Pigmented lesions of the choroid and retina

Chris Hemmerdinger and **Professor Bertil Damato** consider the decisions involved in identifying and treating pigmented lesions of the choroid and retina

Pigmented lesions of the choroid and retina are commonly encountered by optometrists in everyday practice. The increasing use of retinal imaging and indirect ophthalmoscopy among community optometrists means more lesions will be identified. Important clinical decisions must be made about the appearance of the lesion, the likely diagnosis and whether to monitor or refer for a second opinion. In cases where an ophthalmological opinion is required, the priority of referral needs considering. Many texts and online resources are available to the practitioner to help with diagnosis. However, to research a lesion in a standard textbook requires the diagnosis. To help with such quandaries a web-based atlas of ocular tumours has been developed, categorising lesions by their position and colour rather than diagnosis (Figure 1 www.eyetumours.com). This article aims to summarise the important clinical features when seeing such patients and reviews the different pigmented lesions found in the choroid and retina.

History

Careful history taking is an essential part of any clinical assessment. The practitioner is required to extract all relevant facts and document important negatives. As the history is taken before the examination, refinement of the history may be required subsequently. A balance of open and closed questioning will allow the practitioner to quickly and precisely obtain a full and relevant history.

A comprehensive history includes symptoms, ophthalmic history, general medical history, a review of current medications and family history. Many patients presenting with retinal lesions will be asymptomatic. They may be attending for a routine eye examination or be monitored for other conditions such as diabetes. Patients attending for routine examination will not usually require a dilated fundus examination, and screening all patients with a dilated examination would be inefficient.[1]

However, once a lesion has been identified it should be thoroughly examined. Symptomatic patients with an intraocular tumour may complain of blurred vision, field loss, floaters, photopsia, metamorphopsia or pain. Blurred vision, field loss and metamorphopsia may be caused by the lesion itself or an associated retinal detachment. Macular lesions will generally have a more pronounced effect on vision. Photopsia due to choroidal

Figure 1 Eye tumour atlas

lesions is often described as a ball of light which travels across the visual field; it may be intermittent or constant.

Less common symptoms such as floaters, caused by vitreous haemorrhage, or pain due to raised intraocular pressure or inflammation may be reported. It is important to enquire about past ocular history as lesions may have been noticed previously and imaged or referred to the hospital eye service. General medical

Figure 2 Sentinel vessels

Figure 3 Lesion with depigmented 'halo'

history is also important; if there is a history of malignancy, metastases must be considered.

Examination

Any ophthalmic examination should include visual acuity, pupil reactions, intraocular pressure and anterior and posterior segment examination. Once a lesion has been identified it should be examined through a dilated pupil with a binocular indirect viewing system.

Visual acuity may be affected by posterior direct macular involvement, cataract, vitreous haemorrhage or retinal detachment. Intraocular pressure (IOP) may be elevated following vitreous haemorrhage, rubeosis or by lesions causing secondary angle closure. IOP may be reduced when there is an exudative detachment or with intraocular inflammation. Examination of the anterior segment examination may reveal sentinel vessels (Figure 2), segmental cataract, anterior chamber inflammation or rubeosis. Sentinel vessels are dilated episcleral vessels, which are feeder vessels to the tumour. Not all prominent episcleral vessels are sentinel vessels, and it is useful to look for asymmetry. Visual field loss may be noticed by the patient or picked up during the examination. Such field loss may be due to the lesion itself or secondary to a retinal detachment. Posterior segment examination of both eyes is essential, with relevant features being documented as described below.

Documentation

Once a pigmented lesion is identified it should be imaged and stored for comparisons at future consultations. An annotated diagram should be included in the notes documenting the level of the lesion, colour, size, shape, position, surface features, elevation, and the presence of any fluid.

● Level of the lesion – The lesion and any associated features such as haemorrhage may be choroidal, sub-retinal, intra-retinal or pre-retinal. The level of the lesion is essential for correct diagnosis, a stereoscopic view is invaluable in assessing this, but other cues such as the retinal vasculature may help.

● Colour – Choroidal naevi generally appear slate grey or brown. Melanocytomas are black. Congenital hypertrophy of the retinal epithelium is brown or black. Sub-retinal haemorrhage may appear red or brown. However, it must be remembered that naevi and melanomas may be amelanotic, and there can be considerable variation in the appearance of retinal lesions.

● Size – The lesion should be measured in relation to the disc (disc diameters) or with the slit lamp beam and indirect lens. When measuring the lesion with an indirect lens it is essential to record the lens used or calculate the size incorporating the lens magnification factor. Both horizontal and vertical dimensions should be recorded.

