INTRODUCTION

An adverse drug reaction (ADR) is defined as ‘an unwanted or harmful reaction experienced following the administration of a drug or combination of drugs, and is suspected to be related to the drug’. Virtually every drug is capable of producing unwanted side effects. The elderly are more likely to experience such effects due to age-related changes in drug metabolism and excretion, coupled with the co-morbidity and polyphathology often associated with ageing.

Drug use in the elderly (those aged 60 and over) is common, accounting for 60% of prescription items dispensed by community pharmacists. Moreover, the elderly are prescribed approximately 4.5 times more prescription items per head than younger adults aged 15-59 (Information Centre, 2008). The population of the UK is ageing and this trend is projected to continue. By 2033, 23% of the population will be aged 65 and over compared to 18% aged 16 or younger. This trend explains in part why the average number of prescription items dispensed in the UK continues to show a year on year rise (Figure 1).

Several studies have shown that the risk of adverse drug reactions (ADRs) is directly related to the number of prescription items taken. For example, the incidence of adverse events has been reported as 4% when less than 5 drugs are taken, rising to 54% in patients taking more than 5 medicines (Doucet et al, 1999). Polypharmacy increases the probability of drug interactions and the toxicity of drug combinations may be synergistic and greater than the risks associated with each drug alone (Routledge et al 2003).

The burden of ADRs on the NHS is high, accounting for 1 in 16 hospital admissions and 4% of hospital bed capacity (Pirmohammed et al 2004). It has been calculated that the additional cost to the NHS is in the region of £0.5 billion each year (Audit Commission 2001). The classes of medicine used most commonly in the elderly include: cardiovascular drugs, anti-infectives, analgesics, hypoglycaemics, psychotropic drugs and anti-rheumatics.

A recent systematic review found that four drug groups accounted for >50% of preventable drug-related hospital admissions (Howard et al 2006). These include: antiplatelets (16%), diuretics (16%), non-steroidal anti-inflammatories (11%) and anticoagulants (8%). A summary of drugs that commonly cause ADRs in the elderly is shown in Table 1.
A Review of Drug-induced Side Effects in the Elderly

Eighty per cent of ADRs requiring hospital admission are dose-related and represent an accentuation of the normal pharmacological effect of the drug (Routledge et al., 2003). These so-called Type A reactions are predictable and potentially avoidable. Unpredictable or idiosyncratic Type B reactions are rare, although when present can be life threatening.

![Figure 1](image1.png)

**Figure 1:** Growth in number of prescription items for the top five BNF sections from 1998-2007 (source Information Centre 2009).

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs</td>
<td>GI bleeding, peptic ulcer, haemorrhagic stroke</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Renal impairment, hypotension, electrolyte disturbance</td>
</tr>
<tr>
<td>Warfarin</td>
<td>GI bleeding, haematoma</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>Renal impairment, hypotension, electrolyte disturbance</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Confusion, hypotension, constipation</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>Bradycardia, heart block, hypotension</td>
</tr>
<tr>
<td>Opiates</td>
<td>Constipation, vomiting, confusion, urinary retention</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Symptomatic toxic digoxin levels</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>Gastritis, GI bleeding, hyperglycaemia, osteoporosis</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>GI bleeding</td>
</tr>
</tbody>
</table>

**Table 1:** Drugs causing ADRs (adapted from Pirmohammed et al., 2004).

Frail elderly patients appear to be particularly vulnerable in terms of ADRs, particularly those resident in nursing homes. A study in the USA found evidence of probable ocular ADRs in 67% of 332 patients residing in two nursing homes in Georgia (Cooper, 1996). A likely contributing factor to the high incidence of ADRs in the frail elderly is that prescribers do not make the necessary dose adjustment for low body mass or impaired hepatic and renal elimination of drugs.

**OCULAR SIDE EFFECTS OF SYSTEMIC DRUGS COMMONLY PRESCRIBED IN THE ELDERLY**

Due to its small size, rich vasculature and diversity of tissue types, the eye is particularly susceptible to drug-induced side effects. Causation is often difficult to prove by conventional scientific method. Re-challenge studies are rarely performed. The drugs discussed in this section are those that are associated with well-recognised side effects that have been reasonably well documented (Table 2).

