Melanocytic lesions (ML) can be difficult in both their diagnosis and management, especially as melanoma skin cancer displays great variability in its presentation. In the first of a two part feature, the authors describe some commonly presenting melanocytic lesions.

Melanomas are cancers which arise from naevi or within normal looking skin. They are becoming increasingly common and urgent excision is the best hope of cure for affected patients. Although melanoma is more common than in the past, many GPs will see relatively few in their working life, so that diagnosis may be challenging. Moreover, moles do change through life (slowly) and a key guide to diagnosis in primary care is to make oneself familiar with how common naevi evolve and therefore to be able to recognise when something is different. Melanocytic lesions may be broadly classified as congenital or acquired according to their time of onset. Melanocytes originate from neural crest cells; they subsequently proliferate and migrate to the skin, central nervous system, eyes and the ears during embryogenesis. When these melanocytes proliferate excessively, hamartomatous growths known as congenital melanocytic naevi (CMN) result. This can happen in all of these body sites.

Common melanocytic naevi (moles) are acquired naevi. These start to appear in the first year of life and may continue to develop up to the age of 40 years. New melanocytic lesions (ML) developing after the age of 40 are less common and should therefore be treated with some caution.

**High risk factors**
The assessment of risk factors predisposing patients to melanoma is important in the complete evaluation of a ML. Even relatively banal appearing naevi with subtle atypia or a history of change should be treated with caution in high-risk patients. Melanomagenesis may be contributed to by external or genetic factors.

**External factors in melanomagenesis**
Environmental factors such as significant sun exposure and sunbed usage causes ultra violet radiation related melanocyte DNA damage which is a well known precursor for melanoma. The most robust measure of this damage is a history of sunburn. Other external causative factors include immunosuppression, due to underlying medical conditions such as lymphoma or HIV/AIDS or secondary to drugs such as tumour necrosis alpha inhibitors.

**Genetic factors in melanomagenesis**
Most melanomas (90%) are sporadically inherited, i.e. indicating damage to a gene after the patient is born – therefore conferring no risk to their offspring. Melanoma itself is not inherited; however the risk of developing melanoma is passed on from one generation to the next, i.e. familial melanoma (FM).

Melanoma results from genetic changes in melanocytic cells in the skin in response to sunburn, and people with familial inherited red hair, freckles, fair skin with a tendency to burn and multiple moles are considered to be at an increased risk of melanoma. Some specific gene mutations in CDK4 and CDKN2A are associated with increased melanomagenesis.

Genetic testing may be considered for patients with in excess of 50 atypical moles and a family history of two or more first degree relatives with melanoma or pancreatic cancer, as they carry a higher risk for FM. These patients are often referred to as having familial atypical multiple melanoma mole syndrome (FAMMM), or atypical naevus syndrome.

**Mole development**
Normal moles arise early in life and the cells undergo a relatively ordered phase of proliferation, then they age and the naevus matures. During this process they change from flat brown lesions to dome shaped lesions or they may simply fade away over time. They are usually less than 5mm in diameter. As the proliferation is ordered the naevi are symmetrical and evenly coloured (even blue naevi). In cases where the proliferation carries on for a longer period, the naevi are larger, and as the proliferation is more disordered then the naevus will be irregular in shape. The host may respond to that proliferation, so the mole may become pinker. This is then termed an atypical naevus.
Atypical naevi are more likely to change into a melanoma and should be treated with caution. When melanocyte proliferation becomes severely disorderly an irregular pigment network and shape is visible, suggestive of the development of melanoma.

A variety of benign versus malignant lesions are presented in Figure 1.

**Commonly presenting benign melanocytic lesions**

**Banal melanocytic naevus**

These are usually pale brown to dark brown dependent on the Fitzpatrick skin type, symmetrical with a regular outline and usually found scattered over the body. They may be multiple and usually remain dormant. They may be macules, papules or nodules (Figure 1a).

