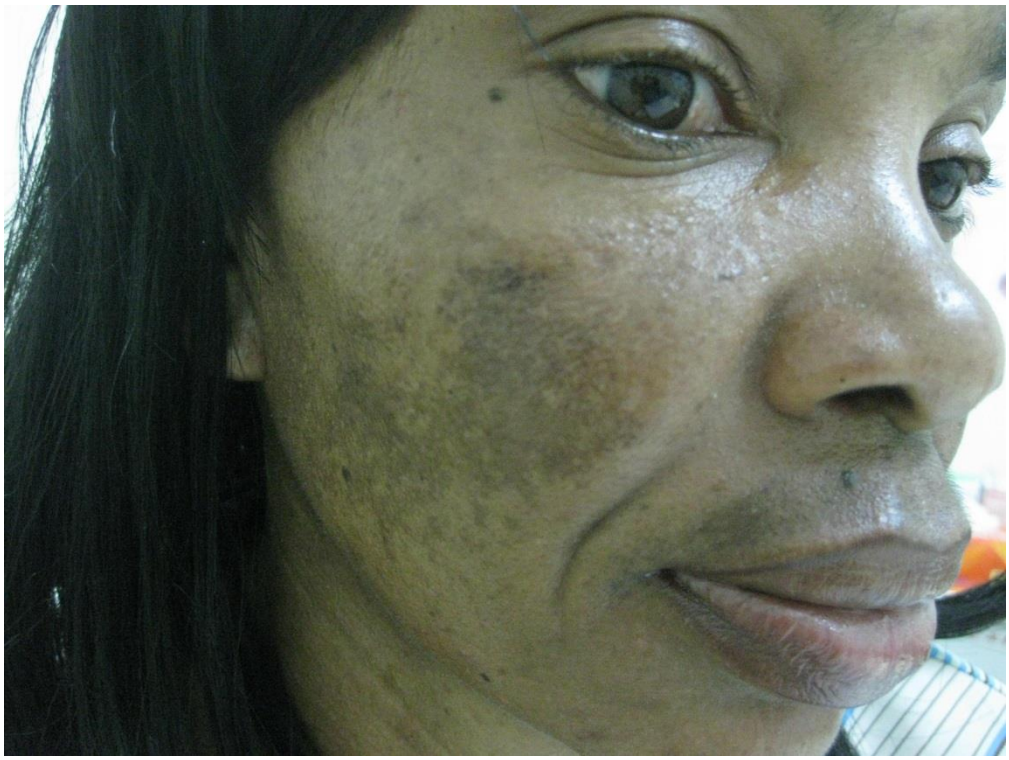
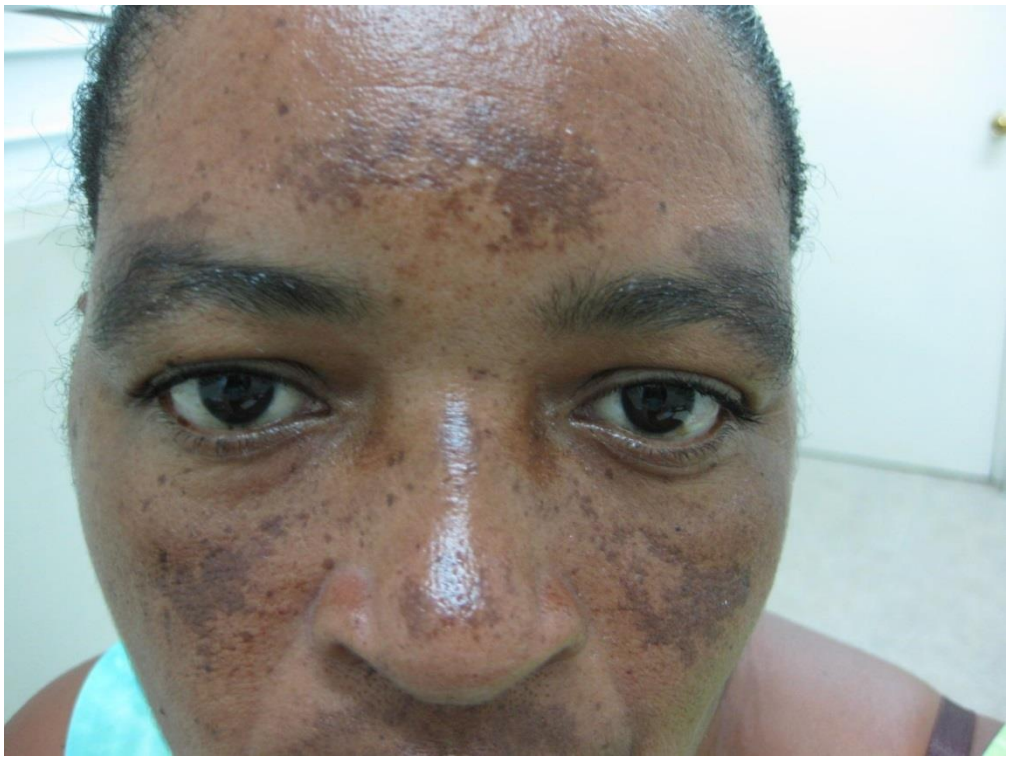
Melasma is a common, acquired disorder of hyperpigmentation that occurs commonly in women with skin of color. Clinical patterns of disease include centrofacial, malar, mandibular and forearm types.[1] Although the exact pathogenesis remains unknown, exacerbating factors include hormonal contraceptives, pregnancy, and ultraviolet-light exposure (Figure 1).