**Corticosteroids**

The association between corticosteroids and ocular ADRs has been known for many years. Steroid-induced ocular hypertension is well documented and can occur with both topical and systemic steroids. Whereas the IOP rise with topical ocular steroids tends to occur over a period of weeks, the response to systemic steroids occurs over a longer time frame, even years (Kersey and Broadway, 2006). Population studies have shown that elderly users of systemic steroids (oral or inhaled) are at greater risk of developing ocular hypertension and steroid glaucoma than non-users (Williamson et al., 1969, Mitchell et al., 1999). Ideally, patients on long-term steroid therapy should be screened annually for glaucoma and those receiving >10mg prednisolone daily should additionally have their IOP’s checked at 1, 3, and 6 months after commencing treatment and at 6 month intervals thereafter (Kersey and Broadway, 2006).

Posterior subcapsular (PSC) cataracts are another well-documented side effect of corticosteroids (Figure 2), irrespective of the route of delivery. For example, prolonged administration of high doses of inhaled corticosteroids increases the likelihood of developing cataracts in elderly patients (Garbe et al., 1998). The risk is dose-dependent and patients receiving <10 mg/day of prednisolone for less than a year are at a low risk of developing cataracts, however cataracts are present in 75% of patients treated with more than 15 mg/day for > 1 year (Black et al., 1960).

![Figure 2](image2.png)

**Figure 2:** Steroid-induced posterior subcapsular cataract
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**Amiodarone**

Amiodarone is a potent anti-arrhythmic agent used in the treatment of ventricular and supraventricular tachycardias. Corneal deposition (amiodarone keratopathy) is the most common ADR. The first cases were reported soon after the drug's release in the 1960's. The prevalence of amiodarone keratopathy varies between 70-100% and is present in all patients who are using the drug long term (Fraunfelder et al, 2008). Drug deposition progresses through a series of stages (Figure 3) ranging from a simple horizontal linear pattern in the inferior cornea to a complex branching vortex pattern (Figure 4). The severity of the keratopathy is dose dependent and is usually reversible on discontinuation of the drug. Most patients are asymptomatic, although halos around lights, glare and dry eye have been reported.

Amiodarone has also been linked to the development of optic neuropathy. Reported cases have had a slow onset with bilateral field loss and disk swelling which can take many months to resolve. Although the association is unproven, any patient experiencing visual disturbance whilst taking amiodarone should be referred to an ophthalmologist (Fraunfelder et al, 2008).

![Figure 3: Progression of amiodarone keratopathy](image)

**Digoxin**

Digoxin remains a frequently prescribed drug for the treatment of supraventricular dysrhythmias and congestive cardiac failure. Digoxin has a narrow therapeutic index, and there is considerable overlap in serum concentration of the drug between patients with and without toxicity. Although the clinical diagnosis of digoxin toxicity has fallen substantially over the past 20–30 years, it remains a common medical problem, particularly in the elderly, where it is often difficult to diagnose. Features of digoxin toxicity are usually non-specific and consist of cardiac and non-cardiac effects. Non-cardiac manifestations include symptoms of fatigue, anorexia, nausea, vomiting, headaches, and confusion. Disturbances of vision—for example, blurring, central scotomas, glare effects, and altered colour perception, are a less common but more specific presenting complaint. Symptomatic colour vision disturbances—for example, xanthopsia, has been reported in up to 15% of intoxicated patients, although formal testing reveals a much higher incidence of colour deficiency. (Lawrenson et al, 2002). Slight to moderate red-green impairment was observed in approximately 20–30% of patients taking digoxin, and approximately 20% showed a severe tritan deficiency. There was no correlation between colour vision impairment and serum digoxin level (Figures 5 and 6).

![Figure 5: Histogram showing the total red-green and total tritan error scores from a battery of colour vision tests for age-matched controls and patients receiving digoxin therapy (from Lawrenson et al. 2002).](image)

![Figure 6: Graph comparing serum digoxin levels with combined error scores for red-green (R/G) and tritan tests (from Lawrenson et al. 2002)](image)

**Biphosphonates**

Biphosphonates, such as disodium pamidronate, alendronate sodium, and risedronate sodium, are used in the treatment of osteoporosis. This class of drug has been reported to cause anterior uveitis and non-specific conjunctivitis. There have also been case
reports of biphosphonate-induced episcleritis and scleritis. Pamidronate has been the best-studied drug in this class and positive rechallenge testing has been carried out, with scleritis recurring after a repeat drug exposure. Onset is usually within 6-48 hours of IV administration (Fraunfelder et al, 2008).

