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Medical Investigations for Optometrists

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In a TED talk by Abraham Verghese (TED.com), he jokes that if a patient arrives at an American hospital with a leg missing, no one will believe the leg has gone till a scan proves it. It is argued that there is an overreliance in many healthcare settings on medical investigations. Optometrists and ophthalmologists both know that there is a sense of certainty given by a number, for example on a blood test result, and reassurance given by an image, for example by a scan. However we are all also taught early in our clinical training that the history is key. With a good history the list of differential diagnoses can be narrowed down considerably, allowing a thorough examination to point towards one or a few possibilities. Medical investigations used correctly, are the final step in the diagnostic process. They should only be used to seek confirmation, if necessary, of a suspected diagnosis, to rule out a rare but serious condition or to allow grading of extent or severity of a disease. For example we use optical coherence tomography (OCT) to demonstrate aspects of age-related macular degeneration which may be treatable and we use the blood test, erythrocyte sedimentation rate (ESR), to rule out giant cell arteritis (GCA): ESR is classically raised in GCA.

The pre and post-test probabilities of a diagnosis should be considered to help decide which investigations to use and when. The pre-test probability is the likelihood that a disease exists in a patient before the investigation. The post-test probability of the diagnosis indicates the extent to which the result of an investigation can be trusted. These probabilities are based on a combination of the evidence and the subjective estimate of the clinician. For example when deciding whether to request an ESR to diagnose GCA, consider the clinical features present: the pre-test probability of GCA would be low in a 35 year-old patient with a headache and so an ESR result is unlikely to be helpful, but the probability would be much higher in a patient who was elderly and had a temporal headache. For the second patient, a raised ESR could usefully confirm a diagnosis that was suspected from the history alone.

The ultimate aim of our practice, whether we are optometrists or doctors, is to be safe, in particular to be aware of cases requiring urgent medical assessment (Williams MA 2012). Over-investigating patients may be perceived to be safe, but in fact wastes healthcare and patients' resources and time, may uncover abnormalities that represent normal variation but still induce anxiety, and perhaps even lead to

further but invasive tests or treatment when none were necessary. The 'Choosing Wisely' campaign is an initiative from the American Board of Internal Medicine (ABIM) designed to cause clinicians to pause and consider the necessity of a test, and its potential for harm, before requesting it, though barriers exist to this change in practice (McMillan and Ziegelstein 2014). There is a 'sweet spot' of investigating in order not to over investigate, while not missing anything of clinical importance, and it is only through experience and keeping up to date with current guidelines and research that we can find this.

This article aims to discuss some clinical scenarios that optometrists may encounter as examples of the use of medical (as opposed to ocular) investigations. The conditions discussed are by no means an exhaustive list, but are selected to illustrate the role of medical investigations of patients with visual complaints.

Diplopia

Diplopia is the phenomenon of seeing more than one image of an object. Medical investigations in diplopia are not usually needed, but on occasion are absolutely vital. The key symptomatology to establish is a) if the diplopia is monocular or binocular and b) if it is painful or painless. If diplopia is still present when the patient covers the unaffected eye, then it is monocular and it indicates a problem with the visual media of that eye, such as keratoconus or cataract. This is not considered a medical emergency on its own. Binocular diplopia however disappears on covering one eye. Binocular diplopia has several causes, including a palsy of the third, fourth or sixth cranial nerve, thyroid eye disease or myasthenia gravis. Third cranial nerve palsies can be classified as so-called 'surgical' or 'medical'. The former classically presents as a third nerve palsy with pain and mydriasis, and requires urgent referral as it may be due to a potentially life-threatening intracranial aneurysm. In contrast, a 'medical' third nerve palsy is pain-free and pupil-sparing, and typically occurs in elderly patients with cardiovascular risk factors, due to vascular insufficiency resulting in ischaemia of one of the nerves supplying the extraocular muscles. A good rule of thumb is that a case of painful binocular diplopia must be seen immediately in either an Emergency Department or Eye Casualty where an urgent

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brain scan, such as a CT- or MRI- angiogram, will be arranged. New onset painless diplopia also needs assessed urgently, but a scan is much less likely to be needed (Tamhankar and Volpe 2015). An interesting scenario is that of raised intracranial pressure (ICP), for example due to a 'space-occupying lesion' like a tumour, in which case a sixth nerve palsy can occur as a 'false-localising sign'. The palsy is not due to the causative lesion pressing directly on the sixth nerve, but rather the raised ICP indirectly causing sixth nerve dysfunction. Thus in a case of sixth nerve palsy, if bilateral optic disc swelling is also noted, then raised ICP should be strongly suspected. Another cause of any isolated cranial nerve palsy not to miss is GCA, and a full history and examination (for example for temporal tenderness) is the major means not to miss it, with ESR and CRP if GCA is suspected.