● Shape – The lesion may be regular or irregular and the margins distinct or diffuse. This may be represented by a diagram or annotated in the notes. Certain lesions may have characteristic shapes such as the bear tracks of grouped typical congenital hypertrophy of the retinal pigment epithelium.

● Position – Ideally the lesion will be imaged; however, when this is not possible it is important to document accurately the position of the lesion. Landmarks such as the disc, vascular arcades and fovea are invaluable in locating a lesion. Any contact with the optic disc must be recorded. It is important to remember that the image is both laterally and vertically inverted when using a binocular indirect ophthalmoscope.

● Surface features – Drusen are a feature of chronicity and are reassuring in that they indicate that the lesion is longstanding; the absence of drusen over a dome-shaped, pigmented tumour is ominous. Orange pigment (lipofuscin) implies retinal pigment epithelium dysfunction and always requires onward referral for ophthalmological opinion. Non-pigmented areas such as lacunae in congenital hypertrophy of the retinal pigment epithelium or

atrophy in pigmented scars should also be noted. A ring of RPE atrophy surrounding a lesion tends to occur in longstanding lesions, which may give the appearance of a 'halo' around the lesion (Figure 3).

● Elevation – Viewing the lesion stereoscopically allows assessment of elevation. Tumours should be classified as flat, minimally thickened (<2mm), shallow dome or pronounced dome (Figure 4). Looking at blood vessel deflection may give an indicator to those observers without stereopsis.

● Sub-retinal fluid – The presence or absence of fluid should be noted. This may be surrounding the lesion or may gravitate inferiorly.

Lesions
Choroidal naevus

Choroidal naevi are common, benign lesions that are usually round or oval with fairly well defined although not sharp borders (Figures 5 and 6). The reported incidence of choroidal naevi ranges from 0.2 to 30 per cent.[2-7] This variation is due to different study populations. The largest population-based study; the Blue Mountains eye study[7] reported an incidence of 6.5 per cent in a white population. The majority (90 per cent) are pigmented, with a characteristic, grey, ophthalmoscopic appearance.

A typical choroidal naevus is asymptomatic, less than 5mm in diameter and less than 1mm in thickness, with surface drusen, no orange pigment (lipofuscin), not in direct contact with the disc and not associated with any sub-retinal fluid.

As mentioned above, the presence of drusen overlying the lesion (Figure 6) is indicative of chronicity, and is reassuring. Lipofuscin (Figure 7) suggests RPE dysfunction and should be viewed suspiciously.

Patients with typical naevi should be observed for any evidence of change. The lesion and its relevant features must be clearly documented as described above. Ideally the lesion should be photographed, although it must be remembered that camera artefacts can produce false impression of growth.[8] If the lesion is observed to increase in size, the diagnosis of benign naevus must be questioned although enlargement has been documented in naevi.[9]

The main concerns with choroidal naevi are visual impairment and malignant growth.

The majority of naevi are asymptomatic; however, they may cause reduced visual acuity, flashes, floaters or visual field defects. Up to 11 per

Figure 4
(a) flat lesion;
(b) minimally thickened;
(c) shallow dome;
(d) pronounced dome

(a)
(b)
(c)
(d)
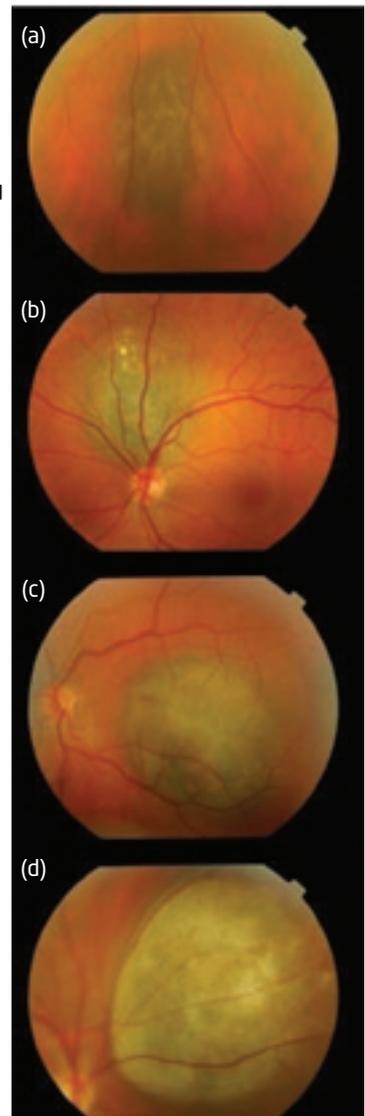
Figure 5 Typical choroidal naevus