Table 2: Selected systemic drugs causing ocular ADRs in the elderly

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticosteroids</td>
<td>Cataract, ocular hypertension, decreased resistance to infection, mydriasis, myopia, exophthalmos</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Colour vision defects, visual field disturbance</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Keratopathy, visual disturbance, anterior ischaemic optic neuropathy</td>
</tr>
<tr>
<td>Biphosphonates</td>
<td>Blurred vision, photophobia, anterior segment inflammation</td>
</tr>
<tr>
<td>Anti-rheumatics</td>
<td>Hydroxychloroquine: visual disturbance (decreased vision, colour vision disturbance), corneal deposition, retinal deposition</td>
</tr>
<tr>
<td></td>
<td>Indomethacin: keratopathy, retinopathy</td>
</tr>
<tr>
<td></td>
<td>Sulphasalazine: induced myopia</td>
</tr>
</tbody>
</table>

**Anti-rheumatics**

Several drugs used in the treatment of rheumatoid arthritis are associated with significant ocular side effects. Hydroxychloroquine has been used for many years in the treatment of autoimmune disorders such as rheumatoid arthritis. Although less toxic than chloroquine, there have been reports of keratopathy, cataract, and the development of an irreversible retinopathy in patients receiving hydroxychloroquine therapy (Fraunfelder et al, 2008). In order to minimise the risks of ocular toxicity, the Royal College of Ophthalmologists have published guidelines for the screening of patients on hydroxychloroquine therapy (RCOphth, 2004). The guidelines recommend baseline vision screening prior to starting treatment followed by annual review where patients are asked about visual problems and their visual acuity rechecked.

Indomethacin is another well-established treatment for rheumatoid arthritis. Although ocular side effects are rare, there have been several reports of corneal deposition and retinal toxicity with associated visual disturbance. It has been recommended that patients on long term therapy should undergo periodic ophthalmic screening (Graham and Black, 1988).

Sulphasalazine can reduce the symptoms and slow the progress of rheumatoid arthritis and other types of arthritis, such as psoriatic arthritis. Optometrists should be aware of the possibility of modest myopic shifts in patients taking this drug or other sulphonamide medications (Santodomingo-Rubido et al, 2003). The mechanism is thought to be due to ciliary body oedema, which may also increase the risk of angle closure.

**Drug-induced angle closure glaucoma**

In most Western countries the ratio of primary angle closure glaucoma (PACG) to primary open angle glaucoma (POAG) is approximately 1:5. However in East Asia, the prevalence of angle closure is much greater (for example in Mongolia, PACG accounts for 4 out of 5 newly diagnosed cases of glaucoma) (Morrison and Pollack, 2003). The prevalence of PACG increases with age and most commonly occurs in the 6th or 7th decade. It has been estimated that at least a third of PACG cases are drug-related (Lockhart and Bouassida, 2007). Certain topical and systemic agents are capable inducing angle closure in susceptible individuals. Optometrists are well aware of the risk of angle closure with anti-muscarinic drugs such as tropicamide, however several systemic drugs have similar anti-cholinergic side effects e.g. anti-depressants, anti-anxiety agents and antihistamines. Adrenergic agents such as ephedrine and naproxolone, which are often used in over the counter cold and flu remedies, can similarly cause angle closure by inducing pupillary block. (Lachkar and Bouassida, 2007).