Thyroid eye disease (TED) (Verity and Rose 2013) can occur with overactivity of the thyroid gland, underactivity or sometimes with normal thyroid activity but as a prelude to thyroid dysfunction. The classic signs are conjunctival injection, lid retraction, proptosis and a risk of compressive optic neuropathy, and extraocular motility deficits; classically restriction of upgaze initially, causing binocular diplopia on upgaze. If TED is suspected, then as well as a history and examination directed towards thyroid status, a blood test for thyroid function may be useful, and if the thyroid gland is swollen, an ultrasound of the gland can help delineate the nature of the swelling. In TED, orbital swelling can cause optic nerve compromise, necessitating urgent referral for orbital imaging, like a CT scan, and intervention such as intravenous steroids, or orbital decompression surgery. For this reason, reduced visual acuity and colour vision with a swollen optic disc and afferent pupillary defect should raise alarm bells in the setting of TED.

Another but less common cause of diplopia is myasthenia gravis, an autoimmune condition in which antibodies attack and destroy the receptors on muscle cells. This condition can present as a painless binocular diplopia or ptosis. The key feature, obtainable from the history, is that the diplopia is *variable*, occurring or worsening with fatigue, for example towards the end of each day. Myasthenia gravis is not limited to the extraocular muscles, but can also involve other muscles of the head and neck, and even intercostal muscles, thus affecting speech, swallowing and sometimes breathing. For this reason investigations are needed to confirm the diagnosis (a blood test for antibodies such as anti-acetylcholine receptor antibodies

to raise or lower the likelihood of what's usually an already suspected diagnosis) (Sieb 2014), and to assess the extent of extraocular involvement, pulmonary function tests are key to quantifying breathing ability. Myasthenia gravis used to have a high mortality due to involvement of the respiratory muscles, but now with anticholinesterase drugs patients can expect a full life expectancy.

Uveitis

The most common form of uveitis is iritis, in which there is inflammation of the iris. This generally presents with a unilateral red, painful eye, which is classically very photophobic. The role of investigations in iritis is usually nil, but occasionally investigations help to build a case for a diagnosis (Guly and Forrester 2010). The stereotypical junior ophthalmologist requests a range of unnecessary blood tests on patients with iritis, such as an array of antinuclear antibodies some of which come back as falsely positive, giving the clinicians a dilemma about what to do next. Most cases of iritis have no systemic association and do not merit systemic investigations, but in patients with uveitis that is recurrent, bilateral, unusual, intermediate or posterior, key symptoms should be enquired about and a systemic cause suspected. For example these include lower back stiffness and pain each morning, preventing easy movement for at least 30 minutes. If present, this raises the suspicion of ankylosing spondylitis, an inflammatory condition typically affecting young men. If a threshold of suspicion is reached, and this as always depends on the clinician's interpretation of the history and examination findings, then imaging of the lumbosacral region by x-ray or CT can be justified to confirm or deny the diagnosis of ankylosing spondylitis, treatable by immunosuppression. Breathlessness, ongoing cough or chest pain could indicate other conditions occasionally associated with iritis, specifically sarcoidosis (a multisystem auto-immune condition affecting mainly the lungs) or tuberculosis (TB). A history of travel to areas where TB is common would raise the suspicion of TB further, as would symptoms of night sweats or unintentional weight loss. Blood tests can be done to demonstrate prior exposure, or not, to TB, and a chest x-ray can also show signs of old TB. A diagnosis of TB may be relevant not only as it may be the cause, directly or indirectly, of the uveitis, but

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also as if there is latent TB then anti-tuberculous treatment may be appropriate if the patient needs systemic immunosuppression for their eye condition (Hoppe, Kettle et al. 2016). Another blood test, angiotensin-converting enzyme ('ACE') is quite specific for sarcoid, and again sarcoidosis can cause classic chest x-ray changes. Ultimately a lung biopsy may diagnose active pulmonary TB or sarcoidosis if present, but without a biopsy these diagnoses have to be made on the balance of probabilities, and investigations serve as important pieces of evidence to consider. A blood test for syphilis serology is always worth considering, as although uncommon, syphilis is a curable cause of uveitis (Davis 2014).

