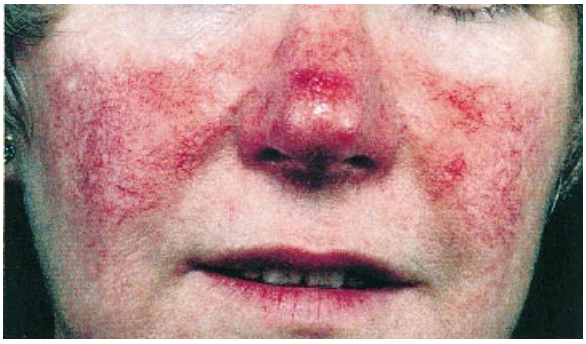

Figure 6 Erythrodysaesthesia.

The second group of red-faced patients is the most difficult to elucidate and to deal with. Many terms have been used for this disorder, including telangiectatic rosacea and vasomotor instability. They have been extensively studied by Wilkin in many publications. It should, however, be remembered that treatment with a number of drugs such as nifedipine, nicotinic acid, alcohol and some systemic conditions such as polycythaemia and the carcinoid syndrome may induce identical symptoms. Wilkin has suggested that the idiopathic condition results from an exaggerated vasodilator response of the facial capillaries in response to a thermal stimulus in the floor of the mouth, thereby passing heat from the internal jugular vein to the internal jugular artery and thence to the hypothalamus.[16] I think it unlikely that this type of patient suffers from an extreme form of rosacea as often suggested and David McGibbon has proposed the term facial erythrodysaesthesia for the condition, which is accurately descriptive [Fig. 6].

The third group of red facial disorders is particularly challenging and yet again is sufficiently different from the preceding two groups to be recognized separately. The term perioral dermatitis is often used to describe this disorder patients but, I believe, rather incompletely because there is often an overlap of several diagnoses in the patients although varying from one to another and with time. I have therefore called the condition the MARSH syndrome indicating Melasma, Acne, Rosacea, Seborrhoeic eczema and Hirsutism. The combination of small pinhead acne, rosacea and sensitivity, and mild seborrhoeic scaling is the most commonly encountered. The acneiform lesions appear first in two triangles

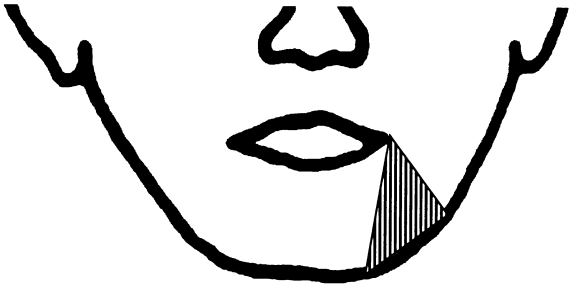

Figure 7 Triangles of putative hormone sensitivity.

delimited by the angle of the mouth, the crease down to the jaw line and the lateral point of the chin (Figs 7 and 8), which are possibly areas of high androgen sensitivity; soon the condition spreads to involve the whole perioral region, the naso-labial folds and occasionally the periocular regions. The anatomy of this region is interesting, the mental artery emerges from the mental foramen at this point and divides to richly supply the overlying skin (Fig. 9). A thermogram of this area shows a hot spot (Fig. 10) and it is possible that there is an overabundant and continuous supply of androgens to the area as a result although a difference in the density of hormone receptors could also be responsible. It should also be noted that the mental nerve also emerges from the same site. Finally, I do not believe that the features focused on by the term perioral dermatitis are in fact caused by the use of pearlized lipstick, contact with toothpaste ingredients or the application of topical steroids.