**SIDE EFFECTS OF TOPICAL OPHTHALMIC DRUGS**

**Preservative toxicity**

Iatrogenic ocular surface toxicity can occur following short-term and long-term use of topical ophthalmic medications (Wilson, 1983, Pissella et al, 2002, Dart, 2003, Baudouin, 2008). An epidemiological study reported that 13% of consecutive cases of external eye disease presenting in a tertiary care setting were drug-induced (Wilson, 1983). Signs associated with drug-induced toxicity include punctate keratopathy, focal erosions and variable degrees of conjunctival involvement e.g. papillary or follicular conjunctivitis. Clinical signs are usually associated with symptoms such as discomfort on instillation, burning, stinging, foreign body sensation or dryness. Adverse events can result from an allergic reaction to the drug itself or more likely caused by a toxic reaction to the preservative or other excipients included in the formulation. Benzalkonium chloride (BAK) is the preservative found in the vast majority of ophthalmic drugs. Laboratory and clinical studies have demonstrated that BAK causes damage to the ocular surface by disrupting cell membranes. Preservative toxicity should always be considered in the differential diagnosis of poorly controlled external disease. Patients taking multiple preserved preparations are at greater risk (Pissella et al, 2003) and switching to preservative–free preparations should always be considered whenever possible.
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Anti-glaucoma drugs
Primary open angle glaucoma (POAG) is a disease of the elderly, affecting 1-2% of the population over 40 rising to 4-5% of those over 80. Once diagnosed, the disease requires lifelong treatment, usually with topical ocular hypotensive agents. Patients often require 2 or more drugs to control intraocular pressure. Commonly prescribed anti-glaucoma preparations include:

- Beta blockers
- Prostaglandin analogues
- Alpha-adrenergic agonists
- Carbonic anhydrase inhibitors

Each group of drugs is associated with a particular ADR profile (see Table 3) and the risk of an ADR increases with the number of drugs prescribed.

Beta-blockers
The development of newer anti-glaucoma drugs has led to a decline in the use of topical beta-blockers as monotherapy, however they are still extensively used in combination products with other drugs. Most topical beta-blockers e.g. timolol, are non-selective and interact with both beta-1 and beta-2 adrenergic receptors. A large volume of a drug administered topically to the eye gains access to the systemic circulation via the naso-lacrimal duct and nasal mucosa. Drugs absorbed in this way avoid first-pass metabolism in the gut and the liver, leading to an elevated plasma concentration (for example a standard dose of 0.5% timolol approximates to a 10mg oral dose) (Diggory and Franks, 1997). Precipitation of asthma and exacerbation of chronic obstructive pulmonary disease (COPD), via blockade of beta-adrenergic receptors in the lung, are significant complications of topical beta-blockers. Although these drugs are contraindicated in patients with a history of airways disease, many elderly patients have undiagnosed respiratory impairment. A survey of drugs given to a population of 125,000 elderly patients in the USA commencing topical beta-blockers for glaucoma, found 21,096 first prescriptions for bronchodilators were subsequently issued (Avorn et al, 1993). This emphasises the need for the prescribing clinician to take a careful respiratory history prior to commencing treatment with beta-blockers or switching to a combination product. Beta-blockers should be discontinued immediately if there is any respiratory impairment (Diggory and Franks, 1997).

The risk of falls increases with age and topical beta-blockers have been implicated as a major risk factor for falls in elderly glaucoma patients due to systemic side effects e.g. orthostatic hypotension (Glynn et al 1991). Topical beta-blockers should therefore be used with caution in elderly patients, particularly those with cardiovascular morbidity.

Prostaglandin analogues
Compared to topical beta-blockers, prostaglandin analogues (latanoprost, brimatoprost, travoprost and the newly released tafluprost) have an excellent safety profile (Alm et al, 2008). However, all drugs in this class are commonly associated with ocular ADRs, including: conjunctival hyperaemia, iris darkening, eyelash changes and cystoid macula oedema. Conjunctival hyperaemia occurs more commonly with travoprost and brimatoprost than with latanoprost. Iris darkening is most evident in patients with mixed coloured irises; uniformly blue or gray irises carry little or no risk. If iris darkening is to occur it usually does so within 8 months of initiating therapy. Darkening and increased growth of eyelashes is relatively common but not usually problematic. By contrast, the risk of cystoid macula oedema (CME) is extremely low but should be considered in eyes at high risk of this condition (aphakia, pseudophakia or retinal vascular or inflammatory disease).

Alpha-adrenergic agonists
The most common ADR associated with selective alpha-2 adrenergic agonists (brimonidine) is an ocular allergic reaction consisting of hyperaemia, follicular conjunctivitis and eyelid swelling (Fraunfelder et al, 2008). Systemic side effects of brimonidine include dry mouth, fatigue or drowsiness and headaches.