Dr R Newaj





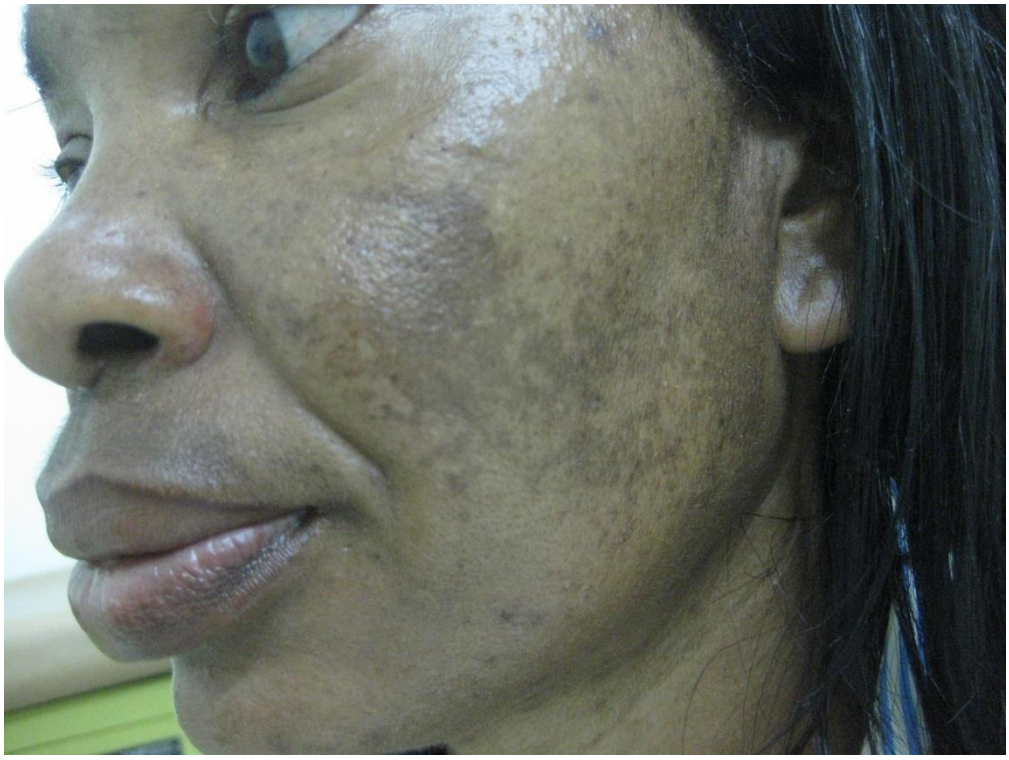


Figure 1: Melasma (images via https://www.dermquest.com/image-library/)

It is imperative that clinicians appreciate the significant and sometimes devastating psychological impact of melasma on the patient and treat it accordingly. Avoidance of exacerbating factors, including photoprotection (clothing, sunscreen, seeking shade, window protectors) is vital. In addition, cosmetic camouflage may be helpful, especially for women.[1] Hydroquinone has long been used with good effect in melasma[2] and its efficacy is undoubted.[3] A plethora of other topical agents, including retinoids, ascorbic acid, azelaic acid and other 'natural' compounds and peels, have been described in the treatment of melasma,[1] although combination hydroquinone (4%), tretinoin (0.05%) and flucinolone acetonide (0.01%) at night has been labeled as being the gold standard.[4]