Management

The following therapeutic suggestions for the treatment of the three groups of conditions described above are

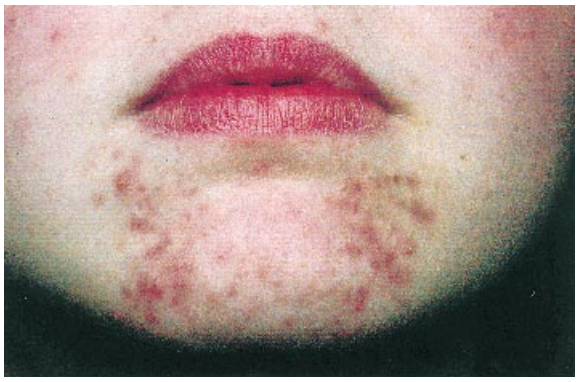

Figure 8 Initial papules in MARSH syndrome.

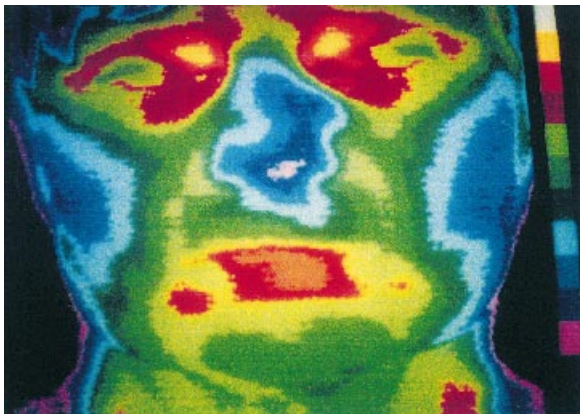

Figure 9 Thermogram of face. Note 'hot spots' below and lateral to angles of mouth. (Courtesy of Prof. J. Ortonne).

tentative and are based on a personal empirical approach to this difficult subject.

For group 1, mainly erythromelanosis, I use the following:

- nongreasy emollients;
- 1–4% menthol in a nongreasy emollient;
- cosmetic camouflage;
- psychological support;
- tunable dye laser to 'feather' the lines of sharp demarcation often seen in the pretragal region of the face. (We have had promising results in those who realize that the objective of the treatment is to make the demarcation less prominent rather than restore the overall colour of the face to normal.)

Group 2 is much more of a problem:

- pimozide has been used by some, but I have not generally found this to be of much help in the relief of symptoms, while the signs also remain unchanged;
- amitriptylene may be helpful in those patients who experience marked anxiety in relation to the disorder;

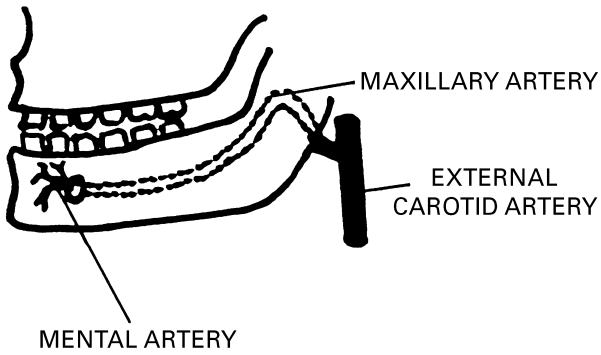

Figure 10 Blood supply of mental artery.

• hormone replacement therapy offers no help for the problem in my experience;
• Wilkin has stated that there is no broad-spectrum antiflushing drug presently available.

The group 3 patients with the MARSH syndrome offer more chance of success:
• topical steroids should not be applied because although they work well initially, encouraging the patient to continue, the steroid rebound phenomenon is very likely to occur;
• minocycline 100 mg daily for 3–4 months works well particularly if used in combination with a topical agent as below;
• topical imidazole, or short-term imidazole and hydrocortisone, or clindamycin lotion;
• low dose (0.3 mg/kg) isotretinoin has proved most valuable in my experience;
• topical oestrogen creams have given promising results in a few patients but data are insufficient to draw firm conclusions about their value.

In focusing on this difficult group of patients I am conscious of the fact that many questions remain unanswered. However, it is hoped that, with more attention to the complexities of the red face as described here, we may be able to develop more effective help for this distressed group of patients.

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