Carbonic anhydrase inhibitors
Topical carbonic anhydrase inhibitors (dorzolamide, brinzolamide) are used as second-line therapy in the treatment of POAG. The most common side effect of drugs in this class (up to 33% of patients) is a bitter metallic taste (Fraunfelder et al 2008). Systemic side effects are uncommon and include gastrointestinal disturbance (occurring in approximately 10% of patients) and headache.

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<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta blockers</td>
<td>Bronchoconstriction, bradycardia, arrhythmia, syncope, impotence</td>
</tr>
<tr>
<td>Alpha adrenergic agonists</td>
<td>Allergic reactions (follicular conjunctivitis), bradycardia, hypotension, headaches, fatigue, somnolence</td>
</tr>
<tr>
<td>Prostaglandin analogues</td>
<td>Conjunctival hyperaemia, iris darkening, eyelash changes</td>
</tr>
<tr>
<td>Carbonic anhydrase inhibitors</td>
<td>Bitter taste, gastrointestinal disturbance, headaches</td>
</tr>
</tbody>
</table>

Table 3: ADRs of topical anti-glaucoma medication

REPORTING ADVERSE DRUG REACTIONS
Before a drug can be used to treat patients in the UK, pharmaceutical companies have to apply for a product licence (also referred to as a marketing authorisation). A licence is only issued following the demonstration of the products safety and effectiveness. The Medicines
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and Healthcare Products Regulatory Agency (MHRA) is the government agency that is responsible for the licensing of medicines in the UK (MHRA, 2008). Pharmaceutical companies also have the option of applying to the European Medicines Agency (EMEA) for a centralised marketing authorisation so that the product is valid simultaneously in all EU member states. Despite a rigorous evaluation by the regulatory authorities, pre-marketing assessment can only give limited information on a drug's safety. Clinical trials generally involve a small number of highly selective subjects who only take the drug for a short time. Although these trials allow common ADRs to be detected, certain side effects may not be detected until large numbers of patients receive the medicine. A process of pharmacovigilance is therefore required in order to permit the identification of less common or delayed ADRs. The most common way in which regulatory bodies collect data on adverse reactions of licensed medicines is through voluntary spontaneous reporting schemes. In the UK, the ‘Yellow Card Scheme’, which is run jointly by the MHRA and the Commission for Human Medicines (CHM), is used to collect data on ADRs from healthcare professionals and patients. When the Yellow Card Scheme was introduced in 1964 following the thalidomide tragedy, only doctors and dentists were allowed to submit reports. The scheme has subsequently been extended to other healthcare professionals and in 2008 patient reporting was introduced. Despite the fact that the scheme is well established, ADRs are clearly being under-reported (BMA, 2006). The number of reports received annually by the MHRA has remained fairly constant over the last 20 years even though the number of prescription drugs over the same period has dramatically increased. Although optometrists have been able to submit reports since the late 1990’s, it is disappointing that less than 50 reports have been received over this time (MHRA, personal communication).

A very good example of the value of post-marketing surveillance concerns the anti-epileptic agent, vigabatrin. During its pre-marketing development, vigabatrin was known to be associated with rare (<1:1000) cases of symptomatic visual fields defects and retinal disorders (Royal College of Ophthalmologists, 2008). However, following its release in 1989, several cases of severe persistent field constriction were reported and it was subsequently established that a third of patients taking the drug show some degree of field loss. The MHRA issued guidance in 1997 restricting its use and provided guidance on monitoring.

Optometrists are well placed to identify ocular ADRs to systemic and ophthalmic agents. The MHRA advises that well-documented side effects should not be reported unless they are severe. In this context, severe ADRs would include any change in visual function or physical change in ocular tissues. However, all suspected ADRs should be reported in children and to newly licensed drugs, irrespective of severity. Newly licensed drugs are indicated in the BNF by an inverted black triangle. A full list of current black triangle drugs can be downloaded from the MHRA website (www.mhra.gov.uk). A flow diagram indicating when ADRs should be reported is shown in Figure 7.

Figure 7. Flow diagram to shown when an ADR should be reported (source: BMA 2006)

Paper copies of the Yellow Card are available in the BNF and a reporting form can also be downloaded as a pdf from the MHRA website. Reporting has recently been made easier with online reporting.