Optic Disc Swelling.

There are many distinct clinical entities causing optic disc swelling, including but not restricted to optic neuritis, anterior ischaemic optic neuropathy (AION), papilloedema and retinal vein occlusion. Most require ophthalmic, or often systemic investigations. The first step to take in Eye Casualty is to measure blood pressure (BP) as disc swelling can be due to severe hypertension. AION is most commonly related to cardiovascular risk factors, and so a cardiovascular workup is appropriate, including testing lipid levels, testing for diabetes and measuring blood pressure. However any case of AION is worth immediately discussing with ophthalmic colleagues as rarely AION is a manifestation of GCA, and if this is suspected then further assessment and blood tests for ESR and C-reactive protein (CRP) are appropriate. When optic disc swelling is detected incidentally by an optometrist during routine testing, referral to ophthalmology is always indicated unless a cause has been diagnosed previously. It is important to find out how well the patient is systemically, as symptoms such as vomiting and headache, especially in the setting of bilateral optic disc swelling could indicate that the disc swelling is in fact papilloedema, i.e. due to raised ICP, and which must be investigated immediately with some form of head scanning, such as CT or MRI. Such scans may also reveal a less obvious cause of optic nerve swelling such as an orbital mass. A central retinal vein occlusion (CRVO) causes disc swelling: dilated tortuous retinal veins, retinal haemorrhages and possibly cotton wool spots and exudates will also be apparent. Investigations following RVO are discussed below.

Although it is always safer to seek advice if in any doubt, children with optic disc swelling who are asymptomatic may have optic disc drusen (Chiang, Wong et al. 2015), and if this diagnosis is made, extensive investigations such as brain scans and lumbar puncture can be avoided. Optic disc drusen are calcific collections which can give the *appearance* of optic disc swelling, usually have no clinical impact and which are not related to the drusen seen in the aged macula. Disc drusen are usually confirmed using either OCT of the optic nerve head to identify them as rounded hyporeflective areas within the nerve head, or b-scan ultrasound to show hyperreflective bumps on and in the optic nerve head. Retinal autofluorescence photography can also reveal the autofluorescent drusen. When diagnosed, these do not need to be followed up and the patients are discharged with information about their condition, so that they can tell any eye care practitioners examining them in future to avoid further duplication of testing unless new signs have emerged.

Optic Neuritis.

Optic neuritis is a specific diagnosis due to inflammation of the optic nerve and characterized by mild pain and reduction in visual acuity, classically worsening over 2 weeks before slowly improving in most. There is often an associated reduction in colour vision and a relative afferent pupillary defect. Ophthalmic examination can often be normal if the inflammation is retrobulbar, but if inflammation is located in the nerve head then disc swelling will be seen. Visual function recovers variably following optic neuritis, and its assessment should include visual field testing as diffuse, central and paracentral loss can occur (Keltner, Johnson et al. 2010). If the symptoms, signs and course of the condition are typical of optic neuritis, then it may be the presenting episode of multiple sclerosis (MS) (Sicotte 2011). NICE guidelines, CG186, published in October 2014 state that all patients with an isolated optic neuritis should be referred to a neurologist

(<https://www.nice.org.uk/guidance/cg186?unlid=78105260620151125164952>)

(accessed October 2016). The decision on whether to have a brain scan (an MRI of brain and spinal cord to look for the classical white matter lesions of MS) following a first presentation of optic neuritis is a controversial one, as half of patients who have

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an episode of optic neuritis will develop MS within 15 years (Voss, Raab et al. 2011). Analogous to the idea of Schrodinger's cat, 'opening the box' and getting an MRI of the head may show subclinical lesions consistent with MS, while an MRI showing no such lesions will lower the probability of MS as an underlying diagnosis. Some patients prefer to know, especially as disease-modifying treatment for MS exists, while others choose to live with the 50% figure, waiting and wondering if another neurological episode will occur.

Retinal Vascular Conditions.