Figure 6 Atypical choroidal naevus with overlying drusen

cent of naevi become symptomatic.[10] Symptoms may be caused by serous retinal detachment, photoreceptor atrophy or choroidal neovascularisation (Figure 8). Visual acuity is generally affected when the naevus is subfoveal.[11] Treatment modalities for symptomatic naevi include transpupillary thermotherapy and photodynamic therapy.[12] All symptomatic naevi should be referred to an ophthalmologist for further investigation.

Malignant transformation of a naevi to a melanoma has been estimated to occur at an annual rate of one in 4,800 and one in 8,845.[2,13] Whether a naevus has actually transformed to a melanoma or whether the melanoma was malignant from its inception is uncertain. In any case, risk factors for progression include the increased lesion size (especially thickness), associated retinal detachment, presence of symptoms, orange pigment on the lesion, and contact with disc margin.[14] If a patient has any of these risk factors the rate of malignant growth is increased so that monitoring is required. Differentiating large naevi from small melanomas can be difficult, even for experienced observers.[15]
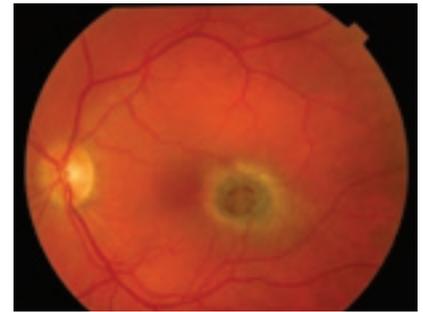
Uveal melanoma

Melanoma of the uvea is the commonest primary intraocular malignancy in adults, with an annual incidence of approximately six per million. Approximately 80 per cent of uveal melanomas are choroidal, with approximately 12 per cent occurring in the ciliary body and 8 per cent in the iris. This article only discusses choroidal melanomas.

Choroidal melanoma may present with a variety of symptoms or may be a chance finding on routine eye examination. Presenting symptoms may include photopsia, floaters, visual field loss, blurred vision and pain. Occasionally choroidal melanomas present as a visible lesion, due to extra-scleral extension. Clinical examination of a patient with any symptoms suggestive of melanoma must include anterior segment examination, intraocular pressure measurement and indirect examination of the fundus through a dilated pupil as described earlier.

Choroidal melanoma is usually seen as an elevated, solid, pigmented mass (Figures 9-12). Associated features may include orange pigment on the surface, sub-retinal fluid overlying the tumour or an inferior retinal detachment. If the melanoma breaks through Bruch's membrane it will have a collar-stud appearance, which may be associated

Figure 7 Lesions with lipofuscin (orange pigment)

Figure 8 Naevus with choroidal neovascularisation
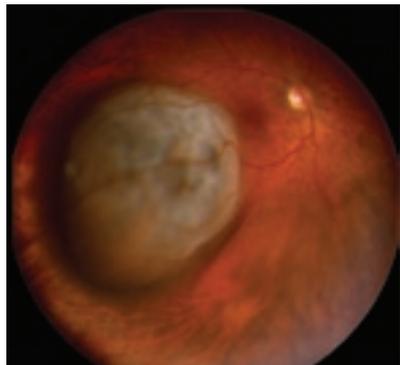
Figure 9 Choroidal melanoma – pronounced dome

Figure 10 Choroidal melanoma – juxtapapillary

with retinal haemorrhages (Figure 11). Some melanomas are amelanotic, which makes them diagnostically more challenging; other conditions such as choroidal metastasis must be considered in these cases. Melanomas develop *de novo* or transform from a naevus and can be found anywhere in the fundus. Lesions located pre-equatorially are more easily missed on routine examinations and therefore present later, whereas posterior lesions are more likely to be detected early. Lesions near the macula are more likely to be symptomatic.