Table 1: Some topical agents used for hyperpigmentation

Drug	Strengths	Weakness
Ascorbic acid	Less cutaneous irritation compared with hydroquinone	Rapidly oxidized and highly unstable; not good as monotherapy
Azelaic acic	Reasonable response for epidermal melasma	Erythema, burning, stinging
Arbutin	Less irritation than hydroquinon; may have sustained lightening effects (seen in studies for lentigines	May cause paradoxical hyperpigmentation in concentrations >3%; no studies in melasma
Glycolic acid	Inexpensive, available as cream or peel	Cutaneous irritation; best in combination with other agents
Hydroquinone	Excellent, well-established efficacy	Cutaneous erythema, burning, itching, irritation
Kojic acid	Less cutaneous irritation compared with retinoids and triple therapy	Mixed efficacy in split-face trials; may be best in combination with hydroquinone
Licorice extract	Good response in epidermal melasma	More robust studies needed

Nicotinamide	Effective for skin lightening	Cutaneous irritation; more studies needed
Retinoids	Good effect in melasma; other benefits on fine lines, texture of skin	Cutatneous irritation, slow (months) to show improvement as monotherapy
Rucinol serum	Satisfactory effect in melasma in one study	'Tolerable' side effects; more studies needed
Soy12	Modest effect on lentigines	No studies on efficacy in melasma

With interest surrounding the advent of low-fluence Q-Switched (QS) laser for treating melasma, it is necessary to evaluate this treatment modality. In early studies, high-fluence neodymium-doped yttrium aluminum garnet (Nd-YAG) caused an unacceptably high incidence of post-inflammatory hyperpigmentation in those with skin of color.[5,6] Since then, Polnikorn described a new technique (also known as 'laser toning') of repetitive sub-threshold pulse 1,064-nm QS-Nd-YAG laser for the treatment of melasma.[7] This technique is thought to result in less melanocyte and keratinocyte damage[8] and is now widely used in East Asia.

Wattanakari[9] evaluated weekly low-fluence QS Nd-YAG for five weeks plus 2% hydroquinone nightly versus 2% hydroquinone alone for dermal and mixed melasma. Although excellent improvements were cited, mottled hypopigmentation, rebound hyperpigmentation and confetti-like hypopigmented macules were reported. A total of eight out of 24 subjects were noted to develop the latter problem, with relapse in all patients at Week 12.

Another randomised study[8] reviewed three groups of patients. The first was treated with low-fluence QS Nd-YAG, the second with glycolic acid peels fortnightly (35-70% with pre-treatment retinoid priming) for 12 weeks and the third with high-fluence Nd-YAG fornightly.[8] Best results were seen with low-fluence Nd-YAG, with high-fluence Nd-YAG causing the most adverse effects. All groups' MASI scores were increased at Week 12, indicating worsening of pigmentation.

Park *et al*.[10] reported that combination QS Nd-YAG plus 30% glycolic acid peels every two weeks were superior to QS Nd-YAG treatment alone, but some recurrence was noted five months post-treatment. Mild adverse events (erythema, transient burning) were noted but no pigmentary problems were cited.

These and other studies suggest that low-fluence QS Nd-YAG laser may be useful in severe, refractory melasma when patients are carefully selected, risk factors for complications are excluded, and a combination of laser treatment and peels is utilized.[11,12] The cost of treatment, inevitable relapse and the increasing side-effect profile with subsequent treatments urges the clinician to use multi-modality treatments and emphasize the need for ongoing photoprotection.

Table 2: Lasers use in melasma

Laser	Strengths	Weakness
High fluence Nd-YAG	NIL	Worsens melasma
Low fluence QS Nd-YAG	Modest - good effect on severe, refractory melasma	Mottling, hyperpigmentation, confetti hypopigmentation
Intense Pulsed Light	Good effect in skin phototype I-III	Unpredictable pigmentary side effects in skin phototype IV-VI
Fractional resurfacing and copper bromide lasers	Some good effects seen with melasma	Further studies required

Oral tranexamic acid (TNA) is a novel treatment in melasma and also deserves some attention. Although traditionally used for bleeding diatheses and menorrhagia, it has been successfully used for the treatment of melasma.[13] Although its mechanism of action is not entirely known, decreased tyrosinase activity in melanocytes is one possibility.[14] Possible side effects include nausea, vomiting and diarrhea. Thromboembolism, pulmonary embolism and myocardial infarction have rarely been reported.

Cho *et al*.[13] showed that TNA at a dose of 500 mg/day plus intense pulsed light, and QS Nd-YAG (four treatments) was superior to laser therapy alone. Shin *et al*.[14] performed a randomized prospective trial, revealing that eight weeks of TNA at a dose of 750 mg/day enhanced the efficacy of low-fluence QS Nd-YAG laser therapy. Further studies are required to more fully evaluate this therapeutic option for melasma.

With the advent of new treatments, including lasers, and more therapeutic options on the horizon, it is an exciting time to be managing pigment disorders. This heralds the inevitable need for ongoing evidence-based research and trials.

References