Retinal vascular conditions are investigated in the ophthalmic clinic to help grade the nature and severity of the condition, and the prognosis with treatment, but systemic investigations are also appropriate. One of the most common causes of blindness in Western Europe is diabetic retinopathy (DR) (Bourne, Stevens et al. 2013). DR can cause irreversible loss of vision at a relatively young age for patients with type 1 diabetes mellitus (DM), and so it is vital to educate these patients about risk factors for DR progression: glucose and blood pressure control, and in the UK attending (or not) DR screening. The most important medical investigation is the capillary blood glucose (historically though inappropriately known as the "BM"), which is a quick and easy medical investigation that patients can perform themselves. The landmark Diabetes Control and Complications Trial (DCCT) assigned participants randomly to intensive or conventional control of blood glucose levels. Those in the intensively controlled group, with consequently lower HbA1c levels, had a significantly lower risk of DR development or progression. Following the trial the participants were followed, and the average blood glucose levels of the two groups converged. However despite this convergence, after 20 years of follow-up those who were originally in the intensively controlled group still benefitted: they had approximately half the risk of DR progression compared to those originally in the conventionally treated group. This durability of effect is known as 'metabolic memory' (Aiello and Group 2014). Tight blood pressure control has an additive benefit to tight blood glucose control too as the UK Prospective Diabetic Study showed (1998). Such simple medical investigations as blood glucose and blood pressure therefore have direct relevance to the visual prognosis (Williams 2014).

Retinal vein occlusion (RVO) occurs when the venous drainage of the retinal blood supply is interrupted due to occlusion of a retinal vein, either the central vein or a branch thereof. The occlusion is thought to be caused by compression of the retinal veins by an adjacent atherosclerotic retinal artery. As such the risk factors for RVO are similar to those for atherosclerosis in general, such as raised blood pressure and diabetes. Occasionally, especially in patients under 40 years of age, other causes are identified. In all patients however, a specific and limited set of blood tests is suggested by the Royal College of Ophthalmologists following RVO: a full blood count, for example to exclude leukaemia, an ESR to exclude systemic inflammatory conditions and a blood glucose to exclude DM (<http://www.rcophth.ac.uk/wp-content/uploads/2015/07/Retinal-Vein-Occlusion-RVO-Guidelines-July-2015.pdf>) (accessed October 2016).

Central Serous Chorioretinopathy (CSR).

CSR characteristically causes a drop in central vision, and is more common in men aged 20-50. Although usually idiopathic, CSR can be associated with several factors, including excess steroid levels from exogenous steroid use, Cushing's disease or pregnancy. A simple enquiry may reveal an unexpected source of steroids, such as in eyedrops, tablets or locally applied agents, for example a lotion being applied to the face, or an inhaler or nasal spray. Cushing's disease is a condition in which endogenous steroid levels are raised, with various possible causes including a pituitary gland or an adrenal gland tumour. Medical investigations are often discussed for patients with CSR, but if there is a strong clinical suspicion of Cushing's disease, referral to a physician for several tests may be appropriate. For example a dexamethasone suppression test helps to confirm Cushing's disease, a test in which blood cortisol levels are measured before and after administration of dexamethasone. A urine collection over 24 hours analysed for free cortisol is also used, but such tests are not done in ophthalmic clinics.

Retinal Artery Occlusion (RAO).

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This is one of the few true ophthalmic emergencies, occurring when a retinal artery is occluded. This is rapidly sight threatening and even with prompt treatment there is only a slim hope of recovering vision. It is generally caused by an embolus passing from the carotid arteries into the retinal vasculature. Even when hope is lost for vision of the affected eye, follow up investigations are important as RAO can be a harbinger of stroke, as the next embolus may just as easily pass to the cerebral circulation. Thus appropriate tests assess cardiovascular risk, such as fasting lipids and glucose, urea & electrolytes (and as it is important to rule out giant cell arteritis as the other major cause of retinal artery occlusion, the blood test should include ESR and CRP). The source of the probable embolus should be sought using ultrasound of the carotid arteries, and an ECG may identify an irregular pulse, a risk factor for embolus.

Age Related Macular Degeneration (AMD).

This is one of the most common retinal conditions affecting the elderly population. It does not require systemic investigations but advanced AMD is associated with smoking, a full history must be taken.

Conclusions.

Investigations for visual conditions play various roles, as illustrated in the conditions discussed. Common to them all however is that their use and interpretation is guided by the specific history and examination findings elicited from the individual patient. Over-investigating may seem the safest approach but has downsides for the patient and practitioner, as incidental findings may cause undue concern and unnecessary referral, as new users of OCT may be finding, and some investigations carry a small risk of harm, such as radiation or allergy. Ongoing collaboration within and between the optometric and ophthalmic professions is needed to learn from each other, and optimize quality of care for our patients.

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