For best results, early detection of choroidal melanomas is important. A mnemonic, MELANOMA, has been devised to alert the clinician to signs and symptoms of an intraocular tumour (Table 1). The acronym refers to: Melanoma visible externally; Eccentric visual phenomena (eg photopsia); Lens abnormality, such as cataract or astigmatism; Afferent papillary defect; No optical correction with spectacles; Ocular hypertension; Melanocytosis, which predisposes to melanoma; and Asymmetrical episcleral vessels. Another mnemonic has been created to remind clinicians of risk factors for tumour growth: To Find Small Ocular Melanomas (Table 2).[16] Tumours that display none of these factors are most likely naevi and have a less than 4 per cent chance for growth at five years. Tumours with one feature have a 38 per cent chance of growth at five years

| TABLE 1 |
|---|
| **MELANOMA acronym** |
| **M** - Melanoma visible externally |
| **E** - Eccentric visual phenomena |
| **L** - Lens abnormality (cataract) |
| **A** - Afferent pupillary defect |
| **N** - No optical correction |
| **O** - Ocular hypertension |
| **M** - Melanocytosis |
| **A** - Asymmetrical episcleral vessels |

TABLE 2
To Find Small Ocular Melanomas mnemonic
T - Thickness greater than 2mm
F - Fluid (sub-retinal)
S - Symptoms
O - Orange pigment
M - Margin touching the optic disc

and those with two or more features have a greater than 50 per cent chance of growth at five years. Tumours with two or more features should probably be considered as small choroidal melanomas.[16]
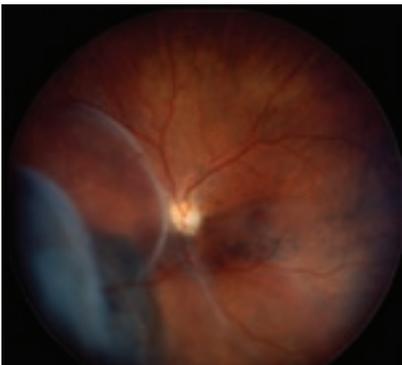
Patients with suspected melanoma should be referred urgently, as early treatment enhances any opportunities for preserving the eye and maintaining some functional vision. The best route for referral may vary around
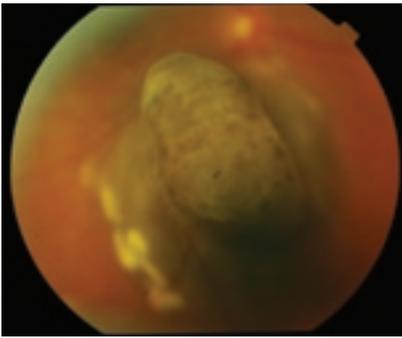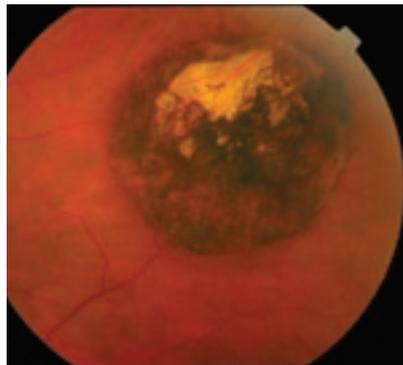
Figure 11 Choroidal melanoma – collar stud

Figure 13 Indeterminate melaoncytic lesion

Figure 12 Choroidal melanoma with inferior exudative retinal detachment

Figure 14 Typical solitary CHRPE

the country; however, the patient will usually see a general ophthalmologist who will then refer them to a tertiary ocular oncology unit. The patient should be seen by an ophthalmologist within one week. If this is achievable locally via an urgent GP referral, this is an appropriate route. If not, then referral should be directly to an ophthalmologist. It is important to keep patients informed, and advise them whom to contact should they not receive an appointment by a specified date. This will act as a safety net to ensure prompt treatment.

Diagnosis of malignant melanoma will be confirmed by the ocular oncologist following thorough history and examination. In addition to indirect ophthalmoscopy, an ultrasound scan of the eye will usually be enough to confirm the diagnosis. When the diagnosis is in doubt, biopsy of the lesion may be required.

The primary treatment goal is to destroy the tumour. Preserving the eye or useful vision is often achieved, but only if the tumour is killed at the same time. The Collaborative Ocular Melanoma Study (COMS) was unable to demonstrate a significant difference in survival between patients whose eyes where enucleated and those who had radiotherapy.[17] Available treatments include plaque radiotherapy, proton beam therapy, transpupillary thermotherapy, trans-scleral local resection,

trans-retinal endoresection and enucleation. The optimal treatment will vary according to patient requirements and tumour characteristics. A combination of the above treatments may be used.