SOURCES OF INFORMATION ON ADVERSE DRUG REACTIONS

Several sources providing information about adverse reactions are available including: the British National Formulary (BNF), The Monthly Index for Medical Specialties (MIMS), and the ABPI Medicines Compendium (a collection of monographs (Summary of Product Characteristics) provided by the pharmaceutical industry on their products). There are also a number of textbooks, notably ‘Clinical Ocular Toxicology’ (Fraunfelder et al, 2008) and a daunting array of scientific papers. However, none of these sources are particularly well suited to use by optometrists in the consulting room. In general, the BNF and MIMS contain little information about ocular adverse reactions while the Summary of Product Characteristics contains so much information that searching for ocular adverse reactions is a time consuming process. A dedicated resource that has been specifically developed for optometrists is the electronic database ‘Electronic Medicines Information (EMedInfo). This is the product of over ten years’ research and development at City University (Thomson and Lawrenson, 2008). The program currently contains information about all licensed medicines available in the UK. A number of powerful search tools are
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provided to help practitioners find information about specific drugs and the information is displayed in a simple and user-friendly data sheet (Figure 8). Further details of the program are available at http://www.thomson-software-solutions.com/html/emedinfoinfo.html

CONCLUSIONS

Age-related morbidity results in a greater use of drugs in the elderly population. Optometrists should be aware of the greater potential for ADRs in this age group. Since the eye is particularly susceptible to drug-induced side effects practitioners should remain vigilant regarding the possibility that an unexpected finding during an eye examination maybe a drug-induced side effect. This is more likely of the timescale of the problem coincides with the period of taking a particular drug. Optometrists should report severe ADRs to the MHRA using the Yellow Card Scheme. Since newly licensed drugs are more closely monitored, any suspect ADR should be reported for these drugs.

REFERENCES


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Office for National Statistics, 2009


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Royal College of Ophthalmologists, 2008. The Ocular Side-Effects of Vigabatrin (Sabril). Information and Guidance for Screening


MULTIPLE CHOICE QUESTIONS

1. What % of prescription items is dispensed by community pharmacists to persons over 60 years of age?
   A. 20%
   B. 40%
   C. 60%
   D. 80%

2. Which of the following classes of medicinal product are responsible for the majority of drug-related preventable hospital admissions?
   A. Beta-blockers
   B. NSAIDs
   C. Anti-platelets
   D. Corticosteroids

3. Which of the following statements regarding the side effects of corticosteroids is false?
   A. Ophthalmic steroids produce a more rapid increase in IOP than systemic steroids
   B. Patients receiving less than 10mg of prednisolone per day for a year are at low risk of developing cataracts
   C. Ocular complications can occur irrespective of the route of steroid delivery
   D. It is sufficient for patients on long-term steroids to be screened for ocular side effects bi-annually

4. What type of cataract is typically associated with corticosteroid use?
   A. Cortical
   B. Sutural
   C. Nuclear
   D. Posterior sub-capsular

5. What is the most common ocular side effect associated with amiodarone?
   A. Keratopathy
   B. Cataract
   C. Optic neuritis
   D. Colour vision disturbance

6. Approximately what % of patients taking digoxin show a slight or moderate red-green impairment?
   A. 10-20%
   B. 20-30%
   C. 30-40%
   D. 40-50%

7. Which of the following systemic drugs has been linked to a myopic shift in refraction?
   A. Sulfasalazine
   B. Hydroxychloroquine
   C. Indomethacin
   D. Sodium palmidronate

8. Which of the following drugs has been linked to inflammation of the anterior segment?
   A. Sulfasalazine
   B. Hydroxychloroquine
   C. Indomethacin
   D. Sodium palmidronate

9. What is the most commonly used preservative used in topical ophthalmic preparations?
   A. Benzylkonium chloride
   B. Phenyl mercuric nitrate
   C. Thiomersal
   D. Quaternary ammonium compounds

10. What is the most common side effect of topical beta-blockers?
    A. Hypertension
    B. Bronchospasm
    C. Iris darkening
    D. Tachycardia

11. Which of the following anti-glaucoma drugs is most likely to cause taste disturbance?
    A. Timolol
    B. Lantanopost
    C. Dorzolamide
    D. Brimonidine

12. Which of the following adverse reactions should not be reported to the MHRA on a ‘Yellow card’?
    A. ‘Serious’ reactions
    B. Reactions to ‘Black triangle drugs’
    C. Reactions in children
    D. Reactions to medical devices