**Lentigo/lentigines**

Lentigines are usually small, pigmented macular or papular lesions with well defined margins occurring anywhere on the body. They are identified pathologically by an increase in normal appearing melanocytes in the epidermis. The basal layer of the epidermis also shows keratinocytes replaced by melanocytes. There are differing types of lentigines:

- **Lentigo simplex:** This is a uniformly pigmented, small macule usually present since childhood or birth which may have a dry scaly surface. These lesions may not result directly from sun exposure and are benign.

- **Solar lentigo:** Solar lentigines occur on sun-damaged sites and present as uniformly pigmented macules or patches. They are commonly referred to as age or liver spots and present commonly with darkening of pigmentation after sunny holidays (Figure 2a).

- **Ink spot lentigo:** As the name suggests these are darkly pigmented (often black) pigmented macules, appearing as an ink splash on the skin on a background of sun damaged skin, often on the shoulders after sunburn. They occur commonly on pale Fitzpatrick type 1 skin.

**Labial melanotic macules**

These are benign brown macules often occurring on the lower lip although they may occur anywhere on the lip or the buccal mucosa (Figure 3).

Similar pigmented macules may be found on the penile shaft or glans in men and on the vulva in females and are termed penile and vulvar lentigo respectively. As the latter are less common such patients should be referred to the pigmented lesion clinic for review.

**Syndrome associated lentigines**

Some very rare genetic syndromes are characterised by multiple lentigines, e.g. xeroderma pigmentosum, LEOPARD, myxoma syndromes (LAMB, Carney, NAME).
Blue naevi
Deep dermal pigmented lesions appear blue on the skin surface due to the Tyndall effect, i.e. the differential reflection of different wavelengths of life by deep melanin in the skin. These are benign, and malignant transformation is very rare (Figure 2b).

Naevus of Ota and Ito
Deep dermal proliferation of melanocytes from birth may result in blue-slate grey pigmented patches around the eye (Naevus of Ota) or on the shoulder or upper arm (Naevus of Ito). These are a form of birthmark and the pigment may become more apparent later on in life.

Other commonly presenting non-melanocytic pigmented lesions

Seborrheic keratosis (basal cell papilloma)
Seborrheic keratoses are benign pale to dark brown warty lesions, which commonly present when inflamed and itchy. They appear as a ‘stuck on’ lesion and have a rough surface. They are not due to sebum production as the name suggests, but in fact are an overproduction of keratin on ageing skin. The exact etiology has not yet been elucidated. These lesions are universal over the age of 50 but may occur much earlier in life. They do cause diagnostic concern when pigmented and indeed melanomas may rarely simulate pigmented, seborrheic keratoses (Figure 2c-d).

Dermatofibromas
These are commonly occurring benign fibrous lesions and mostly present as small nodules on the extremities. They are usually skin coloured with a characteristic ‘pellet under the skin’ like consistency on palpation, although they may become pigmented or inflamed over time. Dermatofibromas are histiocytic lesions, which may occur at sites of trauma.

Dysplastic naevi
Moles usually greater than 5mm in diameter with variegated pigment and an irregular or diffuse edge are termed dysplastic naevi or atypical naevi (Figure 5). Dysplastic naevi often have a ‘fried egg’ appearance, with a pale papule in the centre and adjacent variable pigment in a symmetrical distribution.

Spitz naevi
These are melanocytic naevi but are unusual, being usually pink coloured papules or nodules. They are most common in children. They are benign but are difficult to distinguish from melanomas clinically, so they cause concern especially when seen in older children or adults. As a result of this diagnostic uncertainty affected patients should be referred for review in the pigmented lesion clinic where they are commonly removed.

References
1 Agnieszka W. Kubica, BS, Jerry D. Brewer; Melanoma in Immunosuppressed Patients; Mayo Clinic Proceedings Volume 87, Issue 10, Pages 991-1003, October 2012