Metastatic disease is obviously a concern to patients. They need to be appropriately counselled within the oncology service. As previously mentioned the primary treatment is to kill the tumour, estimations from doubling times of untreated metastasis show most would have seeded in the five years before primary treatment, ie if the tumour is one which has the potential to metastasise, it does so very early, well before the lesion is clinically identified.[18]

If a tumour is removed (local resection, endoresection or enucleation) or biopsied, then it can be studied for histological and cytogenetic features, which can provide prognostic information. Histiologically, tumours may be composed of spindle cells, epithelioid cells or may be mixed. Spindle-cell tumours have a better prognosis than those composed of epithelioid cells. Other features associated with a poorer outcome are closed vascular loops, high numbers of mitotic cells and lymphocytic infiltration. Cytogenetic studies involve looking at the chromosomes of the tumour cells; this can be done by fluorescent *in situ* hybridisation (FISH) or more recently by multiplex ligation probe amplification

(MLPA). Choroidal melanomas have been associated with multiple cytogenetic abnormalities, the most important being monosomy 3 (ie loss of one copy of chromosome 3). Patients with this cytogenetic abnormality within the melanoma have a significantly reduced survival rate.[19] Estimations of survival can be made using neural networks.[20] Further counselling must be given to patients who elect to have cytogenetic studies. Although treatment for metastatic disease only rarely seems to prolong life, patients with a non-lethal melanoma are greatly reassured by their good prognosis.

Indeterminate melanocytic lesions

Although many melanocytic lesions can be classified as choroidal naevi or melanoma, even with a comprehensive examination it is not always possible to be certain of the diagnosis (Figure 13). Such cases may be classified as indeterminate melaoncytic lesions. These must be monitored regularly to look for any evidence of change. In certain cases it may be appropriate to obtain a histological diagnosis by trans-retinal or trans-scleral biopsy. Such biopsies are only carried out after careful patient counselling as there are surgical risks and with small lesions the biopsy may not yield enough material to provide a conclusive diagnosis.

Congenital hypertrophy of the retinal pigment epithelium (CHRPE)

First described by Reese and Jones in 1956,[21] CHRPE consists of hypertrophy with hyperpigmentation of the retinal pigment epithelium. Lesions are typically flat and pigmented, at the level of the retinal pigment epithelium (Figure 14). They are most commonly detected by chance on routine ocular examination as they are generally asymptomatic. In one review of patients referred with suspected choroidal melanoma, CHRPE was fourth in conditions simulating choroidal melanoma (10 per cent of referrals), after choroidal naevi, disciform macular degeneration and disciform peripheral degeneration.[22] It must therefore be emphasised that atypical lesions should be referred for ophthalmological review.

CHRPE lesions may be solitary or multiple, typical or atypical. Multiple atypical lesions include CHRPE-like lesions associated with familial adenomatous polyposis (FAP), which need to be identified as patients are at risk of associated colon cancer.

Typical solitary CHRPE lesions are unilateral, pigmented, well defined and completely flat. They may contain small

non-pigmented areas known as lacunae and may be surrounded by a non-pigmented ring. Less commonly, non-pigmented lesions may be seen. Rarely, vascular sheathing may be noted over the lesion or there may be an intralesion nodual.[23] While the lesions are benign, flat enlargement and enlargement of the lacunae is well documented when lesions are followed over many years.[24] Multiple typical CHRPE are often recognised by the so-called bear-tracking appearance (Figure 15). These lesions need to be differentiated from spindle-shaped, atypical lesions associated with familial adenomatous polyposis.

FAP is a dominantly inherited condition in which multiple polyps are present throughout the colon. Patients have a very high risk of developing colon cancer. A sensitive marker for FAP are atypical, flat, CHRPE like lesions. It should be noted that there is no relationship between classic CHRPE and FAP.[25] These atypical lesions share several features with typical CHRPE in that they are well circumscribed, flat, may contain lacunae or have a surrounding halo. Atypical lesions in contrast to CHRPE are pisciform (fish-shaped) or spindle-shaped, bilateral and multiple.[26]

Melanocytoma

Clinically, melanocytomas are typically black. Optic nerve melanocytomas, which are the most common, are located partly or entirely within the optic disc, often extending over the disc margin into adjacent choroid or neurosensory retina (Figure 16). The vast majority of lesions are unilateral, although cases of bilateral optic disc melanocytomas have been reported.[27]

Historically, melanocytomas were thought of as malignant neoplasms of the optic nerve; however, they are now recognised as benign with an excellent prognosis.[28] The term melanocytoma was adopted by Zimmerman based on similarities to ocular melanocytosis. Others have suggested terms such as hyperpigmented magnocellular naevus of the optic disc (HMNOD) may be more appropriate,[28] although this terminology has not been widely accepted.

Melanocytomas cause mild visual loss in about a one in four patients.[29,30] Severe visual loss is uncommon, but may be caused by central retinal vein occlusion, tumour necrosis or malignant transformation. Afferent pupillary defects have been reported in up to 30 per cent of patients and field defects in up to 90 per cent; these include enlargement of the blind spot, nerve fibre bundle defects and nasal steps.[31] The mechanism for pupillary and field loss

Figure 15 Typical grouped CHRPE
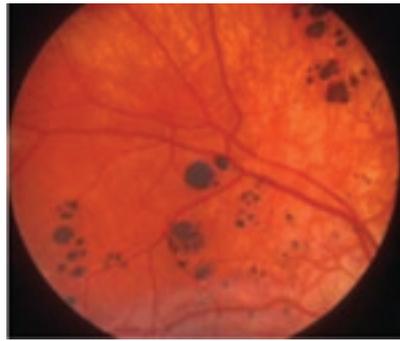
**Figure 17 Peripheral exudative haemorrhagic chorioretinopathy**
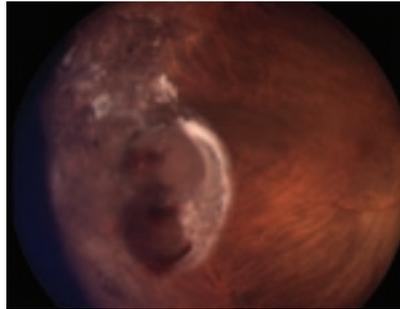
is probably due to mild compression of the optic disc fibres.

Although considered a benign lesion subtle growth is seen in up to 15 per cent, the main predictive factor for enlargement being a thickness of 1.5mm at presentation.[29] Malignant transformation has been reported in 1-2 per cent. It is important to differentiate melanocytoma from uveal melanoma. Both present at a similar age; however, melanomas are rare in dark-skinned individuals, whereas melanocytomas have an equal incidence in all races. There appears to be a slight preponderance for females.[29]

Management of melanocytoma is generally observation with serial photography. Annual follow-up is required due to the risk of malignant transformation. Given the variable clinical appearance and malignant potential of melanocytoma, patients with this tumour should be referred for ophthalmological assessment and surveillance.

Peripheral exudative haemorrhagic chorioretinopathy

Neovascular changes in age-related macular degeneration are well known to optometrists. These changes, which usually occur in the macular area, do not usually represent too much of a diagnostic challenge. Peripheral neovascular changes are well documented,[32] and are often mistaken for melanomas on initial examination[33] (Figure 17). In cases where ultrasound and visualisation of the tumour are not sufficient for diagnosis, serial examinations will show haemorrhagic lesions to decrease in size whereas melanomas grow.
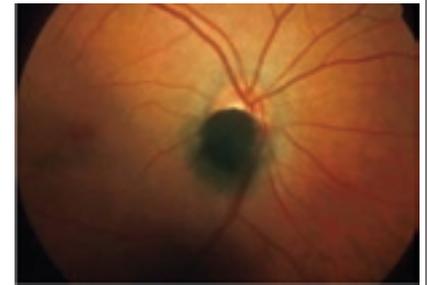
Figure 16 Melanocytoma

Differential diagnosis

Other pigmented lesions may resemble melanoma but are beyond the scope of this article because of their rarity. These include: combined hamartoma of retinal pigment epithelium and retina, pigmented choroidal metastasis, adenoma and adenocarcinoma of the retinal pigment epithelium and retinal pigment epithelial hyperplasia.

Patient counselling

Patients found to have a pigmented lesion all need to be carefully and tactfully informed of the findings. This requires skill so as not to cause excess anxiety in a patient with an apparently benign lesion, at the same time, not giving false reassurance to a patient with a malignant melanoma. It is perfectly acceptable to inform patients of any diagnostic uncertainties. All patients referred with pigmented lesions must be informed of when they are likely to be seen by an ophthalmologist and what they should do if they do not receive an appointment within a specified time. It is not within the remit of the optometrist to provide counselling about treatment and prognosis, which will be done by a multidisciplinary team at an ocular oncology centre.

Conclusions

Optometrists are becoming increasingly involved in primary eye-care provision. Given the ever-increasing use of indirect viewing techniques and availability of retinal photography, pigmented lesions in the ocular fundus will present important management issues to optometrists. Optometrists need to be able to decide which lesions can be safely observed and which patients should be referred on for ophthalmological opinion. ●

A list of references is available from the clinical editor: william.harvey@rbi.co.uk

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